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An exploration of the patients' lived experience with antineoplastic medicines for colorectal cancer in Malta.

BRINCAT, A.

2023

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AN EXPLORATION OF THE PATIENTS' LIVED EXPERIENCE WITH ANTINEOPLASTIC MEDICINES FOR COLORECTAL CANCER IN MALTA

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PhD 2023

AN EXPLORATION OF THE PATIENTS' LIVED EXPERIENCE WITH ANTINEOPLASTIC MEDICINES FOR COLORECTAL CANCER IN MALTA

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A thesis submitted in partial fulfilment of the
requirements of
Robert Gordon University
for the degree of Doctor of Philosophy

September 2023

Research is to see what everybody else has seen,

and think what nobody has thought.

Dr Albert Szent-Gyorgyi

Biochemist, Nobel Prize winner

1893-1986

Abstract

Cancer is a global health problem, with colorectal cancer being the third most common cancer worldwide. Antineoplastic medicines are considered the backbone of treatment for colorectal cancer, administered with the intent to relieve symptoms and achieve cure or prolong life. Consequently, patients have to cope with the burden of this treatment in addition to the symptoms of a life-threatening illness. This can be challenging and is poorly understood.

The overall aim of this research was to explore the patients' lived experience with antineoplastic medicines for colorectal cancer in Malta.

This research involved three phases. Phase I consisted of a systematic review to appraise, synthesise and present the available evidence of patients' lived experience with antineoplastic medicines prescribed for the management of malignant solid tumours. This review of ten studies showed the dynamic processes and socio-cultural influences that affected the patients' beliefs, practice and burden with antineoplastic medicines. Despite the lack of longitudinal qualitative studies, patients were still noted to undergo a continuous process of reinterpretations about their treatment along its journey. As this review captured almost all aspects mentioned in the original conceptual model of patients' lived experience with medicines (PLEM) for any acute and chronic illness (Mohammed, Moles and Chen 2016), it was likely to be transferable to the oncology setting with minor modifications.

Phase II involved a longitudinal qualitative study which explored the perceptions and experiences of 16 patients receiving a six month cycle of antineoplastic medicines (FOLFOX or XELOX) for the management of colorectal cancer.

In parallel, another longitudinal qualitative study was conducted for Phase III by interviews with significant others nominated by patients participating in Phase II. This phase aimed to explore the significant others' perspective on the patients' lived experience with antineoplastic medicines .

All interviews were audio-recorded and transcribed verbatim, with data analysed using Interpretative Phenomenological Analysis for Phase II and Framework Analysis for Phase III. Five themes were generated from the analyses: (1) perceptions and knowledge of the illness and treatment; (2) the healthcare system in relation to the illness and treatment; (3) patient's involvement in treatment decision-making and their experience of medicine-taking; (4) medicine and illness-related impact on patients and (5) personal support structure. The longitudinal analysis of these themes supported inferences relevant to development in these areas along the treatment trajectory.

Whilst patients faced the prospect of the treatment journey with fear, they had high expectations to achieve cure irrespective of treatment intent. Almost all patients passively consented to the oncologist's recommendations but still criticised the lack of provision of specific treatment information. Patients praised the personalised service of the nurse navigator particularly upon encountering difficulties in between cycles. To mitigate the substantial impact of treatment on their everyday life, patients sought refuge in spirituality and religion in addition to self-regulation coping strategies. Support was crucial for patients as they sought to develop a personal support network, mainly involving their significant other as from initiation of treatment.

In conclusion, this doctoral research showed that the patients' lived experience with antineoplastic medicines is complex and remained challenging long-term. It also highlighted that the patients' needs go beyond the provision of medicines. Despite improvements made in the local healthcare system, further specific patient-tailored interventions are warranted such as the introduction of buddy system and the provision of specific information at appropriate time-points in the treatment journey. Further research is required to explore their potential implementation and adoption into practice.

Keywords: patients' lived experience, antineoplastic medicine, colorectal cancer, systematic review, longitudinal qualitative research, phenomenology

Acknowledgements

My progress through this research and the compilation of the thesis would not have been possible without the assistance of a number of individuals to whom I am grateful. First and foremost, I would like to praise God who helped me get through this journey and fulfil another dream.

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I would like to thank the staff at the School of Pharmacy and Life Sciences at Robert Gordon University, particularly Dr Colin Thompson. Despite being a distance learning student, they encouraged and supported me to participate in activities held at university using virtual means. Also, a special thanks go to the staff at the Graduate School for their guidance and support during difficult periods.

I am greatly indebted to all patients and significant others who willingly participated in this research. Despite facing a difficult time in their life, these individuals kept their commitment throughout the longitudinal study and were looking forward for their next interview to share their experiences. I am also thankful to be awarded a scholarship within the Tertiary Education Scholarship Scheme for their financial support.

Last but not least, I would like to express my special thanks to my family, especially my parents who always believed in me and supported my dreams. I am forever indebted for their love, patience and understanding. Along my doctoral journey, I realised that I required more than just academic support.

Public output from this research

Until to date, findings obtained from the study presented within this thesis were disseminated through the following outputs. Further outputs are planned to be submitted to peer reviewed journals and conferences.

Phase I

Peer-reviewed publications

Brincat, A., Stewart, D., Vella Bonanno, P., Weidmann, AE., 2016. Patients' lived experiences of cytotoxic medications prescribed for the management of malignant solid tumours: a systematic review. [Online] York:PROSPERO. Available from: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=48457 [Accessed 19 January 2023].

Brincat, A., Vella Bonanno, P., Stewart, D., Weidmann, A.E., 2020. Patients' lived experiences with antineoplastic medicines for the management of malignant solid tumours: A systematic review. *Research in Social and Administrative Pharmacy*, 16(4), pp. 450-463. DOI: https://doi.org/10.1016/j.sapharm.2019.06.020.

Oral presentations

Brincat, A., Stewart, D., Vella Bonanno, P., Weidmann, A.E., 2018. Patients' lived experiences with antineoplastic medicines prescribed for the management of malignant solid tumours: a systematic review. Oral presentation at the European Society of Clinical Pharmacy International Workshop, Reykjavik, Iceland, February 2018.
Abstract published in *International Journal of Clinical Pharmacy* (2018) 40, pp.730–736. Doi:https://doi.org/10.1007/s11096-018-0637-5.

Brincat, A., Stewart, D., Vella Bonanno, P., Weidmann, A.E. 2018. Systematic review contributing to an understanding of the patients' lived experience with medicines with reference to antineoplastic medicines. Oral presentation at the International Social Pharmacy Workshop, Leuven, Belgium, July 2018. Abstract published in *Research in Social and Administrative Pharmacy* (2018) 14:e623-e56. DOI: 10.1016/j.sapharm.2018.05.023.

Brincat, A., Stewart, D., Vella Bonanno, P., Weidmann, A.E., 2019. Patients' lived experiences with antineoplastic medicines. Oral presentation at the 13th Regional European Commonwealth Conference, St Paul's Bay, Malta, March 2019.

Posters

Brincat, A., Stewart, D., Vella Bonanno, P., Weidmann, A.E., 2018. Patients' lived experiences with medicines with reference to antineoplastic medicines: a systematic review. Poster presentation at the Robert Gordon University School of Pharmacy and Life Sciences' Research Day, Aberdeen, UK, May 2018.

Phase II

Peer-reviewed publications

Brincat, A., Vella Bonanno, P., Stewart, D., Weidmann, A.E., 2021.Patients' experiences of medicines on initiation of antineoplastic agents for the treatment of colorectal cancer: a qualitative study. *BMJ Open*, 11, pp. e047749. DOI:10.1136/bmjopen-2020-047749.

Oral presentations

Brincat, A., Vella Bonanno, P., Stewart, D., Weidmann, A.E., 2018. A prospective longitudinal study of colorectal cancer patients' lived experience with antineoplastic medicines in Malta. Oral presentation at the Medication Safety and Effectiveness Workshop, Valletta, Malta, August 2018.

Brincat, A., Tonna, A., Vella Bonanno, P., Stewart, D., Weidmann, A.E. 2021. An exploration of the patients' lived experience with antineoplastic medicines. Oral presentation at the Robert Gordon University School of Pharmacy and Life Sciences’ Journal Club, Aberdeen, UK, December 2021.

Brincat, A., Stewart, D., Vella Bonanno, P., Weidmann, A.E., 2022. “They were waiting for me and welcomed me with great love and escorted me to my room”: A qualitative approach exploring patients’ experiences of cancer healthcare services. Oral presentation at the Health Services Research and Pharmacy Practice Conference, University of Bath, UK, April 2022.
Abstract published in *International Journal of Pharmacy Practice* (2022) 30, pp.i1. DOI: https://doi.org/10.1093/ijpp/riac020.000.

Brincat, A., Tonna, A., Vella Bonanno, P., Stewart, D., Weidmann, A.E., 2022. An exploration of the patients' lived experience with antineoplastic medicines. Oral presentation at the Robert Gordon University School of Pharmacy and Life Sciences’ Postgraduate Research Symposium, Aberdeen, UK, June 2022.

Posters

Brincat, A., Vella Bonanno, P., Stewart, D., Weidmann, A.E., 2020. Patients’ lived experience with antineoplastic medicines for colorectal cancer: a qualitative study. Poster presentation at the International Conference on Communication in Healthcare, Online, September 2020.

Brincat, A,, Vella Bonanno, P., Stewart, D., Weidmann, A.E. 2021. Patients’ misconceptions following initiation of antineoplastic treatment for colorectal cancer. Poster presentation at the 25th Anniversary European Association of Hospital Pharmacy, Online, March 2021.
Abstract published in *European Journal of Hospital Pharmacy* (2022) 28 (Supplement 1), pp. A1–A184. DOI: 10.1136/ejhpharm-2021-eahpconf.131.

Brincat, A., Tonna, A., Vella Bonanno, P., Stewart, D., Weidmann, A.E., 2022. An exploration of patients' perceptions of colorectal cancer and its management: A qualitative study at initiation of treatment with chemotherapy. Poster selected for Abstract Poster Walk in the 26th European Association of Hospital Pharmacy, Vienna, Austria, March 2022.
Abstract published in *European Journal of Hospital Pharmacy* (2022) 29 (Supplement 1), pp. A1–A187. DOI: http://dx.doi.org/10.1136/ejhpharm-2022-eahp.204.

Phase III

Further publications of this phase of study are currently in progress.

Award

The research work disclosed in this publication is partially funded by the Tertiary Education Scholarships Scheme and Get Qualified Scheme.

Foreword

This thesis describes my research undertaken to fulfil the requirement of a PhD degree at the Robert Gordon University, Aberdeen UK. The research focused on exploring the patients' lived experience with antineoplastic medicines (PLEM) for colorectal cancer in Malta.

After I graduated as a pharmacist from the University of Malta in 2010, I worked in procurement and supply of medicines for the government health services in Malta for the first three years. During that time, I continued with my studies at the University of Malta to obtain a Master in Pharmacy with specialisation in clinical pharmacy. I was subsequently appointed as a senior hospital pharmacist at the national oncology centre in Malta and as a visiting assistant lecturer at the University of Malta. These opportunities stirred my enthusiasm- and kindled my passion for academia and research. My work enabled me to embark on my PhD journey to incorporate my experience into research aimed at the improvement of clinical practice. This research empowered me to make an original contribution to my field of study.

Whilst working at the national oncology centre in Malta full-time I was fortunate to have a line manager who had just completed her PhD herself and who provided me with the necessary advice and assistance in devising my own PhD work.

In August 2016, I was appointed as one of the Maltese National Implementation Ambassadors in the European Association of Hospital Pharmacy and a delegate in the European Association of Oncology Pharmacy, through which I was able to share our local practice with European and international fora. Towards the end of 2021, I was appointed as a Principal pharmacist in Mount Carmel Hospital in Malta. This had increased further pressure on my research.

Along my doctoral journey, I learned about different research philosophies, methodologies and methods which have shaped and expanded my research expertise. Furthermore, I had the opportunity to present my work at various national and international conferences intended for different audiences. This also allowed me to network with individuals from different spheres of life. Overall, this research process allowed me to develop as a researcher.

I am confident that by exposing unmet needs of patients with colorectal cancer as part of the outcome of this research, this research has the potential to make a positive impact on the provision of cancer care in Malta. This is in line with the objectives set in the Europe’s Beating Cancer Plan (European Commission 2021) and the National Cancer Plan 2017-2021 (Ministry for Health 2017) to improve patients’ experience and quality of life during and beyond their cancer treatment.

This doctoral research is presented in six chapters, as outlined below:

Chapter one gives a brief overview of cancer with particular emphasis on colorectal cancer and its treatment. It also defines the overall aim of this doctoral research together with specific aims and objectives of each phase of research.

Chapter two focuses on the different philosophical worldviews, research designs and methods that encompass the research process. The rationale of adopting specific methodology for this research is also described. Measures to promote rigour and robustness of the research are explained.

Chapter three presents Phase I of the research which was an original systematic review about the patients’ lived experience with antineoplastic medicines for the treatment of malignant solid tumours. This reports comprehensive information about the search strategy and findings.

Chapter four describes Phase II of the research which is a longitudinal qualitative study with patients. This phase aimed to explore longitudinally the patients’ lived experiences with antineoplastic medicines for colorectal cancer during the treatment journey and beyond. The changes in patients’ beliefs, practice and burden with regards to treatment with antineoplastic medicines are reported.

Chapter five describes Phase III of the research which is a longitudinal qualitative study with significant others. It aimed to explore longitudinally the significant others’ perspective on the patients’ experiences with antineoplastic medicines for the duration of the treatment journey for colorectal cancer.

Chapter six, the final chapter of this thesis, provides a summary of key findings of each phase of the research with respect to the overall aim. The originality and impact of research together with some potential future studies are described.

Abbreviations

5-FU/LV	Fluorouracil and leucovorin
CASP	Critical Appraisal Skills Programme
CEA	Carcinoembryonic antigen
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CRD	Centre for Reviews and Dissemination
CT	Computed tomography
ESMO	European Society for Medical Oncology
EU	European Union
FOLFIRI	Fluorouracil and irinotecan
FOLFOX	Fluorouracil, leucovorin and oxaliplatin
FOLFOXIRI	Fluorouracil, leucovorin, oxaliplatin and irinotecan
IARC	International Agency for Research on Cancer
IPA	Interpretative Phenomenological Analysis
MeSH	Medical Subject Headings
OECD	Organisation for economic co-operation and development
PLEM	Patients’ lived experience with medicine
PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analysis
PRISMA-P	Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol
PROMs	Patient-reported outcome measures
TNM classification	T for tumour size, N for nearby lymph nodes, M for metastasis
UK	United Kingdom
UKRI	United Kingdom Research and Innovation
USA	United States of America
WHO	World Health Organisation
XELIRI	Capecitabine and irinotecan
XELOX	Capecitabine and oxaliplatin

Table of contents

List of Tables

List of Figures

List of Appendices

Chapter 1

Introduction

1. Introduction to the chapter

This chapter provides a brief overview of cancer with particular emphasis on colorectal cancer and its management. Information about the incidence and prevalence of cancer in Malta, the setting where the study is conducted, together with a description of the healthcare system in Malta is provided. The concept of the patients' lived experience with medicine (PLEM) is also explored. This information provides a background for the rationale of the study. The chapter concludes with the overall aim of the doctoral research together with the specific aim and objectives of each phase of the research.

1.1. Cancer

The term cancer refers to a group of around 200 different illnesses characterised by uncontrolled growth of abnormal cells which may also spread to adjacent organs (Cancer Research UK 2020, World Health Organisation 2022a). As a term, it was first mentioned around 400BC by Hippocrates and etymologically derived from the Latin meaning a crab (Pestle and Colvard 2013) secondary to its likening to "a moving crab, infiltrating tissues with its claws" (Inchingolo et al. 2020 p.3172). The process of carcinogenesis, as shown in Figure 1.1, involves the transformation of healthy normal cells into malignant cells as a result of a complex series of steps namely initiation, promotion, progression and metastasis (Siddiqui et al. 2015).

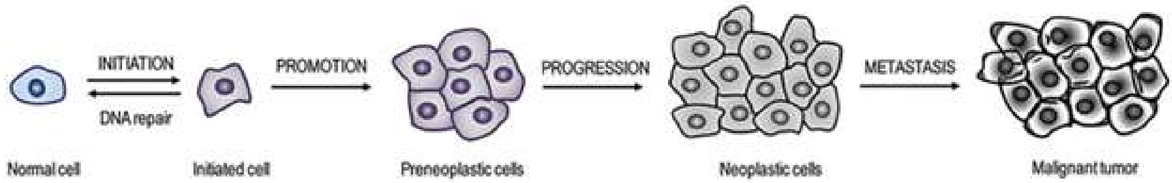

Figure 1.1: Phases of carcinogenesis. © 2015 The New York Academy of Sciences. (Siddiqui et al. 2015)

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1.1.1. Epidemiology of cancer

The cancer research agency of the World Health Organisation (WHO), International Agency for Research on Cancer (IARC), estimated a global occurrence of 19.3 million new cancer cases in 2020 (Sung et al. 2021). Of these, over 4 million (22.8%) new cancer cases occurred in Europe; translating to the identification of around 11,000 new cancer cases daily (Dyba et al. 2021). Recent epidemiology data shows that globally 1 in 5 individuals develop cancer during their lifetime (Sung et al. 2021). For both genders, breast cancer was the most commonly diagnosed cancer worldwide (11.7% of total cases, 2.3 million new cases), followed by lung cancer (11.4% of total cases, 2.2 million new cases) and colorectal cancer (10.0% of total cases, 1.9 million new cases) (Sung et al. 2021). This is represented in Figure 1.2.

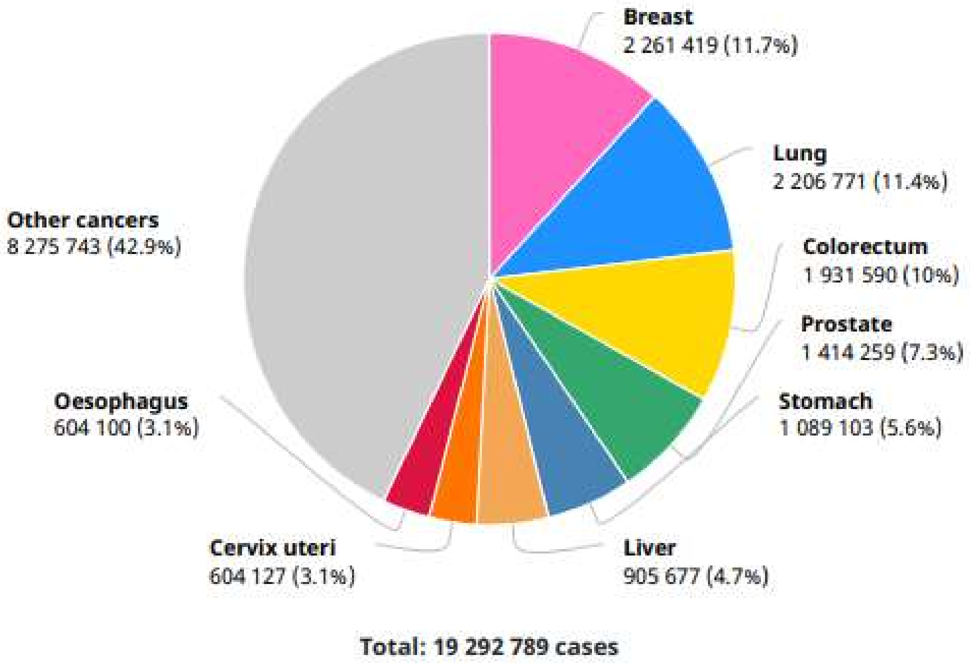

Figure 1.2: Number of new cancer cases for both genders and all ages in 2020 © 2022 IARC. (WHO – IARC 2022[a])

In 2020, cancer accounted for around 10 million deaths, with around 2 million deaths (19.6%) occurring in Europe (Dyba et al. 2021, Sung et al. 2021). This equates to 1 cancer death in every 8 men or 11 women. Globally lung cancer was considered as the leading cause of cancer deaths (18.0% of total deaths, 1.8 million deaths), followed by colorectal (9.4% of total deaths, 0.9 million deaths) and liver cancer (8.3% of total deaths, 0.8 million deaths) (Sung et al. 2021). This is represented in Figure 1.3.

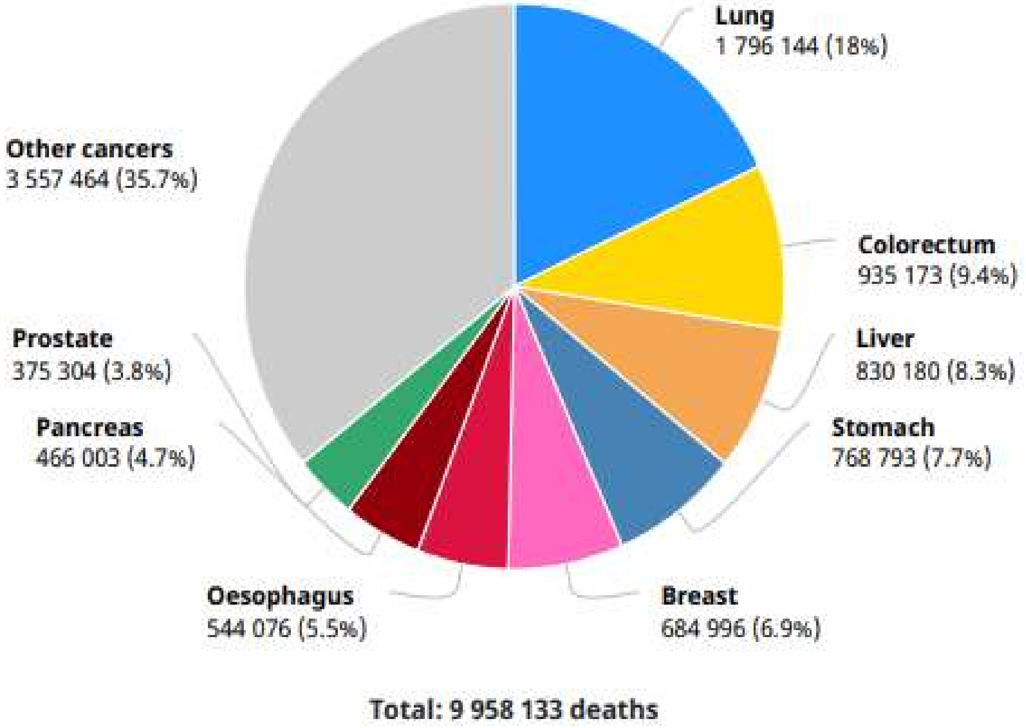

Figure 1.3: Number of cancer deaths for both genders and all ages in 2020 globally © 2022 IARC. (WHO – IARC 2022[a])

Recent epidemiological trends indicate that in most countries cancer deaths may eventually surpass deaths related to cardiovascular disease (Bray et al. 2021). As a result of a growing and aging population, the annual incidence of new cancer cases is projected to increase by 47.0% (9.1 million new cancer cases) by 2040. This will likely lead to an increase in the premature death rates in individuals between 30-70 years of age (Sung et al. 2021) (Figure 1.4).

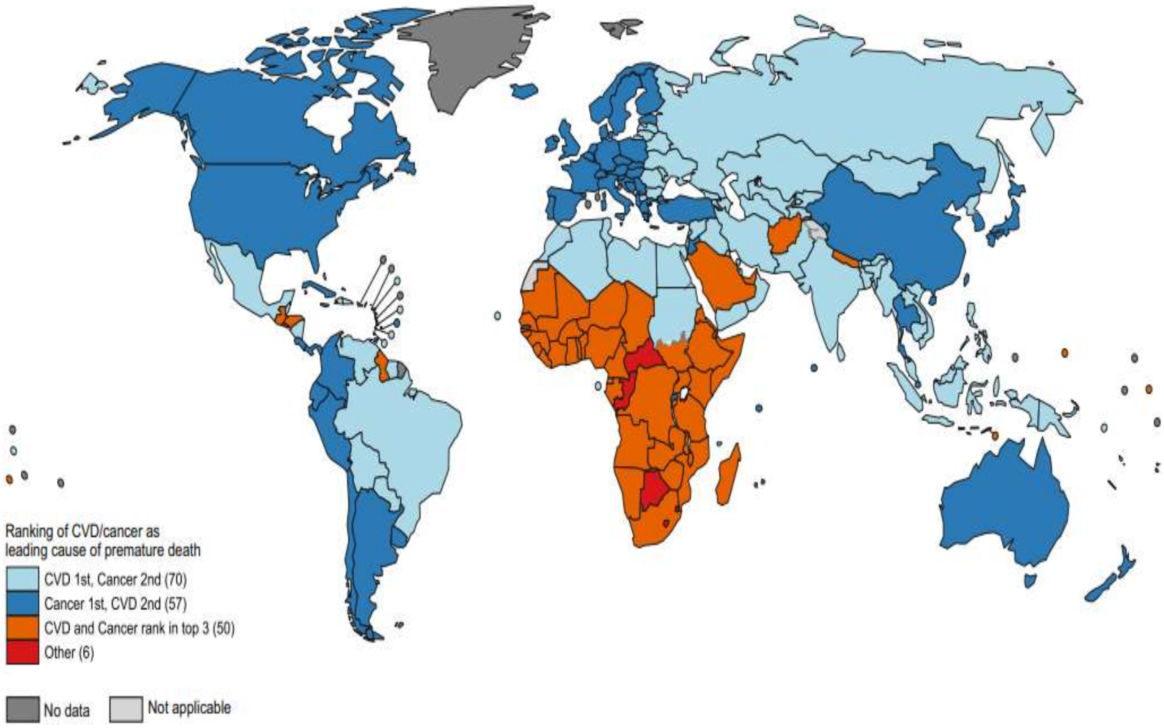

Figure 1.4: World map displaying the leading cause of premature deaths of individuals between 30-70 years old [CVD: cardiovascular disease] © 2021 WHO (Bray et al. 2021)

1.2. Colorectal cancer

Colorectal cancer encompasses any cancer of the large bowel or rectum originating from the colorectal mucosa (Thrumurthy et al. 2016). It poses a growing public health concern as it accounts for 10% (1.9 million new cancer cases) of all cancers; ranking third in terms of incidence in both genders worldwide. The incidence rate for colorectal cancer differs between countries, with the highest rates found in highly developed countries in Europe, North America and Australia (Sung et al. 2021).

Colorectal cancer is responsible for 9.4% (0.9 million deaths) of all cancer related deaths (Sung et al. 2021, Xi and Xu 2021). As a result of earlier cancer detection through the implementation of screening programmes, there has been a progressive decline in the mortality rate of colorectal cancer patients in many Western countries since the mid-1980s (Stintzing 2014, European Commission and European network of cancer registries 2021, Haggstrom and Cheung 2022). In fact, with the advancement in medicines from the beginning of the 21st century, colorectal cancer started to be considered as a chronic illness, with patients requiring extended treatment over many years (Chua et al. 2012, Benson 2014, Jacobsen, Nipp and Ganz 2017, Siddiqui and Cruz 2019).

1.2.1. Risk factors

Risk factors which increase the likelihood for developing colorectal cancer include genetic and environmental factors. Despite the fact that sometimes colorectal cancer is inherited, most of the reported cases are sporadic rather than familial. Environmental and lifestyle factors linked with a possible increased risk of colorectal cancer include consumption of red and processed meat, obesity, tobacco and high alcohol consumption (Argiles et al. 2020, Macrae 2022). In fact, colorectal cancer is often considered as marker of socio-economic development (Sung et al. 2021). Age is a major unmodifiable risk factor, with the median age at onset of colorectal cancer being 67 years (Argiles et al. 2020, Biller and Schrag 2021). Though this illness rarely presents in individuals prior to the age of 40 years, an increased incidence is noted by Western cancer registries amongst individuals 40 to 44 years old (Argiles et al. 2020).

1.2.2. Clinical presentation

Patients with colorectal cancer typically present with abdominal pain, rectal bleeding, unexplained weight loss, generalised weakness, altered bowel habits and microcytic anaemia (Argiles et al. 2020, Biller and Schrag 2021). However, the clinical symptoms at presentation may differ depending on the location and stage of the cancer (Argiles et al. 2020). Approximately a quarter of patients would already have distant metastasis at presentation of symptoms whilst half of patients with colorectal cancer would eventually develop metastatic illness in the near future (Vatandoust, Price and Karapetis 2015).

1.2.3. Investigations

Colorectal cancer is mainly diagnosed using endoscopy together with histological confirmation achieved by biopsy. Tumour markers, including carcinoembryonic antigen (CEA), may be elevated in colorectal cancer (Van Cutsem et al. 2014, Argiles et al. 2020). Staging of colorectal cancer is performed using x-ray imaging such as computed tomography (CT) and magnetic resonance imaging (MRI) in case of rectal tumours. Staging criteria include tumour size (T), regional lymph node involvement (N) and distant metastasis (M). The most common sites of colorectal metastasis include the liver and lungs (Biller and Schrag 2021).

1.2.4. Management

Colorectal cancer is managed using a multimodal approach. The selection of treatment for the management of colorectal cancer is influenced by the stage of the illness, the performance status of the patient as well as the molecular characteristics of the cancer (Stintzing 2014, Brown et al. 2019). Table 1.1 shows the indicated modality of treatment according to the stage of colorectal cancer.

Table 1.1: Treatment options for colorectal cancer by stage
(Colorectal cancer alliance 2022)

Stage	Surgery	Antineoplastic medicines +/- Targeted therapies	Radiotherapy
0 Earliest stage of cancer	Yes	No	No
I	Yes	No	No
II	Yes	Yes – FOLFOX or XELOX for rectal cancer and high risk colon cancer	Yes – for rectal cancer, given in tandem with 5-FU/LV or capecitabine
III	Yes	Yes - FOLFOX or XELOX	Yes – for rectal cancer, given in tandem with 5-FU/LV or capecitabine
IV Most advanced stage of cancer	Yes – usually only for cases of cancer obstructing the gastrointestinal tract. Some patients may be candidates for liver, lung or peritoneal surgery	Yes - FOLFOX or FOLFIRI plus bevacizumab or cetuximab or panitumumab or aflibercept or trifluridine/tipiracil or regorafenib	Yes – mainly for rectal cancer. Also considering interventional radiology for liver and lung metastases

The standard curative treatment for colon cancer is surgical resection with optimal lymph node dissection. This is the mainstay treatment for early-stage disease (Stage 0 and I). In case of locally advanced stage disease (Stage II and III), the benefits of antineoplastic medicines in combination with surgery have been established. In these cases, antineoplastic medicines can be used as neoadjuvant (prior surgery) or adjuvant (after surgery) treatment to maximally reduce and stabilise the cancer (Argiles et al. 2020, Xie, Chen and Fang 2020). Parenteral fluorouracil and oxaliplatin (FOLFOX) regimen is the standard adjuvant treatment for colon cancer, with oral capecitabine and parenteral oxaliplatin (XELOX) administered to patients who are unable to tolerate FOLFOX. Single-agent treatments with fluorouracil with leucovorin (5-FU/LV) or capecitabine are recommended alternative treatment options for frail patients who cannot tolerate oxaliplatin. The management of metastatic colorectal cancer (Stage IV) involves the use of multiple antineoplastic medicines given either in combination or as single agents; these are 5-FU/LV, capecitabine, irinotecan and oxaliplatin. Their use is aimed at the reduction in cancer size as well as the suppression of further tumour spread and growth. Additional treatment with targeted therapy such as anti-epidermal growth factor receptor agents cetuximab and panitumumab or anti-angiogenesis agent bevacizumab is a recent approach aiming to further control the illness and successfully prolong the overall survival of patients with colorectal cancer (Wolpin and Mayer 2008, Van Cutsem et al. 2014, Van Cutsem et al. 2016, Xie, Chen and Fang 2020).

Treatment for rectal cancer may differ with regards to perioperative management in comparison to treatment for colon cancer. In fact, the use of local pelvic radiotherapy is more often reserved for rectal cancer in comparison to colon cancer (Stintzing 2014, Brown et al. 2019). The use of antineoplastic medicines and targeted therapies are associated with treatment toxicity, with patients exhibiting different adverse effects depending on the treatment taken. Alopecia and severe diarrhoea are associated with irinotecan whilst peripheral neuropathy is more linked to the use of oxaliplatin (Van Cutsem et al. 2014, Van Cutsem et al. 2016). Table 1.2 outlines first-line treatment regimens with antineoplastic medicines and/or targeted therapies and the associated toxicities.

Table 1.2: Treatment regimens with antineoplastic medicines and/or targeted therapies used for first-line treatment of advanced and metastatic colorectal cancer
(Biller and Schrag 2021)

Regimen name and component	Dosing schedule	Selected adverse effects
FOLFOX (Fluorouracil, leucovorin and oxaliplatin)	Every 2 weeks, with infusion of oxaliplatin over 2 hours and infusion of fluorouracil over 46-48hours	Pancytopenia, neuropathy, hypersensitivity
XELOX (Capecitabine and oxaliplatin)	Every 3 weeks with infusion of oxaliplatin over 2 hours and oral capecitabine for 2 weeks and 1 week off	Pancytopenia, diarrhoea, hand-foot syndrome, neuropathy, hypersensitivity
FOLFOXIRI (Fluorouracil, leucovorin, oxaliplatin and irinotecan)	Every 2 weeks, with infusion of oxaliplatin over 2 hours, 1.5 hours irinotecan and 46 hours fluorouracil	Pancytopenia, diarrhoea, neuropathy, hypersensitivity
FOLFOX plus cetuximab or panitumumab	Every 2 weeks, with infusion of cetuximab over 2 hours or panitumumab over 60 minutes, oxaliplatin over 2-6 hours and infusion of fluorouracil over 46 hours	Pancytopenia, diarrhoea, hand-foot syndrome, hypomagnesaemia, hypersensitivity, neuropathy, skin toxicity
FOLFIRI (Fluorouracil and irinotecan)	Every 2 weeks, with infusion of irinotecan over 0.5-1.5 hours and infusion of fluorouracil over 46-48 hours	Pancytopenia, diarrhoea
XELIRI (Capecitabine and irinotecan)	Every 3 weeks with infusion of irinotecan over 0.5-1.5 hours and oral capecitabine for 2 weeks and 1 week off	Pancytopenia, diarrhoea, hand-foot syndrome
FOLFIRI plus cetuximab or panitumumab	Every 2 weeks, with infusion of cetuximab over 2 hours or panitumumab over 60 minutes, irinotecan over 0.5-1.5 hours and infusion of fluorouracil over 46-48 hours	Pancytopenia, diarrhoea, hypomagnesaemia, infusion reaction, skin toxicity
Fluorouracil and leucovorin (5-FU/LV)	Intravenous infusion over 5 minutes	Pancytopenia, mucositis
Capecitabine	Oral regimen given daily for 3 weeks of every 4 weeks	Pancytopenia, hand-foot syndrome
Bevacizumab plus FOLFOX or XELOX, FOLFIRI, XELIRI, FOLFOXIRI, 5-FU/LV or capecitabine	Infusion time depends on specific treatment regimen given	Hypertension, bowel perforation, poor wound healing, proteinuria, thrombosis

1.2.5. Response evaluation and follow-up

The European Society for Medical Oncology (ESMO) Clinical Practice Guidelines recommend that patients should be reviewed every 2-3 months during treatment with antineoplastic medicines. The review should involve evaluation of the patient's general condition including physical examination and investigations with imaging such as CT scan. The occurrence of adverse effects of treatment and their impact on patient's quality of life should be assessed (Van Cutsem et al. 2014).

Follow-up care for patients after completion of treatment is essential to identify a recurrence at an early stage, and hence maximise the patients' overall survival (Argiles et al. 2021). As outlined in Figure 1.5, the follow-up care should spread over at least 5 years post-surgery and would include regular investigations such as tumour markers, imaging and endoscopy (Argiles et al. 2021).

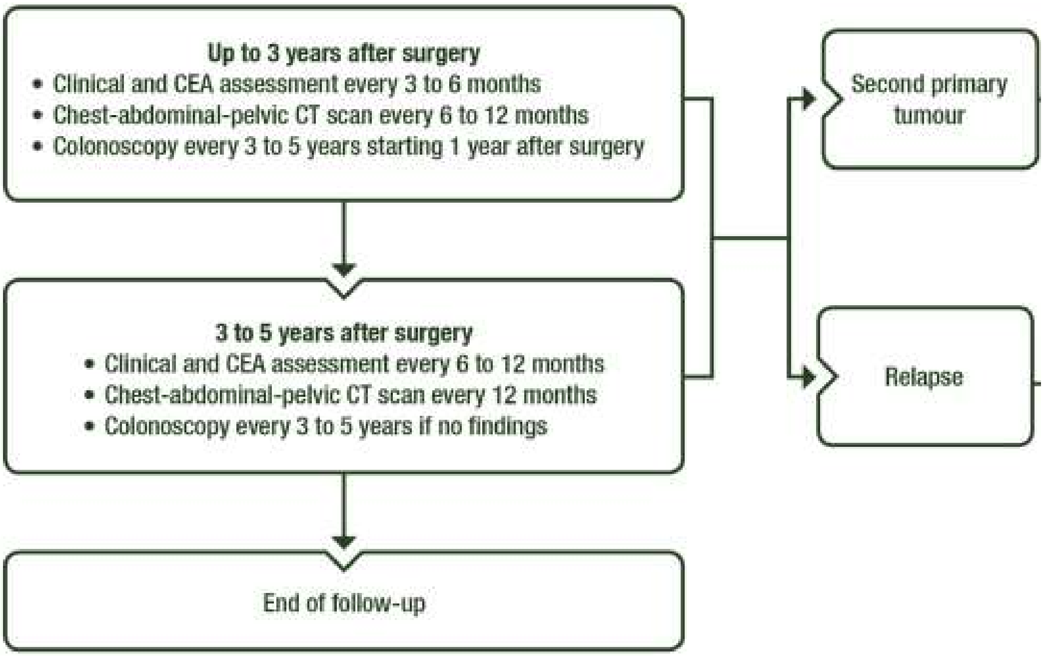

Figure 1.5:Recommendations on follow-up post colorectal cancer surgery ©2020 ESMO, Elsevier Ltd (Argiles et al. 2021)

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1.2.6. Prognosis

Prognosis was defined by Hansebout et al. (2009 p.328) as “the prospect of recovering from injury or disease, or a prediction or forecast of the course and outcome of a medical condition.” The prognosis of cancer depends on the staging of cancer described in accordance to TNM classification (Rosen and Sapra 2022). Table 1.3 provides a summary of the 5-year survival rates according to colorectal cancer stage. This varies between >90% in case of Stage 1 colorectal cancer to <10% for Stage IV metastatic colorectal cancer (Wolpin and Mayer 2008), emphasising the importance of early detection and provision of treatment (Siegel et al. 2020).

Table 1.3: TNM stage grouping and their respective 5-year survival
(Wolpin and Mayer 2008)

Stage	**TNM classification**	**5-year survival**
I	T_{1-2}, N_0, M_0	>90%
IIA	T_3, N_0, M_0	80-85%
IIB	T_4, N_0, M_0	70-80%
IIIA	T_{1-2}, N_1, M_0	65-80%
IIIB	T_{3-4}, N_1, M_0	50-65%
IIIC	T_{1-4}, N_2, M_0	25-50%
IV	T_{1-4}, N_{0-2}, M_1	5-8%

1.3. A background on Malta

The Maltese Archipelago is composed of 3 main inhabitable islands namely Malta, Gozo and Comino. As shown in Figure 1.6, Malta is a small European country strategically positioned at the centre of the Mediterranean Sea in the passageway between the European and the North African continents (Debrincat 2014). With an estimated total population of 516,100 in year 2020 covering an area of 316km^2, it is one of the smallest and most densely populated countries worldwide (National Statistics Office – Malta 2021).

The Maltese Islands are rich in history and culture, influenced from their roots dating back to the prehistoric period. On 21st September 1964 Malta gained its political independence from Britain and then became a republic on 13th December 1974 with the president considered as the head of state. On 1st May 2004, Malta became a Member State in the European Union. Malta is also a member of the United Nations, Commonwealth and various other international organisations (Azzopardi Muscat et al. 2014).

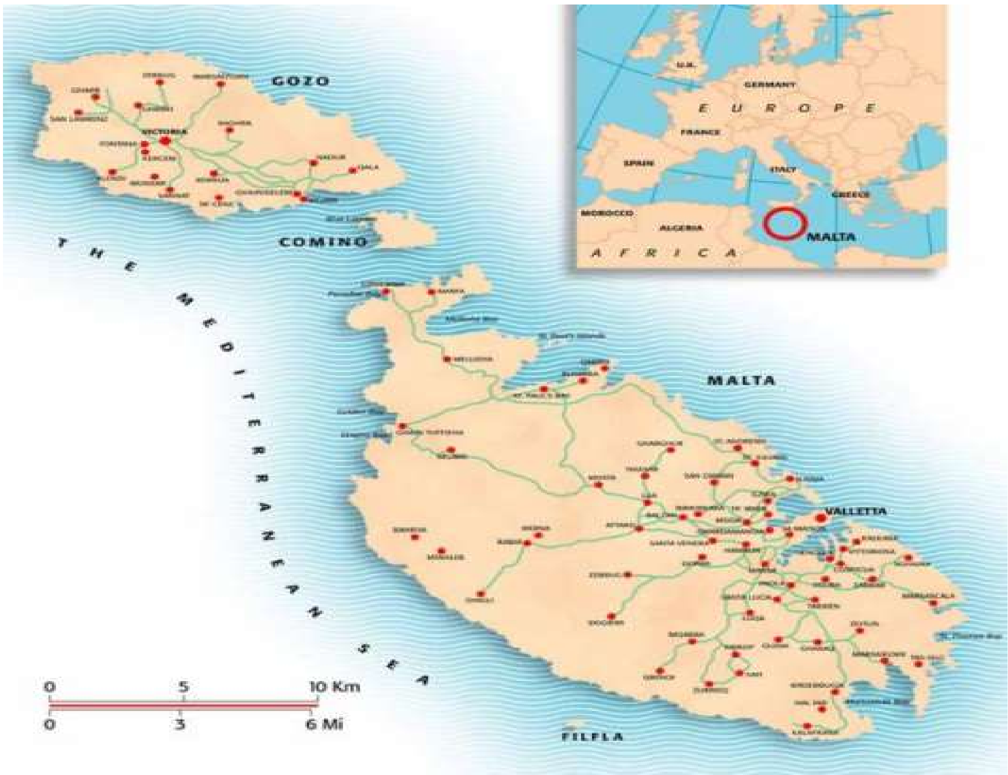


Figure 1.6: Map of the Maltese Islands © 2009 Paul Refalo (Refalo 2009)

1.3.1. Epidemiology of cancer in Malta, particularly colorectal cancer

According to the WHO IARC (2022^b), a total of 2500 cancer cases were newly diagnosed in Malta in 2020. As shown in Figure 1.7, the most commonly diagnosed cancer in both genders is breast (16.1%, 403 new cases), followed by prostate (13.4%, 336 new cases), and colorectal cancer (11.6%, 289 new cases).

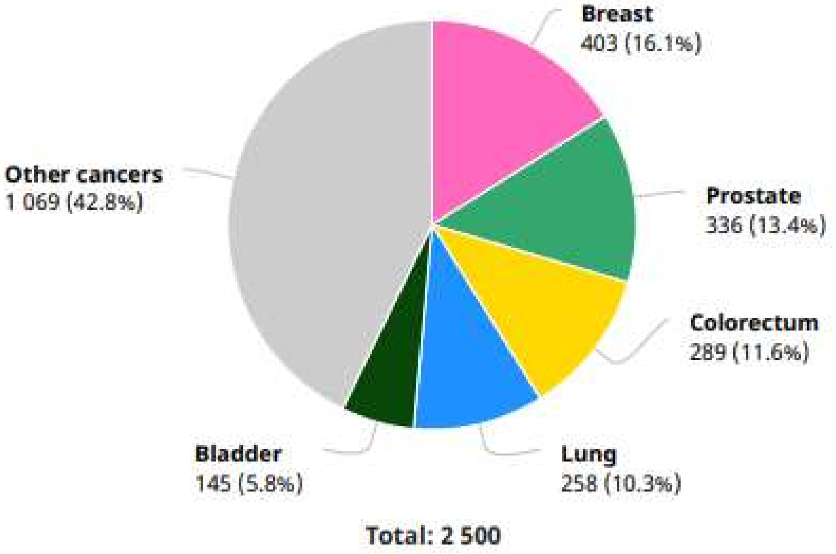


Figure 1.7: Number of new cancer cases for both genders and all ages in Malta in 2020 © 2022 IARC. (WHO – IARC) 2022^b)

For the year 2020, lung cancer (20.1%, 194 deaths) was the leading cancer death in Malta, followed by colorectal cancer (9.3%, 90 deaths) and pancreatic cancer (9.2%, 89 deaths) (WHO IARC 2022^b). The life expectancy of citizens in Malta in 2020 was 82.6 years, placing it as the second highest amongst European countries. The improvement in life expectancy since the year 2000 is attributed to the decline in cancer deaths. Local data showed that age - standardised mortality rates per 100,000 population for cancer reduced by 14% between 2000 and 2018 (Organisation for Economic Co-operation and Development (OECD) and European Observatory on Health Systems and Policies 2021). With respect to colorectal cancer, Malta ranked amongst European countries with low incidence and mortality for colorectal cancer in 2020 (Figure 1.8) (European Observatory on Health Systems and Policies 2022). Despite this, cancer incidence is still expected to continue to rise till 2030 by approximately 2% each year due to ageing population, dietary factors, sedentary lifestyle and obesity (Ministry for Health 2017).

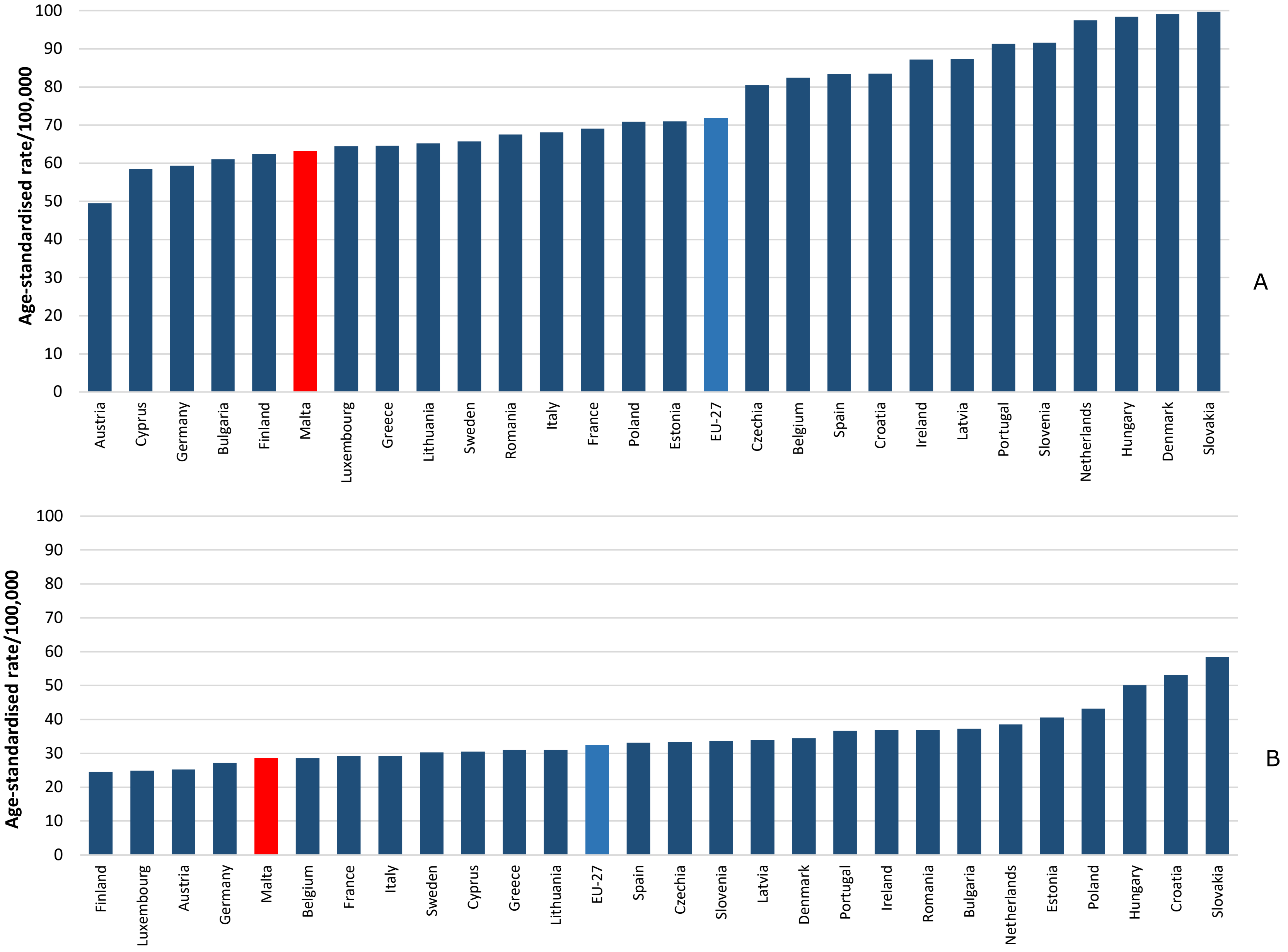


Figure 1.8: Incidence (A) and mortality (B) of colorectal cancer in both gender in European countries, in 2020, expressed in age-adjusted standardised rate per 100,000 (European Commission 2022)

The age-adjusted ten-year survival rate for patients with common cancers diagnosed and treated in Malta (2008–2012) has approached 50% with the exception of lung cancer, as shown in Figure 1.9. With respect to colorectal cancer, Malta registered a lower death rate in comparison to EU average and a slightly lower five-year survival rate for patients diagnosed between 2010 and 2014 (Malta 58%, EU 60%). This poses further challenges to the local healthcare system due to increasing demand for cancer services (Ministry for Health 2017, OECD/European Observatory on Health Systems and Policies 2021).

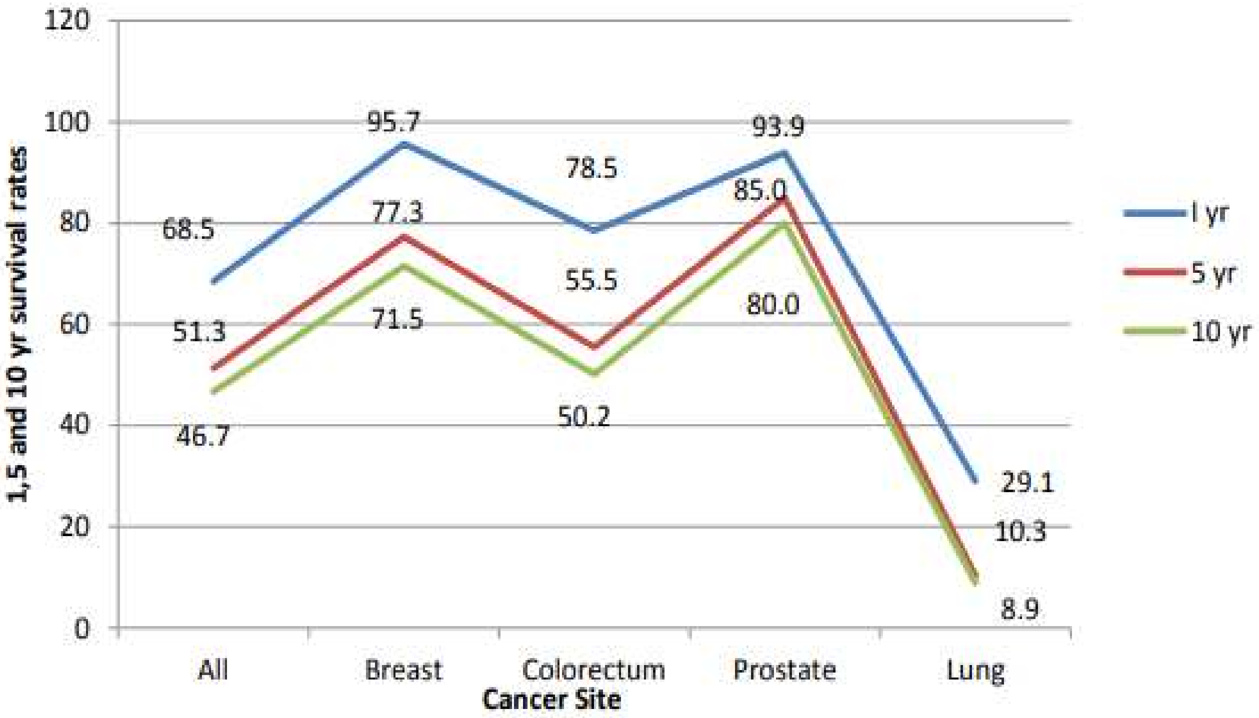


Figure 1.9:Age-adjusted ten-year relative survival for patients diagnosed in 2008 till 2012 with a follow-up till end of 2014 © 2017 Ministry for Health (Ministry for Health 2017)

1.3.2. Healthcare system in Malta

The National Health Service is the principal provider of health services in Malta. It is composed of five public funded hospitals; whereby two hospitals offer acute services (one acute hospital in Malta and Gozo respectively). The remaining hospitals offer specialised care in the areas of oncology, rehabilitation and mental health (Azzopardi Muscat et al. 2014, Azzopardi Muscat et al. 2017). The private sector acts as a complementary service for healthcare service delivery (Azzopardi Muscat et al. 2017, OECD/European Observatory on Health Systems and Policies 2021).

In 2018, Malta spent €2646 per capita on healthcare, amounting to 8.8% of Gross Domestic Product. Though Malta ranked third with the highest growth in health spending, it is still below EU average (OECD/European Observatory on Health Systems and Policies 2021). The public healthcare system on the Maltese islands follows the Beveridge model since it is funded through tax revenue (Physicians for a national health program 2010, Azzopardi Muscat et al. 2014). It is free of charge at the point of use to all residents covered by social security legislation or humanitarian exemption. This includes inpatient hospital care along with the necessary treatment, medication and a three day supply of post-discharge medicines (Azzopardi Muscat et al. 2017, OECD/European Observatory on Health Systems and Policies 2021).

Private out-of-pocket expenditure is still substantial, amounting to 34.3% of the total health expenditure in 2018 (OECD/European Observatory on Health Systems and Policies, 2021). In fact, Malta ranked fourth in the EU with a high out-of-pocket expenditure related to buying of medicines as well as fees for service provision by private general practitioners and specialists related to primary and outpatient care. This was attributed to socio-cultural reasons where traditionally individuals with high income and education sought care from the private sector. Also, individuals resort to outpatient care directly from private specialists in order to bypass long waiting lists in public tertiary care and without the need of referral (OECD/European Observatory on Health Systems and Policies, 2021).

According to the Euro Health Consumer Index of 2018, the Maltese healthcare system is ranked in 27th place out of 35 countries (Bjonberg and Phang 2019). It was reported that the local healthcare system had an improved cancer survival rate and adequate accessibility to healthcare services. However, the patients' involvement in decision-making relating to their care was still lacking (Bjonberg and Phang 2019, Ganado 2019).

1.3.3. Oncology services in Malta

In an effort to prevent cancer and improve quality of cancer care, a National Cancer Plan was first launched by the Government of Malta in 2011 (Ministry for Health, the Elderly and Community Care 2011) and reviewed in 2017 (Ministry for Health 2017). In keeping with the National Cancer Plan (Ministry for Health, the Elderly and Community Care 2011), a national cancer screening programme for colorectal cancer was set up in 2012. This is currently offered to all persons aged between 56 and 72 years. In addition, they are invited to do a home-testing faecal immunochemical test every 2 years (Ministry for Health 2021a).

In order to improve the cancer services, a new haemato-oncology hospital was built, which opened in 2015 (Figure 1.10). Sir Anthony Mamo oncology centre is the single secondary care centre in Malta that provides specialised care for oncology and haematology patients with various inpatient and outpatients services. This spearheaded the introduction of new cancer services which brought about changes in clinical practice and aimed to provide seamless cancer care pathways (The Malta Independent 2016, Ministry for Health 2017, Government of Malta 2021).

Figure 1.10: Setting in Malta for data generation – Sir Anthony Mamo Oncology Centre ©2016 Times of Malta (Dalli 2016)

Two new services were implemented, namely the fast-track services and the introduction of nurse navigators. The fast-track services allowed family physicians to directly refer patients with suspected cancer to be reviewed in a timely manner by the oncologist (The Malta Independent 2016, Government of Malta 2021). Also, the service of nurse navigators specialising in a specific cancer type was launched in February 2016. This service intends to assist patients with cancer in their medical care throughout their journey. Whilst being a point of contact for patients, nurse navigators act as a liaison between the healthcare provider and the patient to ensure better communication and assist in overcoming any barriers to care. This brought about a shift from the traditional follow-up care being provided by the oncologist to the nurse navigator (The Malta Independent 2016). Recently, this service was commended by the WHO (2022b) as it truly embraces patient-centred care.

Other available cancer care services include the focal nurses, Aurora Support Service and clinical support services. Focal nurses are responsible to educate patients and their significant others about specific treatment modalities such as chemotherapy and radiotherapy and support patients in self-care activities during treatment. The focal nurses specialised in chemotherapy also run the Aurora Support Service, which is a nurse-led free of charge service aimed to educate newly diagnosed patients about the use of antineoplastic medicines and management of adverse effects of such treatment by primarily organising a group information session. They also organise well-being days for all patients with cancer where patients are provided with educational talks about skin care, improvement in physical appearance, meditation techniques and aromatherapy (Government of Malta 2021). Furthermore, there are clinical support services dedicated for cancer patients namely occupational therapy, physiotherapy, psychological and social work services. These services, with the exception of the focal nurses and psychological services, can be accessed following referral by a healthcare professional (Government of Malta 2021).

1.4. The patient journey for patients with cancer

The patient journey is defined as "the chronological chain of events that constitutes the patient's encounter with various parts of health and care services" (Pfannstiel and Rasche 2019 p.331). As shown in Figure 1.11, the cancer patient moves horizontally across the different hospital departments to receive his care, involving various healthcare professionals (Giunti 2018). In each department, there is a process where both patient and healthcare professional share an action with the resultant information flowing between persons and systems (Gualandi et al. 2019). Though the hospital management strives to ensure a smooth flow to provide safe and efficient patient care, it needs to ensure the most effective and efficient use of hospital resources. As a result, healthcare professionals are only aware of the provision of care for which they are responsible. Only the patient fully experiences the entire journey. The patient's journey is rarely linear and is unique for each individual patient. Each patient seeks to receive the appropriate care with a high standard of service (Ben-Tovim et al. 2008, Trebble et al. 2010, Pfannstiel and Rasche 2019, Gualandi et al. 2019). According to the Institute of Medicine, quality of healthcare services is based on 6 domains, namely safety, effectiveness, patient-centredness, timely, efficiency and equitability (WHO 2020). In order to satisfy the patient's aim and improve the quality-of-service provision, the hospital management must explore and understand the individual patient's journey (Gualandi et al. 2019).

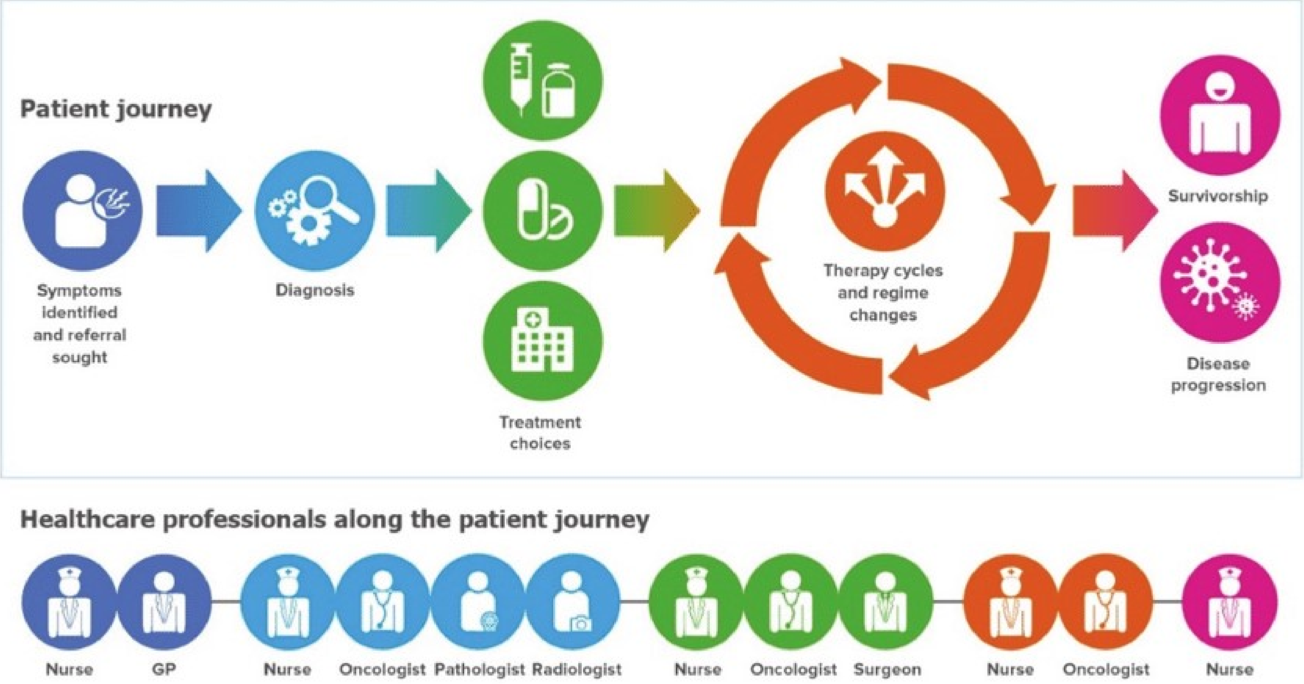


Figure 1.11:The cancer patient journey from presentation of symptoms to survivorship or disease progression ©2018 DeepDive Oncology (Giunti 2018)

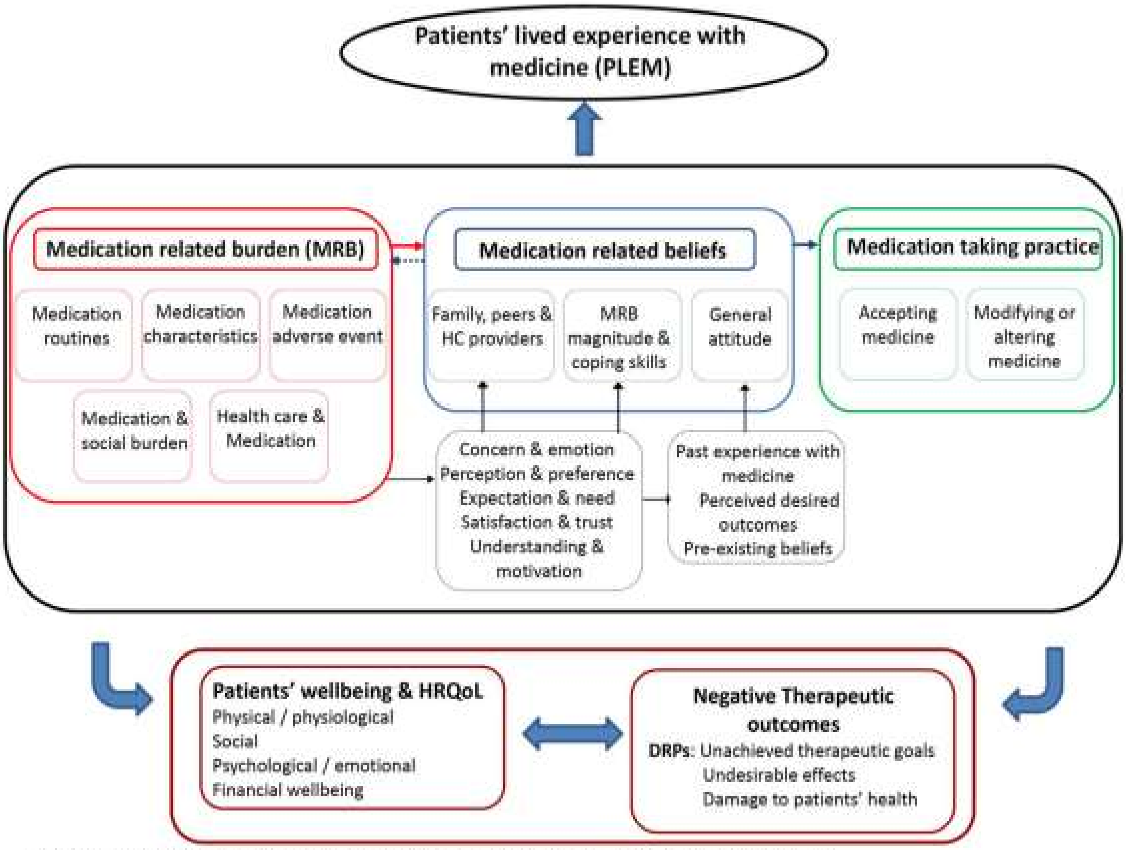
1.4.1. Lived experience

Lived experience is defined as "personal knowledge about the world gained through direct, first-hand involvement in everyday events rather than through representations constructed by other people" (Chandler and Munday 2011 p.243). Capturing the perspective of the individual provides a more complete understanding of their own experience and offers insights that cannot be identified through any other means (Fujisawa and Klazinga 2017).

With time, the concept of the patients' lived experience is being more commonly used as a means of assessing quality of patient care in healthcare systems. The growing interest in capturing the patients' lived experience stemmed from the rising role of the patients' involvement in medical care. Therefore, by gaining a better understanding of the patients' lived experience, healthcare professionals and policy makers are directing attention towards the patient's voice with the patient becoming more involved in his/her own health (Fujisawa and Klazinga 2017, Gaille 2019). Literature suggests a positive association between the patients' experience and health outcomes, adherence to medicines, preventive care and healthcare resource use (Haynes et al. 2008, Bridge et al. 2019).

1.4.2. Patients' lived experience with medicine

Patients' medication experience was initially described by Cipolle, Strand and Morley (2004) as "the sum of all events involving drug therapy that a patient encounters in his/her lifetime". In a later publication by Shoemaker and Ramalho de Oliveira (2008 p.86) medication experience was defined as "an individual's subjective experience of taking a medication in his daily life." Based on a meta-synthesis of 34 qualitative studies, Mohammed, Moles and Chen (2016) developed a conceptual framework on PLEM for patients with any illness (Figure 1.12). It identified the various factors that affect the patients' experience with medicine (Mohammed, Moles and Chen 2016).



Abbreviations: DRPs= Drug Related Problems, HC = Health care, HRQoL= Health related quality of life

Figure 1.12:Conceptual PLEM model
©2016 BMJ Publishing Group (Mohammed, Moles and Chen 2016)

As portrayed in Figure 1.12, the PLEM conceptual model is comprised of three key domains, namely medication-related beliefs, medication-related burden and medication-taking practices. These are subdivided into 13 subdomains. Furthermore, medication-related burden was identified as a central component of patients' lived experience of medicine use. This also affected the patient's beliefs about adherence to medicines and their illness as well as their attitude and willingness to follow the treatment regimen. The impact of medicines on health-related quality of life may be regarded as a balance between the benefits and burden (Mohammed, Moles and Chen, 2016).

Since its publication in 2016, the PLEM conceptual model has been used to create tools specifically designed to evaluate the burden of medicines such as the Living with Medicines Questionnaire (Krska, Katusiime and Corlett 2017) and Medication-Related Burden Quality of Life scale (MRB-QoL) (Mohammed et al. 2018). None of these two tools were developed specifically for the oncology setting.

With the expected increase in the incidence of cancer, the demand for antineoplastic medicines is expected to increase by 53% (9.8 million individuals in 2018 to 15 million in 2040) assuming adherence to the current evidence-based guidelines (Jarach 2019). The use of antineoplastic medicines is often used in combination with other treatment modalities such as surgery and radiotherapy and with other medicines such as immunotherapy and supportive medicines. As the incidence of cancer increases with age, patients are expected to deal concurrently with other comorbidities, further increasing the challenges related to cancer management such as tolerability and survival (Lee et al. 2011). Besides this, the use of antineoplastic medicines is associated with the development of severe adverse effects such as immunosuppression and neurotoxicity which present immediately or as late effects during the patients' life with a significant impact on the patients' quality of life (Sawada et al. 2009, Ramasubbu et al. 2021). Quality of life is a dynamic multidimensional construct capturing the subjective well-being (both positive and negative aspects) of patients in all life aspects, namely physical, emotional, functional and social domains (Bottomley 2002, Lewandowska et al.

2020). As the disease process and duration of cancer together with the use of antineoplastic medicines may negatively impact the patients' quality of life (Lewandowska et al. 2020), this further emphasises the need to evaluate PLEM amongst patients with cancer who receive antineoplastic medicines.

1.4.3. Value-based healthcare for patients with cancer

The concept of patient-centred care originated in early 1990s and was defined by Institute of Medicine (2001 p.6) as "providing care that is respectful of and responsive to individual patient preferences, needs and values and ensuring that patient values guide all clinical decisions." Patient-centred care places the patient at the centre of care and is constructed on eight dimensions namely respect for patients' preferences, emotional support, physical comfort, communication needs, continuity and transition, care coordination, involvement of family and friends and access to care. Therefore patient-centredness is a multifaceted construct and a core component of quality (Tseng and Hicks 2016).

All healthcare systems today are under pressure to spend their resources wisely and efficiently due to increasingly complex patients with multiple chronic conditions, increased public expectations, changing clinical practice and costs of new technology developments. As a result of the imbalance between the increasing incidence of cancer and costs of cancer treatment as well as finite healthcare resources, the report 'Delivering High Quality Cancer Care' (Institute of Medicine 2013) concluded that cancer care is in crisis and highlighted the need to change from a volume-driven to a value-based healthcare. This innovative reform proposed healthcare systems to be managed based on outcomes that matter to patients. Also, services should be provided in an equitable and sustainable manner to meet the needs of all individuals (Zanotto et al. 2021, Van Staalduinen et al. 2022).

In addition to patient-centred care, the concept of value-based healthcare was introduced by Porter and Teisberg in 2006. Though there is no single definition of value in context of healthcare, it often refers to the ratio of outcomes to costs (Tseng and Hicks 2016). Hence focusing on the monetary value. In 2017, work conducted in United Kingdom and Italy led to widening of the concept of value-based healthcare. This took in consideration three distinct aspects of value, namely personal, allocative and technical values. Later the fourth pillar of societal value was included by the ‘Expert Panel on Effective Ways of Investing in Health’; developing the “Quadruple Value” Model (Figure 1.13). As a result, value may be achieved across one or more of these pillars. By assessing the value of an intervention at an individual, population and societal level, it informs the optimal use of available resources and achieves the best outcomes (European Commission 2019).

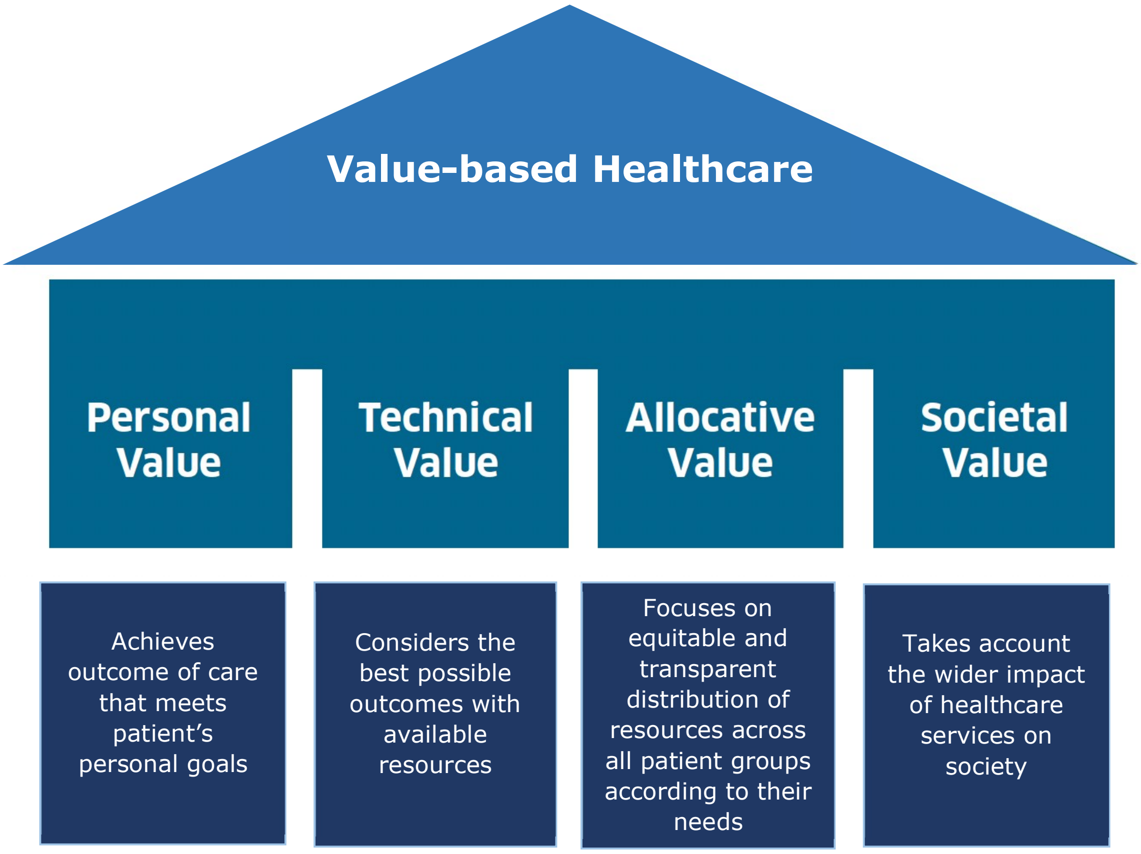


Figure 1.13: The four value pillar of Value-based Healthcare.
© 2019 European Union. (European Commission 2019)

With respect to oncology, healthcare decisions are complex as these are affected by multiple factors and treatment options implying varying degrees of preference for patients and healthcare professionals (Campolina 2018). To enhance value, this requires a multi-faceted and multi-professional approach. By supporting patients’ initiative to engage in shared-decision making, patients will be allowed to make informed choices about their care by considering the available treatment options with their associated risks and benefits. This further promotes better understanding by healthcare professionals about what matters mostly to patients. Thus, leading to better use of resources as well as reduction in waste and harm associated with medicines (European Commission 2019, Scottish government 2022). The use of patient-reported outcome measures (PROMs) allows the patient’s voice to be heard and healthcare professionals to better assist their patients. By sharing information obtained from PROMs, such as allowing patients to have access to their health records, this may improve patients’ engagement with the result of feeling more satisfied with their care (Baumhauer and Bozic 2016). This emphasises the need to explore the patients’ perspectives on their cancer care so that healthcare professionals understand how this affects the patients’ overall health and wellbeing.

1.5. Aims and objectives of this doctoral research

The overall aim of this doctoral research was to explore the patients’ lived experiences with antineoplastic medicines (PLEM) for the treatment of colorectal cancer in Malta. The doctoral research was conducted in three phases. Table 1.4 provides details about the aim and research objectives for each phase of the study.

Table 1.4: Design, aim and research questions/objectives of each phase of study

Phase	Design	Aim	Research questions/Objectives
I	**Systematic Review**	To critically appraise, synthesise and present the available evidence of patients' lived experiences with antineoplastic medicines prescribed for the management of malignant solid tumours	• What is the definition of the patients' lived experience with medicine? • What are the medicine-related beliefs of cancer patients? • What is the medicine-taking practice of cancer patients? • What is the medicine-related burden experienced by cancer patients?
II	**Longitudinal qualitative study from the perspective of patients**	To explore longitudinally the patients' lived experiences with antineoplastic medicines for colorectal cancer during the treatment journey and beyond	• To explore the patients' beliefs and knowledge with antineoplastic medicines • To explore the patient's medicine taking practice of antineoplastic medicines • To explore the burden experienced by patients with colorectal cancer during treatment with antineoplastic medicines and beyond
III	**Longitudinal qualitative study from the perspective of significant others**	To explore longitudinally the significant others' perspective on the patients' experiences with antineoplastic medicines for the duration of the treatment journey for colorectal cancer	• To explore the perspective of significant others on the patients' beliefs and knowledge • To explore the perspective of significant others on the patients' approach to medicine-taking practice • To explore the burden experienced by patients from the perspective of the significant others

Chapter 2

Methodology

2. Introduction to the chapter

This chapter describes the different types of literature reviews and provides a justification to carry out a systematic review as part of this research. It explains the different philosophical worldviews, research designs and methods that encompass the research process. The research approach adopted for this doctoral research is outlined, with details on the strategies utilised for sampling, data generation, analysis and quality assurance. Justifications for the chosen approaches are provided.

2.1. Literature review and other types of reviews

A literature review has been described as "a comprehensive study and interpretation of literature that relates to a particular topic" (Aveyard 2014 p.21). The goals of carrying out a literature review (Booth, Sutton and Papaioannou 2012, Aveyard 2014) are to:

- summarise and compile the available literature on a particular topic to enhance understanding and prevent duplication of work
- identify new approaches for data interpretation
- describe how different pieces of work relate to each other and provide contextualisation
- identify and resolve any contradictions in earlier publications
- highlight gaps in previous studies and justify a way forward for further research

The expansion of evidence-based practice in health and social sciences led to the development of several different types of reviews (Grant and Booth 2009). The purpose, benefits and limitations of the most common types of reviews are outlined in Table 2.1.

Table 2.1: Characteristics of common types of reviews
(Grant and Booth 2009, Booth, Sutton and Papaioannou 2012, Sutton et al. 2019)

Type of review	Purpose	Benefits	Limitations
Literature Review	Examines published material to cover a wide range of topics at different degree of comprehensiveness	• Provides information of what has been accomplished • Generates summation of information • Allows building on previous work and identifies gaps	• Lacks explicit intent to elaborate on the scope or analyse the data collected • Subject to bias due to selective presentation of results and not assessing validity of statements
Mapping Review	Maps and categorises published literature to initiate further reviews and/or primary research after identification of gaps in literature	• Allows contextualisation of in-depth systematic literature reviews as part of broader literature • Characterises studies in other approaches such as different theoretical perspective, setting or population • Guides the researcher whether to undertake in-depth review and synthesis all or a subset of studies • Recognises gaps in the evidence	• Characterises studies at a broad descriptive level, generally based on study design • Usually does not involve quality appraisal
Scoping Review	Identifies the nature and extent of research evidence	• Provides preliminary assessment of the size and scope of available research literature to indicate whether a full systematic review is required • Attempts to be systematic, transparent and replicable	• Does not involve quality appraisal • Subject to bias due to limitations in rigour • Cannot use outcomes to propose change in policy or practice
Systematic Review	Identifies and appraises published studies and synthesises the '*best evidence*' to answer research questions	• Involves an exhaustive, systematic search to allow compilation of all known knowledge on a specific topic • Included literature undergoes critical review • Provides recommendations for practice	• Restricts the inclusion of studies to a single study design may limit application of this methodology
Meta-analysis	Statistically analyse combined numerical data of quantitative studies to postulate a more precise effect of the results	• Combines various individual studies to provide composite evidence to influence practice • Offers time efficient process for decision makers	• Quality of the review depends on its included studies
Umbrella Review	Compiles evidence from multiple systematic reviews in a single usable document	• Focuses on a broad condition for which there are competing interventions • Identifies reviews that address these interventions and compares their outcomes • Provides recommendations for practice	• Requires the availability of specific narrow reviews

The term 'literature review' is widely used as a generic term. However, there are key differences in the methodological approach when compared to systematic review, as outlined in Table 2.2. The Institute of Medicine defined a systematic review as a "scientific investigation that focuses on a specific question and uses explicit, prespecified scientific methods to identify, select, assess, and summarise the findings of similar but separate studies" (Manchikanti et al. 2014 p.E319). Hence this type of review follows explicit and systematic method intended to minimise bias (Sutton et al. 2019).

Table 2.2: Differences in methodological approach of literature review and systematic review (Robinson and Lowe 2015)

Methodological stage	Literature review	Systematic review
Description	Commonly provides summary evidence on a particular topic, often without answering a specific question	High level overview of primary research to a specific question. It is considered as a stand-alone piece of research, which is usually conducted prior undertaking further research
Data collection	Publications are identified through a fairly random process	Several specified databases are used to search pre-determined terms
Data extraction	Publications are read and key messages included in the review	Data extraction tool is utilised to identify information required. Two or more researchers are involved in this process
Amount of publications included	≥150 publications	Usually <50 and may also be fewer than 10
Data analysis	Author interprets the meaning of the results	Standardised methods of analysis are used to appraise methods, assess rigour and strength of evidence
Data presentation	Narrative write-up, generally supported with diagrams	PRISMA or a similar table of the included publications
Publication	Not suitable for publication in journals	Might be suitable for publication in journals
Outcome	Recommendations informed by evidence of various kinds obtained from included papers	Recommendations are supported on evidence from reviewed publications

2.1.1. Review type selected for the doctoral research (Phase I)

In Phase I of this research a systematic review was conducted to critically appraise, synthesise and present the available evidence of patients' lived experience with antineoplastic medicines. From the different types of reviews, a systematic review was chosen because it is comprehensive and is considered as one of the highest level of evidence, as shown in Figure 2.1. The method, results and conclusion of the systematic review are described in detail in Chapter 3 (Systematic Review). The findings of this review informed the subsequent phases of this doctoral research.

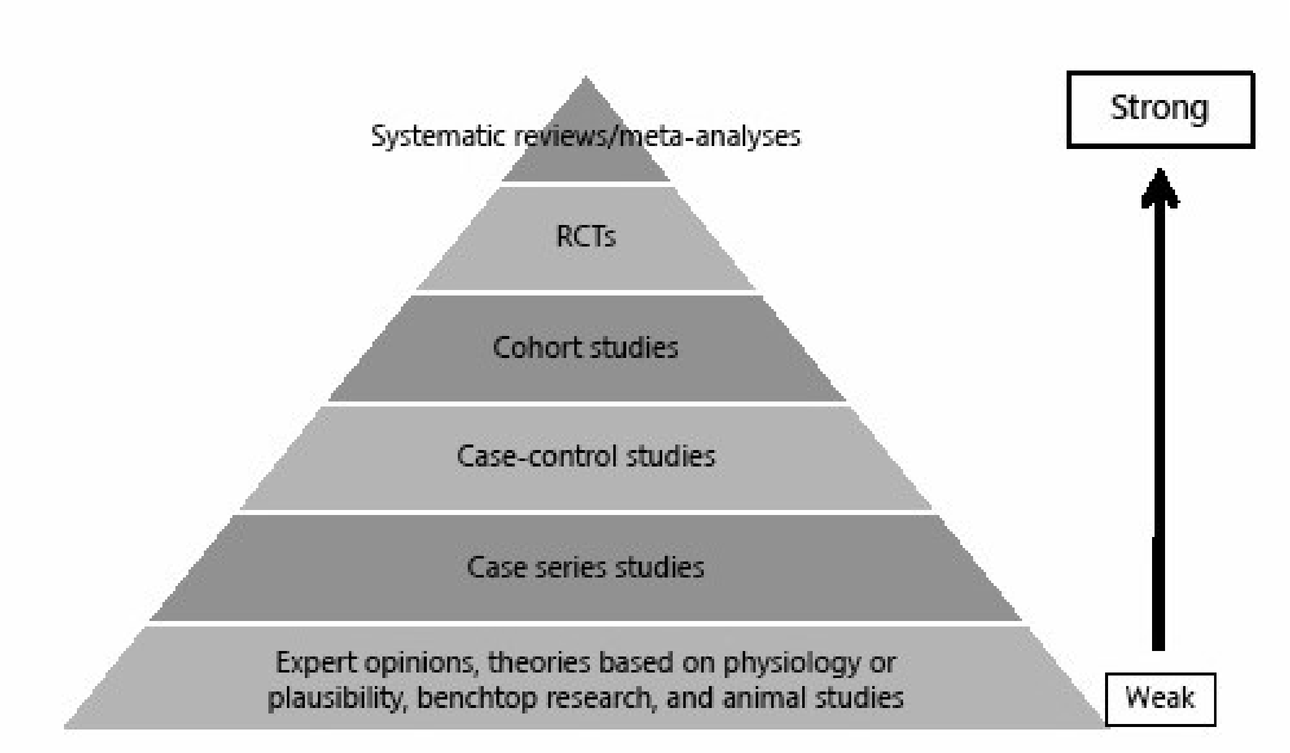


Figure 2.1: Hierarchy of evidence ©2022 Krager AG (Szajewska 2018)

2.2. The research process

Research is defined by Bassey (1990 p.35 as cited in Cohen, Manion and Morrison 2007) as “a systematic, critical and self-critical inquiry which aims to contribute to the advancement of knowledge.” It involves a systematic process that seeks to explore a phenomenon or investigate a problem with the ultimate aim to uncover the truth and enhance the existing knowledge (Cohen, Manion and Morrison 2007, Shah and Al-Bargi 2013).

Crotty (1998) described the research process as being composed of four sequential basic elements, namely epistemology, theoretical perspective, methodology and methods (Figure 2.2). Ontology (the philosophy of being) in combination with epistemology (the theory of knowledge) are known to make up the research paradigm. This leads to a theoretical perspective, which in turn feeds into the methodology and finally into methods (Crotty 1998, Leavy 2017). Conducting the research process in terms of these basic elements ensures that the research is well performed and the outcome is reliable (Crotty 1998).

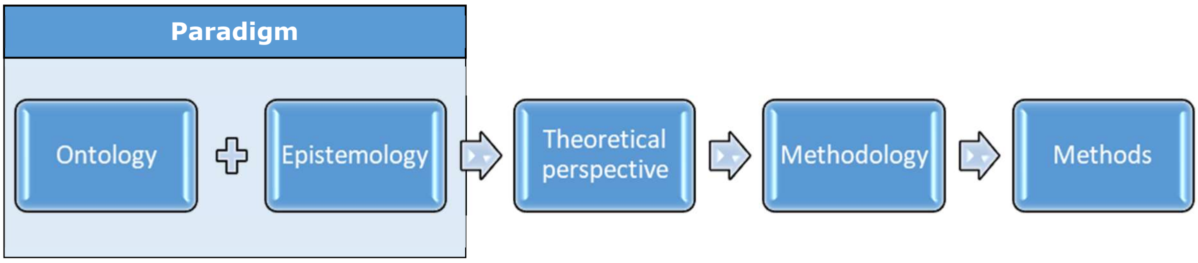


Figure 2.2:The elements of the research process
(Crotty 1998, Leavy 2017)

Furthermore, Creswell and Creswell (2018) explained that the plan to conduct research may be referred to as research approach. As outlined in Figure 2.3, this is composed of a cyclical scheme between the philosophical worldviews, research designs and research methods. This framework shall form the basis of this chapter.

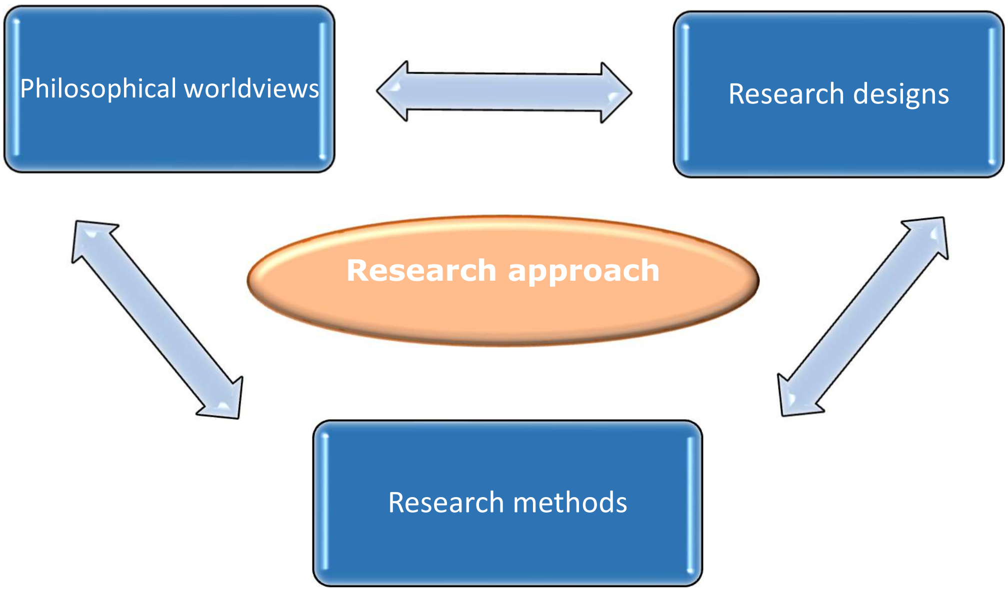


Figure 2.3: The framework for research
(Creswell and Creswell 2018)

2.2.1. Philosophical worldviews

Research is underpinned by the beliefs that guide the thoughts and actions of the researcher (Guba 1990). This was originally referred to as paradigm by Kuhn in 1962 (Bowling 2014), but currently is denoted by various interchangeable terms:

- epistemologies and ontologies (Crotty 1998)
- interpretive framework (Creswell 2013)
- worldview (Creswell 2014)

Creswell (2014 p.6) describes the worldview as "a general philosophical orientation about the world and the nature of research that a researcher brings to a study." Hence in simple terms, the worldview may be compared to the lens through which the researcher looks at the world. This will influence how the research is created, conducted and reported (Shah and Al-Bargi 2013).

Literature makes reference to an increasing number of different worldviews (Creswell 2013, Denzin and Lincoln 2013). Four commonly cited worldviews in health and social sciences research are post-positivism, interpretivism, transformative and pragmatism. These are selected in accordance with the research aim, questions and approach. Typically, quantitative and qualitative research are underpinned by post-positivism and interpretivism respectively (Petty, Thomson and Stew 2012a, Creswell and Creswell 2018). Each worldview, as outlined in Table 2.3, is better described in terms of the four philosophical assumptions, namely ontology, epistemology, axiology and methodology (Carson et al. 2001, Creswell 2013, Creswell and Creswell 2018).

Ontology and epistemology are constructed conceptually together to fully explain the meaning of reality. The ontological notion of realism postulates that reality exists outside the mind. In accordance to Crotty (1998), there are three distinct epistemological positions:

- Objectivism – assumes that the "social entities exist in a reality which is independent or external to consciousness and experience"

- Subjectivism – believes that the reality is dependent on social actors and assumes the "understanding of meanings that individuals attach to social phenomena"
- Constructionism – assumes that "different individuals construct meaning in different ways, even in relation to the same phenomena"

Axiology was first mentioned by Paul Lapie in 1902 and Eduard von Hartmann in 1908. It was considered as a basic philosophical assumption as it affects the way to investigate reality. Whilst axiology is concerned with the role of values (and ethics) within the research process and the researcher's stance, methodology provides an explanation on the process of research (Wahyuni 2012).

Table 2.3: Common worldviews with their associated philosophical assumptions
(Carson et al. 2001, Creswell 2013, Creswell and Creswell 2018)

Philosophical assumptions *Definition*	**Post-positivism**	**Interpretivism**	**Transformative**	**Pragmatism**
Ontology *What is the nature of reality?*	Single reality that exists '*out there*'	Relativist, multiple realities constructed through lived experience	Subjective-objective reality obtained through negotiations with participants	Single and multiple realities, based on what is useful and practical
Epistemology *What counts as knowledge and how knowledge claims are justified?*	Objective; Approximation of reality through empirical observation and measurement	Construction of reality by understanding multiple participant meanings	Multiple ways of knowing the reality; collaboration	Reality is understood through use of different tools
Axiology *What is the role of values?*	Researcher bias must be minimised, unless eliminated and not included in the study	Individualised values honoured and negotiated amongst participants	Indigenous values respected and studied; Biased; researcher is open about their bias	Uses multiple stances; Values identified and discussed to obtain multiple views
Methodology *What is the process of research?*	Quantitative, deductive approach to generate new knowledge, theory verification	Qualitative, inductive approach to emerge ideas and generate theory	Emphasis on collaboration, political involvement, questioning of methods, highlighting concerns and issues	Mixed qualitative and quantitative approaches in data collection and analysis, problem-centred

2.2.2. Research designs

Research designs refer to "the theoretical, political and philosophical backgrounds to social research and their implications for research practice and for the use of particular research methods" (Robson 2011 p. 528). It is also known as methodology (Petty, Thomson and Stew 2012[b]) and strategies of inquiry (Denzin and Lincoln 2011). There are three different designs for undertaking research, namely quantitative, qualitative and mixed methods research. Figure 2.4 shows the integration of both quantitative and qualitative research designs to conduct mixed methods research.

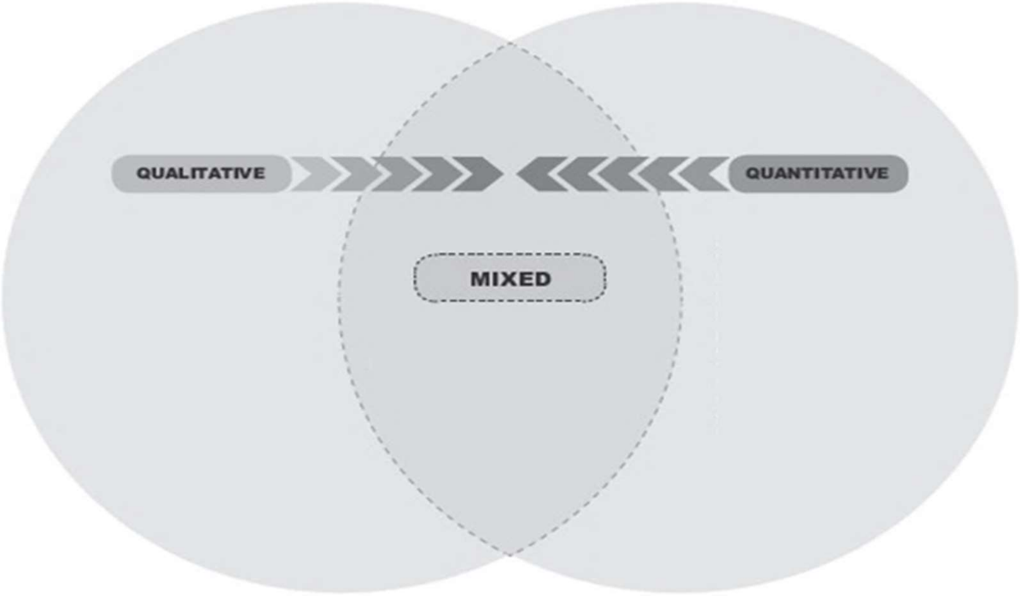


Figure 2.4: The Mixed methods research design
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Each research design has its own strengths and weaknesses. Hence it is crucial to consider the various types of designs and their associated methods to address the posit research question (Creswell 2013). Choosing one approach over the other should not depend only on the type of data collected (numerical vs language data), the sample size or the data collection method employed (Green and Thorogood 2009). It should moreover be based on the research aims and questions to be answered. The differences between qualitative and quantitative designs are detailed in Table 2.4.

Table 2.4: Summary between quantitative and qualitative designs
(Yilmaz 20134, Leavy 2017)

Characteristics	Quantitative	Qualitative
Philosophical worldview	Positivism	Interpretivism
Perception of variables in question	Reductionist, identifying and defining concepts	Holistic, studied in its social context
Type of inquiry	Objective	Subjective
Purpose	• Generalisable • Predictive • Causal explanations • Focuses on depth	• Contextualisation • Interpretation • Understanding perspectives • Focuses on breadth
Motivations for selection	• Test a theory or explanation • Identify factors that influence an outcome • Understand the best predictors of an outcome	• Understand a concept or phenomenon due to insufficient or recent research • Identify unknown variables
Research design	• Experimental designs, non-experimental design such as surveys	• Narratives, phenomenology, ethnography, grounded theory, case-study
Approach	• Begins with hypothesis • Deductive • Seeks consensus or the norm • Reduces data to numerical indices • Abstract language in write-up	• Generates a hypothesis • Inductive • Seeks pluralism or complexity • Makes minor use of numerical indices • Descriptive write-up
Sampling	Random	Purposive
Outcomes	• Variables can be identified and measured • Explaines causal relationships between variables • Statistical significance, measures of association	• Variables are complex and difficult to measure • Provides insights into the nature and social contexts of variables • Recurrent themes, hypothesis, conceptual models, survey measures
Researcher's role	• Detachment and impartiality • Objective portrayal • Etic (outsider's point of view)	• Personal involvement and partiality • Empathic understanding • Emic (insider's point of view)

2.2.2.1. Quantitative research design

Quantitative research is characterised by a deductive approach, where it seeks to establish correlation between variables or determine a causal relationship or predict the results of particular variables through the use of a priori theory (Bowling 2014, Leavy 2017). This correlation or relationship is put forward as a hypothesis and tested through experimental (such as randomised controlled trials) or non-experimental designs (such as surveys) (Creswell 2014). Summary of the characteristics of two common quantitative research designs are outlined in Table 2.5.

Table 2.5: Types of quantitative research designs
(Creswell and Creswell 2018)

Characteristics	Experimental designs	Non-experimental designs
Purpose	Determine whether a specific treatment influences an outcome	Provide numeric description of trends, attitudes or opinions of a population by studying a sample of that population, with the intent of generalising from sample to population
Data collection	Provide specific treatment to one group and withhold it from another group followed by determination of how both groups score an outcome	Use of questionnaires or structured interviews
Study type	True experiments with random assignment of subjects to treatment conditions or quasi-experiments that use nonrandomised assignments	Cross-sectional or longitudinal studies

2.2.2.2. Qualitative research design

Qualitative research design provides "a detailed description of how practices actually work" (Giangreco and Taylor 2003 p.135). It is characterised by an inductive approach to knowledge seeking to develop a theory through interpretation of different meaning (Ritchie and Lewis 2003, Creswell 2013). Qualitative research takes into consideration the individual subjective experience and meaning-making processes to achieve depth of understanding (Leavy 2017). Data is generated from a variety of sources primarily from interviews, observations and documents such as participant diaries and photographs. There are various designs employed within qualitative research. The characteristics of the most common qualitative strategies of inquiry in health and social sciences are discussed in Table 2.6.

Table 2.6: Types of qualitative research designs
(Petty, Thomson and Stew 2012^{b}, Creswell and Creswell 2018)

Characteristics	Narrative research	Phenomenology	Grounded theory	Ethnography	Case study
Purpose	Explores the experiences of an individual	Understanding the essence of the experience of individuals by exploring the meaning of a phenomenon	Developing a theory grounded in data obtained from the individuals experiencing the phenomenon	Describing and interpreting the culture of group	Developing an in-depth understanding of a single entity
Type of study	To narrate detailed stories or life experiences of an event or a series of events for a small group of individuals	To describe the lived experience of a phenomenon by individuals	To develop a theory which explains the social process, action or interaction based on the views of the participants	To understand and interpret the shared pattern of behaviours, language and beliefs of culture within a group over a period of time	To provide an in-depth understanding of single or multiple cases
Discipline origin	Humanities	Philosophy and psychology	Sociology	Social and cultural anthropology	Multiple fields: health and social sciences
Data analysis strategies	Data is obtained as a story which is restructured in chronological order and selecting key aspects. Interpretation and thematic analysis may follow	The descriptive data obtained undergoes interpretation and analysis to reveal the 'essence' of the phenomenon	Data obtained is coded through the assignment of labels. Similarities and differences between codes are identified to generate relationships and create an explanatory model which form the basis of a theory	Data analysed and interpreted to generate a description of the culture-sharing group	Data analysed to provide a description of the case guided by the research question with no specific method of data analysis
Researcher's role	The meaning of the stories is negotiated between the researcher and the participants to develop a collaborative narrative	The researcher's own views are put on the side (bracketing) to enhance understanding of the phenomenon and determine the essence	The researcher transforms codes into broader concepts and develops to identify the relationship and capture the complexity of the social process	The researcher analyses the meaning of behaviour, language and interaction amongst the group	The researcher extracts and analyse detailed information from various data sources over a prolonged period of time

2.2.2.3. Mixed methods research design

The mixed methods research design integrates both quantitative and qualitative approaches in a single research process. This methodological approach with a pragmatic philosophy offers a comprehensive understanding of the phenomenon being studied by considering multiple perspectives, positions and standpoints (Johnson, Onwuegbuzie and Turner 2007, Leavy 2017). A mixed methods design is considered in the following scenarios (Creswell and Plano Clark 2011), when:

- single data source is insufficient
- results necessitate an explanation
- findings are generalised
- a particular theoretical stance is required and/or phases require enhancement with a second approach to address the research question

This research design makes use of open and closed ended questions and is commonly employed in applied social and behavioural science, especially when seeking to induce a social action or behavioural change (Leavy 2017, Creswell and Creswell 2018). Creswell and Creswell (2018) described in detail three common mixed methods designs in Table 2.7.

Table 2.7: Types of mixed methods research design (Creswell and Creswell 2018)

Characteristics	**Convergent mixed methods**	**Explanatory sequential mixed methods**	**Exploratory sequential mixed methods**
Approach	Provide a comprehensive analysis of the problem	Use in a field with strong quantitative orientation	Build instruments for particular sample, develop interventions for experiments
Data collection	Concurrently collect quantitative and qualitative data	First conduct quantitative research, analyse the results and then build on the results to explain in more detail with qualitative research	First conduct qualitative research and explore the views of participants. Analyse the results and then use this information to build quantitative research
Data Analysis	Quantitative and qualitative data integrated in interpretation of the results	Initial quantitative data results explained further with the qualitative data	Initial qualitative data results explained further with the quantitative data
Challenges	Contradictory findings necessitate further exploration	Unequal sample size for both studies and identify quantitative results for further exploration	Sample selection for both studies and identify the appropriate qualitative results for further research

2.2.3. Research methods

Corbin and Strauss (2008 p.1) defined method as “techniques and procedures for collecting, gathering and analysing data.” The choice of the method depends on the type of information to be gathered which needs to be congruent with aim of the study. In accordance to the research methodology selected, the research employs different methods for data collection, analysis and interpretation (Creswell and Creswell 2018), as outlined in Table 2.8.

Table 2.8: Characteristics of the different methods
(Creswell and Creswell 2018)

Characteristics	Quantitative approach	Qualitative approach	Mixed methods approach
Data type	Pre-determined method	Emerging method	Both pre-determined and emerging methods
Data form	Numeric data gathered from scales of instruments	Text information recording and reporting the voice of the participants	Both numeric and textual data
Data collection tools	Randomised, single-subject questionnaires	Structured, semi-structured interviews focus group, participant observation	Multiple data collection tools incorporating instrument data with observations or in-depth interviews
Questions used	Closed, instrument based questions	Open-ended questions	Both open and closed-ended questions
Data sets	Performance data, attitude data, observational data and census data	Interview data, observation data, document data and audio-visual data	Multiple forms of data drawing on all possibilities
Data analysis	Statistical analysis	Text and/or audio-visual image analysis	Statistical and text analysis
Data interpretation	Statistical interpretation of data	Themes or pattern interpretation from data	Makes interpretation across both the qualitative and quantitative data

2.3. Research approach of this doctoral research (Phase II and III)

2.3.1. Philosophical worldview

Following the systematic review of the literature (Phase I), this doctoral research focused on two parallel longitudinal qualitative studies with patients (Phase II) and their significant others (Phase III). A predominantly qualitative design was adopted in line with the aims of the studies (Phase II and Phase III) to explore, not quantify, the subjective experiences of patients with antineoplastic medicines and identify changes over time. In Phase III, the perspective of significant others on patients' experience allowed the collection of additional information about the external environment that patients themselves might not even be aware of. An overview of the research approaches adopted for Phases II and III are outlined in Table 2.9.

Table 2.9: Research approach of Phases II and III of the doctoral research

	Phase II	**Phase III**
Aim	To explore longitudinally the patients' lived experiences with antineoplastic medicines for colorectal cancer during the treatment journey and beyond	To explore longitudinally the significant others' perspective on the patients' experiences with antineoplastic medicines for the duration of the treatment journey for colorectal cancer
Philosophical worldview	Interpretivism	
Methodology	Longitudinal qualitative approach using interpretative phenomenological analysis	Longitudinal qualitative approach using phenomenology
Method	Face-to-face semi-structured interviews and patient diary	Face-to-face semi-structured interviews

Qualitative research designs have different epistemological and ontological underpinnings depending on the distinct lens used to explore, explain or interpret the phenomenon in real-world contexts (Rodriguez and Smith 2018). Each philosophical assumption in relation to interpretivism relevant to this doctoral research is presented in Table 2.10.

Table 2.10: Philosophical assumptions in relation to interpretivism as relevant to the doctoral research (Crotty 1998, Creswell 2013)

Philosophical assumptions	**Interpretivism**	**Phase II**	**Phase III**
Ontology	Multiple realities are constructed through our lived experiences and interactions with others	Relativist – assuming that there are many versions of truth in the world, with individuals naturally seeking to interpret their experiences	
		Patients newly diagnosed with colorectal cancer and naïve to antineoplastic medicines	Significant others with different relationships to the patient
Epistemology	Reality is co-constructed between the researcher and the researched and shaped by individual experiences	Subjectivism - acknowledging that an external reality exists but its nature is imposed on the object by the individual's experience. Hence ascribing a meaning to the object that may be imported from somewhere else. Subjective processes of self-reflection are accessible through questioning and conversation	
Axiology	Individual values are honoured and negotiated among individuals	Acceptance of influence from both science and personal experiences of participants, as well as the values, social position, cultural context and experiences of the researcher. The researcher forms an integral part of the research process	

As several qualitative methodologies exist, it was essential to consider the approach that was most closely associated with the philosophical underpinning of the study. This ensured that a high quality outcome was obtained based on methodological accuracy. Given that the purpose of this research was not to build a theory, grounded theory was not considered as an appropriate choice of methodology. Phenomenology appeared to be methodologically aligned to this research aim and objectives of exploring the perceptions and experiences of persons with colorectal cancer initiating treatment with antineoplastic medicines (phenomenon) and as they lived through the treatment journey.

2.3.2. Phenomenology

Phenomenology is anchored in the experience rather than theory and hence it is concerned with the way people exist in the world and the significance of everyday phenomena. This allows the researcher to develop meaning and understanding from these experiences (Starks and Trinidad 2007, Gill 2014).

Phenomenology is fundamentally divided into two main schools, namely descriptive phenomenology and interpretive phenomenology. Whilst descriptive phenomenology attempts to understand the essence of a phenomenon free from context and preconceived ideas, interpretive phenomenology is a process of inquiry that goes beyond description of a phenomenon by seeking to reveal meaning that is generally hidden in the human experience. The latter also accepts that the realities of individuals and their life choices are influenced by the world in which they live (Lopez and Willis 2004). There are different types of phenomenological methodologies as described in Table 2.11. This is because they all have a common departure point without essentially progressing towards the same destination or with an identical velocity. Gill (2014) described that phenomenological methodologies are a family of approaches, which are related through five interrelated commonalities:

- Mutual underpinning in phenomenological philosophy
- Definite interest in the meaning of individuals' experiences
- Attempts to understand the point of view of the *"experiencer"*
- Homogenous sampling
- Thematic analysis

The use of interpretive phenomenology approach was adopted in this research as it is useful to achieve a deeper understanding of patients' personal experiences. It also offers the researcher to possibility of interpreting what other hidden meanings may have influenced the patients' experience and response to it (Mackey 2005).

Table 2.11: Comparison between descriptive and interpretive phenomenology
(Gill 2014, Rodriguez and Smith 2018)

Descriptive phenomenology	Interpretive phenomenology
• Dominant scholar: Edmund Husserl (1859-1938) • Known also as Transcendental phenomenology • Epistemological in orientation, questioning knowledge: *How do we know what we know?* • Historical context is irrelevant • The meaning of rich data is subject of analysis • Essences of consciousness or conscious experience can be shared • Meaning is not influenced by researcher belief systems and experiences • Data stands alone but meanings can be reconstructed • Bracketing supports the validity of interpretation enabling a level of objectivity	• Dominant scholar: Martin Heidegger (1889-1976) • Known also as Hermeneutic phenomenology • Ontological in orientation, questioning experiences and understanding: *what does it mean to be the person in this context, with these needs?* • Historical context is implicit to understanding the concept being explored • The interaction between the situation and the individual that we seek to identify and interpret is implicit • One's culture, practices and language can be shared • Meaning is influenced by researcher belief systems • Interpretation explains what is already known • Developing an understanding of the experiences is known as the hermeneutic circle

	Sanders's phenomenology	**Giorgi's descriptive phenomenology**	**Van Manen's hermeneutic phenomenology**	**Benner's interpretive phenomenology**	**Smith's interpretative phenomenological analysis**
Purpose	To make explicit structure (or essences) and meaning of human experiences	To establish the essence of a particular phenomenon	To transform lived experience into a textual expression of its essence	To articulate practical, everyday understandings and knowledge	To explore in detail how participants are making sense of their personal and social world
Participants	3-6	≥3	unspecified	Until new informants reveal new findings	≥1
Key concepts	• Bracketing • Eidetic reduction • Nomematic/ noetic correlates	• Bracketing • Eidetic reduction • Imaginative variation • Meanings units	• In depth writing • Orientation • Thoughtfulness	• The background • Exemplars • Interpretive teams • Paradigm cases	• Double hermeneutic • Idiographic • Inductive

Phenomenology is rooted in the philosophical worldview of interpretivism, which is based on the premise that reality is created for individual persons through their experiences and consequently multiple realities will exist. Within the interpretivist stance, the patients are viewed as the experts of their own experiences and the researcher is interested in understanding these individuals' lived experiences. The core knowledge is derived from how individuals interpret and make sense of their experiences and the world around them (Holloway and Wheeler 2002, Rubin and Rubin 2012, Gray 2017).

In Phase II, this theoretical worldview allowed the research student to better understand the meaning that patients attach to their treatment journey with antineoplastic medicines through their engagement with the world. Phase III complemented Phase II by gaining an in-depth insight into the patients' beliefs, practice and burden from the perspective of their nominated significant other. Multiple realities have been constructed through their shared lived experience.

2.3.3. Longitudinal qualitative research design

Longitudinal qualitative research design is widely recognised for its unique contribution to expanding the qualitative perspective and explore concepts of time and change. These two inseparable constructs are central in the context of human experience (Saldana 2003, Corden and Millar 2007, Calman, Brunton and Molassiotis 2013). In comparison, cross-sectional studies are more commonly utilised to describe a particular phenomenon at the time when the research is carried out (Derrington 2019). Strengths and weaknesses of cross-sectional and longitudinal research designs are outlined in Table 2.12.

Table 2.12: Comparison of research designs
(Calman, Brunton and Molassiotis 2013, Derrington 2019)

Type of research design	Strengths	Weaknesses
Cross-sectional	• Describe a phenomenon at one point in time of the research – ‘snapshot’ • Data collected all at the same time • Reasonably cheap, quick and practical as no follow up is necessary • More easy recruitment of participants due to less commitment • Less ethical considerations	• Less rich detailed data is collected with regards to individual participant differences • Data collected from a snapshot in time, hence more difficult to identify and analyse any development trends
Longitudinal	• Same group of participants followed throughout the entire study on the same variable over two or more distinct time periods. Participant variables do not affect data collected • Provides deeper understanding of a phenomenon • Allows evaluation of changes within individual or trends over time • Allows comparison of findings and may yield more than one study from one data set • Allows significant rapport with participants	• Practical difficulties expensive, time-consuming • Participant attrition • Withdrawal of participants also means that if remaining participants share particular characteristic, findings may be biased

Whitehead (2004) claimed that longitudinal studies with multiple interviews elicit more detailed personal accounts over the duration of the study, resulting in multi-faceted descriptions of the phenomenon (Maguire et al. 2014). This doctoral research utilises temporal points during the treatment journey to capture the subjective understanding of lived phenomena with antineoplastic medicines, which may change, evolve or remain stable across time. It allowed the exploration of how the patients and significant others interpret and respond to such changes. However, the literature did not provide any guidance about the best time points to conduct the interviews throughout the treatment journey.

2.3.4. Data generation in qualitative research design

Data generation refers to the method used to collate data from a source in a qualitative study (Given 2008). There are different types of data generation tools available for qualitative research as outlined in Table 2.13. In-depth one-to-one interviews with patients and significant others were crucial to collate rich data about the patients' lived experience with antineoplastic medicine in this doctoral research as it allows the generation of data from each participant independently. Face-to-face interviews were chosen over telephone or online interviews because this approach permits rapport building, enhances disclosure of the participants' own personal experience and allows the observation of the participants' non-verbal cues (DeJonckheere and Vaughn 2019).

The majority of interviews were conducted in the hospital whilst the patients were receiving their antineoplastic treatment as this transpired to be logistically convenient for both the research student and the participants.

Table 2.13: Types of data generation tools in qualitative research (Creswell 2013)

Data generation tool	Types within data generation tools	Strengths	Weaknesses
Observations	• Data gathered with researcher as a participant • Data gathered with researcher as an observer • Data gathered with researcher being more of a participant than as an observer or vice-versa • Data gathered with researcher being first as an observer and then involved as a participant	• Researcher has a direct real-life experience with participants • Data on participants' behaviour and activities is collected from the research site • Atypical observations may be noted • Suitable to explore subjects which makes the participants uncomfortable to discuss	• Researcher may be considered as intrusive • Personal information which was observed cannot be documented • Researcher may lack good observing skills, that may affect the outcome of the study • Categories of participants, such as children may pose difficulty in establishing rapport
Interviews	• Face-to-face interview • Telephone interview • Focus group interview • Electronic interview	• Suitable in circumstances when participants cannot be directly observed • Historical data may be provided by participants • Researcher takes control of the line of questioning	• Data collection occurs in a designated setting, which is often not their natural environment • Indirect data which is filtered through the perspective of interviewees is collected • Presence of researcher may bias responses • Participants may not all be equally capable to express themselves
Documents	• Public documents, such as minutes of meetings or newspapers • Personal documents such as diaries, medical records, biographies	• Language and words of participants may be obtained • Data has been articulated thoughtfully by the participants • A discreet method of data collection, whereby data source may be accessed at the researcher's convenient time • Since written evidence is collected, this spares the time and expense of transcription	• Confidential information may be protected by restricted access • Data provided may be incomplete and documents may not be authentic or precise • Researcher may have to search for information in hard-to-find locations • Participants may not all be equally capable to document data in the same detail
Audio-visual materials	• Photographs • Videotapes • Art objects • Messages on social media • Sounds • Film • Website pages	• A discreet method of data collection may be used • Participants allowed to directly share their real experience • A creative method of data generation that attract visual attention	• Data may not be highly accessible • Presence of an observer, such as photographer may be distracting and affect the responses • Interpretation may be difficult

2.3.4.1. Types of interviews

Face-to-face individual interviews can either have a structured, semi-structured or unstructured format. The differences are outlined in Table 2.14. Semi-structured face-to-face interviews were chosen for phases II and III of this research, as this approach permits in-depth description and understanding of the participants' perspectives resulting in the generation of very rich data. Although an interview guide was used, it still provided participants with the freedom to express their views in their own words. The research student was allowed to probe responses to gain further detail and clarify any information that was unclear.

Table 2.14: Types of interviews
(Petty, Thomson and Stew 2012**b**)

Interview type	Characteristics
Structured	• Consists of a specific set of questions in a predetermined order and with stipulated response categories • Used when knowledge about the topic is available • Generates a fairly superficial level of response • Commonly used in telephone interviews or interviews in public places with large number of participants
Semi-structured	• Consists of few pre-determined areas of interest with possible prompts to guide the conversation • Use of an interview guide as a set of instructions for researcher but allows discussions to diverge from it • Interviewee's responses determine the way in which the interview is directed • Allows for provision of reliable and comparable qualitative data • Commonly used type of interview in qualitative research
Unstructured	• Involves stories that are based on the unfolding of events or actions from the perspective of a participant's life experience • Interviewees guide the interview and allow information to be revealed that may not have been predicted. The researcher follows the direction of the participant • Often lengthy in duration • Poses more difficulty to analyse as it yields wide and deep themes • Used when knowledge about the topic is limited • Commonly used in exploration of broad areas, such as illness experience

2.3.4.2. Approaches to sampling techniques

Two main sampling techniques exist namely probability and non-probability sampling. Probability sampling technique is based on randomisation whereby each individual of the population has an equal opportunity to be selected. Hence reducing the possibility of recruitment bias (Sharma 2017). Non-probability sampling techniques are typically applied to qualitative research, with purposive sampling being most commonly used to seek out '*information-rich cases*' (Johnson and Waterfield 2004, Patton 2015 p.264). Hence, this section focuses mainly on the different non-probability sampling techniques (Table 2.15).

Purposive sampling forms part of the non-probability sampling techniques. This was used to select participants for Phase II of the research study and allowed participants with specific characteristics to be recruited. Each participant was then asked to nominate at least one person they considered to be a significant other in their care. These nominated significant others were the participants for Phase III of the study. Given the nomination aspect in the recruitment of the participants, the recruitment of the significant others in Phase III can be classified as snowball sampling.

Table 2.15: Types of non-probability sampling techniques
(Creswell 2013, Bowling 2014, Jensen and Laurie 2016, Moule, Aveyard and Goodman 2016)

Sampling technique	Definition	Advantages	Limitations
Convenience sampling	Participants selected based on accessibility	• Low-cost option • Easy to recruit • Ideal for formulating ideas	• Risk of non-representative sample • Results may not be generalisable • Least reliable results • Findings restricted to population under study and subjectivity of researcher
Purposive sampling	Participants selected based on researcher's judgment on who will provide valuable insights based on the study aims	• Easy to recruit • Low cost option • Ideal for formulating theoretical explanations • Accurate data gathered as participants only fulfilling the established criteria are recruited	• Risk of non-representative sample and research bias as the researcher's judgement may inadvertently skew the selection of participants
Quota sampling	Participants selected based on participants characteristics in the same proportion as found within the population	• Quick and easy • Decreases the risk of over or under representations of participants as established quotas ascertain adequate representation of different categories	• Risk of non-representative sample • Systematically biased sample as researcher needs to select participants in each category to fit the inclusion criteria
Snowball sampling	Initial sample of participants (recruited using purposive or convenience approach) nominate other potential participants	• Useful means to identify participants who are hard-to-reach or stigmatised • Ensures trust and credibility	• Risk of non-representative sample • Results may not be generalisable • Findings restricted to population under study and subjectivity of researcher
Theoretical sampling	Participants selected on similar characteristics of interest, hypothesis formulated and tested on exceptional cases	• Identifies new areas by choosing those which result in the greatest theoretical returns	• Findings restricted to population under study and subjectivity of researcher

2.3.4.3. Sample size determination

Marshall (1996 p.523) explained that "an appropriate sample size for a qualitative study is one that adequately answers the research question." The sample size in qualitative research tends to be small to permit in-depth analysis, which is fundamental in this approach (Vasileious et al. 2018). Starks and Brown Trinidad (2007) indicated that sample sizes for phenomenological studies are commonly in the range of 1 to 10 participants. With regards to longitudinal qualitative study, each participant will be interviewed more than once and so this tends to generate a large amount of data for each participant. Morse (2000) emphasised that the richness of the data generated should supersede the quantity of participants recruited in the study. Saldana (2003) advised that the sample size should consist of more participants than initially required due the risk of dropouts. This is particularly important for longitudinal studies where the long-term commitment by the participants is required.

The sample size in qualitative research is often determined by the concept of data saturation (Saunders et al. 2018, Guest, Namey and Chen 2020). This concept was originally introduced as theoretical saturation in grounded theory by Glaser and Strauss (1967 p.61) and defined as the point at which "no additional data is being found whereby the researcher can develop properties of the category." Along the years, the broader term data saturation has become widely used in qualitative research as a methodological element to stop sampling, recruiting and generating data (Saunders et al. 2018). Guest, Namey and Chen (2020) described data saturation as "the point in data collection and analysis when new incoming data produces little or no new information to address the research question." Four different models of saturation were identified in the literature (Table 2.16).

Table 2.16: Models of saturation in qualitative research
(Saunders et al. 2018)

Saturation model	Description	Main focus
Theoretical saturation	Relates to the development of theoretical categories in data analysis as criterion for further data collection	Sampling
A priori thematic saturation	Relates to the degree to which collected data was exemplified in pre-determined codes or themes	Sampling
Data saturation	Relates to the degree to which new data repeat what was expressed in previous data Provides identification of redundancy in data	Data collection
Inductive thematic saturation	Relates to the identification of new codes or themes	Data analysis

In this doctoral research, data saturation was attained in the Phase II study but not achieved for the Phase III study. Attempts were made to achieve data saturation for the Phase III study by increasing sample size as recommended by Francis et al. (2010). Since Phase II and Phase III studies were complimentary, this involved a one-time recruitment of three additional patients followed by a further recruitment of one patient to Phase II to increase the number of participants in Phase III. This resulted in the recruitment of four additional individuals to Phases II and III. However due to the heterogeneity of significant others, data saturation was still not achieved for the Phase III study.

2.3.4.4. Transcription of interviews

Data transcription was defined by Howitt (2019 p. 135) as "the process by which a sound or a video recording of the spoken word is turned into written language for subsequent analysis." It is considered as "a powerful act of representation" (Oliver, Serovich and Mason 2005 p.1273), since it affects the conceptualisation of data. The transcription process is a central task in qualitative research design, which should not be considered as a 'behind-the-scenes aspect of data management" (Agar 1996 p.153, Oliver, Serovich and Mason 2005 p.1273). Transcription is labour-intensive which necessitates investment of time and money, particularly in case of hiring a transcriber or using transcription software programs. The common practice is to transcribe each interview verbatim to preserve a complete record of the interview (Leavy 2017). Despite the time-consuming nature of transcription, this method allowed the research student to reflect on the research activity and immerse herself in the data whilst "honouring both the research process and the participant's voice" (Oliver, Serovich and Mason 2005 p.1286). This can powerfully affect the way in which participants are understood, the knowledge they share, and the resultant conclusion (Oliver, Serovich and Mason 2005). Two commonly used types of transcription are described in Table 2.17.

Table 2.17: Transcription types
(Oliver, Serovich and Mason 2005, Azevedo et al. 2017)

Transcription type	Description
Naturalism	• Preservation of different elements of the interview besides the verbal content such as non-verbal language, contextual aspects and interaction between interviewer and interviewee • Every utterance is captured in detail as much as possible • Language represents the 'real world' with thorough transcription of what is said and how it is said • Analysis presented with speech as it is spoken by the participant rather than overly-filtered through the transcriber • Typically used in conversation analysis studies • Rooted in naïve realism that accepts empirical realities unproblematically
Denaturalism	• Verbal speech is prioritised • Grammatical errors are corrected • Non-standard accents are standardised • Idiosyncratic elements of speech such as pauses or stutters (and non-verbal language) are omitted • Presented as more polished and selective transcription • Interested more in the informational content of speech, with focus on meanings and perceptions made during interview • Often used in critical discourse analysis

In view that the purpose of the study was to generate meanings and perceptions regarding the use of antineoplastic medicines, a denaturalised transcription style was employed. Although this approach was used, attempts were still made to have a "full and faithful transcription" (Cameron 1996 p.33 in Oliver, Serovich and Mason 2005) by following verbatim transcription of speech, with less importance to the transcription of accents or involuntary vocalisation. The use of key quotes from the participants reveals to the readers the participants' complex meaning around the use of antineoplastic medicines.

2.3.5. Data analysis and interpretation

Data generated using qualitative methods is analysed through an iterative process where the researcher continually moves between data collection and analysis (Petty, Thomson and Stew 2012[b]). Corbin and Strauss (2008 p.45) described analysis as a dynamic process of "examining a substance and its components in order to determine their properties and functions, then using the acquired knowledge to make inferences about the whole." According to Leavy (2017), data analysis in qualitative research involves the following stages:

(1) data preparation and organisation
(2) initial immersion
(3) coding
(4) categorising and theming
(5) interpretation

The phases of data analysis and interpretation in qualitative research occurs in a recursive process, whereby analysis leads to interpretation and vice versa (Leavy 2017). Trent and Cho (2014, p.652 in Leavy 2017) distinguished between analysis and interpretation using the following definitions:

- Analysis as "summarising and organising data"
- Interpretation as "finding or making meaning"

Approaches to analysis of interviews include those which focus either on language (example discourse analysis, conversation analysis) or on meaning (example grounded theory) (Ritchie and Lewis 2003). According to Lyons and Coyle (2015), there are five main approaches to analyse qualitative data (Table 2.18).

Table 2.18: Approaches of qualitative data analysis (Lyons and Coyle 2015)

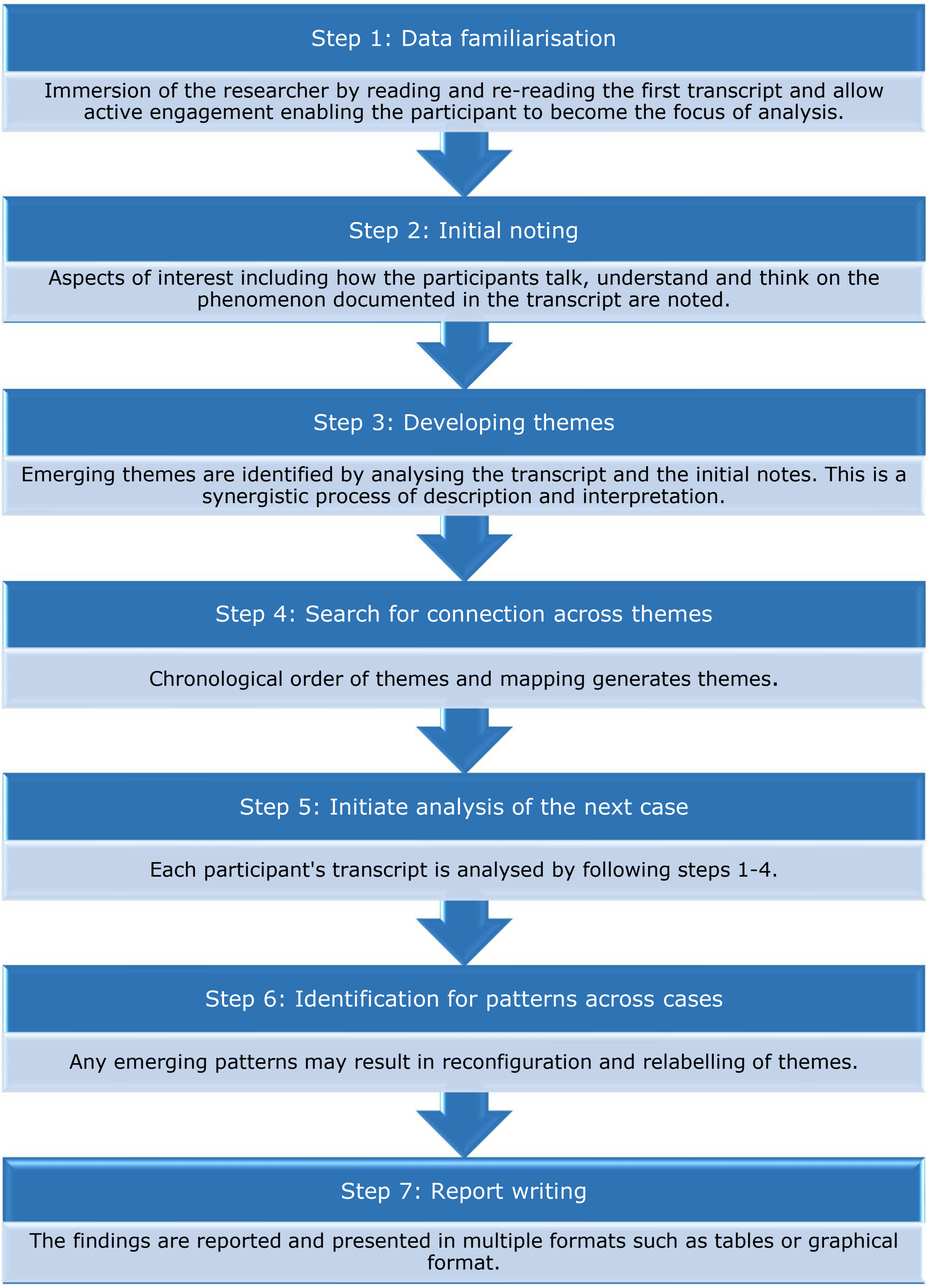
Type of analysis	Description
Thematic analysis	Identifying and interpreting patterns of meaning or themes
Discourse analysis	Analysing the language in texts and context
Narrative analysis	In-depth assessment of the participants' experiences and meanings instead of analysing for commonalities amongst different participants
Interpretative phenomenological analysis	Exploring the participants' lived experiences and assess how the participants are making sense of their personal and social world
Grounded theory	Generating a theory on a given topic inductively

Based on the philosophical worldview chosen and the aim of the Phase II study, interpretative phenomenological analysis (IPA) was selected as a suitable approach for data analysis. It was carried out according to the steps outlined by Smith, Flowers and Larkin (2009), summarised in Figure 2.5. IPA, also known as Smith's interpretative phenomenological analysis is an approach to qualitative, experiential research pioneered in the field of psychology by Jonathan Smith in 1996. It has gained momentum and popularity in other disciplines including human, social and health sciences over the past 25 years (Smith, Flowers and Larkin 2009, Pringle et al. 2011). Being considered as a "variant of phenomenology", IPA is based on three theoretical underpinnings:

- Phenomenology: concerned with uncovering the meaning through exploration of experience in the participants' own terms

- Hermeneutics: focuses on interpretation of the meaning whereby efforts are made to understand how these persons make sense of their experiences. The IPA analytical process is regularly referred to as double hermeneutic; by first allowing the participant to make meaning of their world and then the researcher attempts to understand and interpret that meaning (Smith and Osborn 2008, Smith, Flowers and Larkin 2009)

- Idiography: puts emphasis on the individuals' perceptions and experiences (Pringle et al. 2011). This is achieved by an initial analysis of each participant's experience and then search for similarities and differences across the participants (Smith, Flowers and Larkin 2009).



Step 1: Data familiarisation

Immersion of the researcher by reading and re-reading the first transcript and allow active engagement enabling the participant to become the focus of analysis.

Step 2: Initial noting

Aspects of interest including how the participants talk, understand and think on the phenomenon documented in the transcript are noted.

Step 3: Developing themes

Emerging themes are identified by analysing the transcript and the initial notes. This is a synergistic process of description and interpretation.

Step 4: Search for connection across themes

Chronological order of themes and mapping generates themes.

Step 5: Initiate analysis of the next case

Each participant's transcript is analysed by following steps 1-4.

Step 6: Identification for patterns across cases

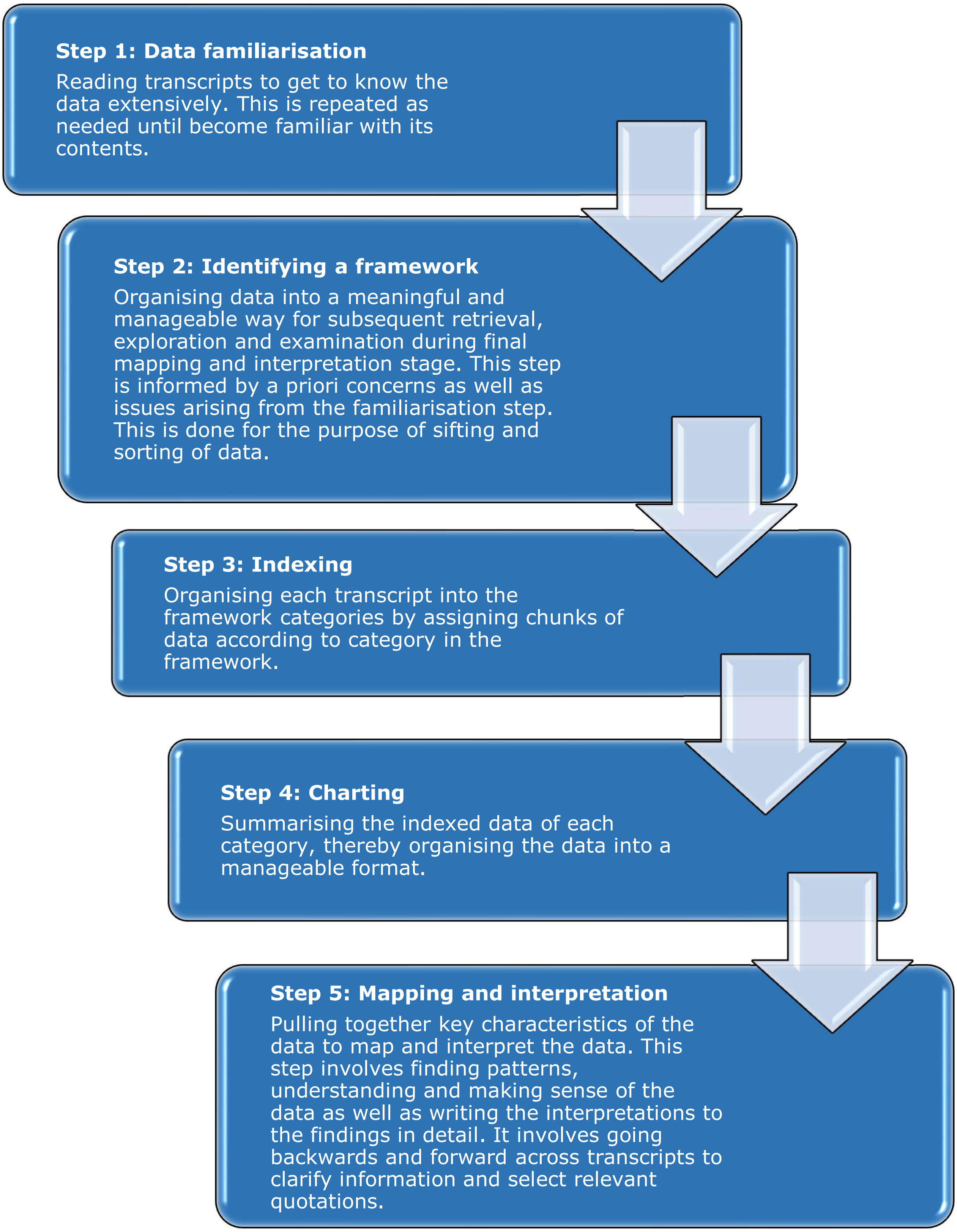
Any emerging patterns may result in reconfiguration and relabelling of themes.

Step 7: Report writing

The findings are reported and presented in multiple formats such as tables or graphical format.

Figure 2.5: Stages of interpretative phenomenological analysis (Smith, Flowers and Larkin 2009)

With regards to the Phase III study, framework analysis was adopted as outlined by Ritchie and Spencer (1994) in Figure 2.6 as this allowed the exploration of patterns in the data. Framework analysis forms part of the broad family of thematic analysis. It provides a flexible, structured form of data management and data analysis and is useful for a large sample size and when a team is working collectively on data analysis (Ritchie and Spencer 1994, Parkinson et al. 2016). The data analysis was performed by following a stepwise approach from transcribing to coding which was guided by the themes and sub-themes generated in Phase II. Therefore, it followed a deductive approach by using themes and sub-themes identified a priori.



Step 1: Data familiarisation

Reading transcripts to get to know the data extensively. This is repeated as needed until become familiar with its contents.

Step 2: Identifying a framework

Organising data into a meaningful and manageable way for subsequent retrieval, exploration and examination during final mapping and interpretation stage. This step is informed by a priori concerns as well as issues arising from the familiarisation step. This is done for the purpose of sifting and sorting of data.

Step 3: Indexing

Organising each transcript into the framework categories by assigning chunks of data according to category in the framework.

Step 4: Charting

Summarising the indexed data of each category, thereby organising the data into a manageable format.

Step 5: Mapping and interpretation

Pulling together key characteristics of the data to map and interpret the data. This step involves finding patterns, understanding and making sense of the data as well as writing the interpretations to the findings in detail. It involves going backwards and forward across transcripts to clarify information and select relevant quotations.

Figure 2.6: Steps of framework approach to data analysis
(Ritchie and Spencer 1994)

2.4. Choice of theoretical framework

Grant and Osanloo (2016 p.12) described theoretical framework as "the foundation from which all knowledge is constructed for a research study." Therefore the theoretical framework provides a lens through which the researcher approaches the topic and looks at the complex phenomenon of medicine experience (Kelly 2010, Garvey and Jones 2021). This improves the rigour of the research findings.

In 2016 Mohammed, Moles and Chen published the meta-synthesis exploring the medication-related burden and PLEM. The authors created a conceptual model describing PLEM, as detailed in Chapter 1. The PLEM conceptual model was selected as a theoretical framework to underpin this research as no other theoretical frameworks were found to be as specific for qualitative exploration of medication experience. It allowed the collection of structured data most relevant to the research question. The outcome of the systematic review (Phase I) was an adaptation of the original PLEM conceptual model of Mohammed, Moles and Chen (2016) specifically for the oncology setting. This adapted model was then used to underpin Phases II and III of this study.

2.5. Quality in research

Irrespective of the methodological approach used, it is important to ascertain the quality and accuracy of the data being collected. This is based on four criteria as shown in Table 2.19. Qualitative research is often criticised for the lack of scientific rigour. This is due to the challenge in exhibiting validity and reliability when compared to quantitative research (Cope 2013). Quality in qualitative research is also referred to as trustworthiness.

Table 2.19: Criteria for quality in research
(Shenton 2004, Petty, Thomson and Stew 2012[b])

Quantitative research Criteria of quality	Qualitative research Criteria of quality	Descriptions
Objectivity	Confirmability	The degree of confidence that the findings of the study represent the participants' responses as corroborated by other researchers
Reliability	Dependability	The extent to which the study could be replicated in similar participants and context as well as ensuring the findings of the inquiry are consistent
Internal validity	Credibility	The degree to which truth may be ascertained in the findings as obtained from the participants
External validity	Transferability	The extent to which the findings may be applied to other contexts or other participants

The concepts of credibility, dependability, transferability and confirmability postulated by Lincoln and Guba (1985) were applied to this research to ensure trustworthiness and minimise analysis bias. The implemented strategies for promoting quality in this doctoral research are described in Table 2.20.

Table 2.20: Strategies for promoting quality in qualitative research as adopted in this doctoral research
(Lincoln and Guba 1985, Cope 2013)

Rigour criteria	Original strategy	Strategy as applied to our study to achieve rigour
Credibility	Prolonged engagement with the setting	• As the data collection of the study was conducted longitudinally over a 9-month period, it allowed the researcher to know the participants more closely • The research student position and stance were clearly described
	Adequacy as a researcher – ensuring appropriate knowledge and skills to perform the role	• The research student received training in qualitative interviewing and performing data analysis using interpretative data analysis [a,b] She also familiarised herself with literature to gain further insight on how to conduct in-depth interviews • The research team was composed of pharmacists with different cultural backgrounds having experience in qualitative research and extensive knowledge in the field of clinical pharmacy. The research student and another member of the research team also had experience in working as hospital pharmacists in oncology setting, hence were acquainted with the key processes of cancer care
	Interviewing process and techniques	• The interview guide developed iteratively and was tested in a pilot study to ensure that it was clear, appropriate and comprehensive • Clear statements about the purpose of the research study were provided at the start of each interview to reduce expectancy bias
	Peer debriefing	• Regular meetings with the research team aided to uncover biases or assumptions and brought additional perspectives
Dependability	Detailed description of the study method	• The research process followed a detailed study protocol • An appropriate method of data collection was selected • A detailed sampling strategy of participants and method of data collection was described • Characteristics of all participants were clearly described • Transcription accuracy was conducted on 10% sample of transcripts. These were randomly selected and cross-checked by a person independent to the study to ensure reliability of transcription • Analysis was compared to the PLEM conceptual model in systematic review • Translation of quotations from the interviews from Maltese language to English language were carried out by the research student who is conversant in both languages. A second researcher fluent in both languages carried out reverse-translation to ensure the precise contextual meaning of the original quotation
	Achieving an audit trail	• Challenges and issues were documented in a research diary to retain cohesion in the research process (aim, design and method)

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[a] Introduction to interpretative phenomenological analysis and advanced interpretative phenomenological analysis – University of Malta (2018)
[b] Academy Seminar "Hospital pharmacy Practice Research – Scientific Quality" - European Association of Hospital Pharmacists (2017)

Confirmability	Reflexivity and reflection on own perspectives	• Regular meetings were held with the research team • Data analysis of all the transcripts was independently reviewed by another researcher from the research team to ensure accuracy. Any discrepancies between the researchers were resolved through discussion, until consensus was reached
	Representativeness of the findings in relation to the phenomena	• The use of semi-structured audio-recorded interviews allowed the research student to revisit the data and remain true to participants' accounts • Use of rich and thick verbatim extracts from patients' account assist the reader to make their judgements
Transferability	Detailed description of setting	• Detailed information on the context of research provided

2.6. Reflexivity

Reflexivity is the process of being aware. Due to the fact that the researcher has an integral role in data collection and analysis in qualitative research, it is essential to bring to light how the researcher influences the research process (Finlay 2002, Peat, Rodriguez and Smith 2019). IPA employs inter-subjective reflexivity, as this approach aims to unravel the dynamic that exist with the researcher-participant relationship (Goldstein 2017). This is of more importance in the double hermeneutic dynamic in IPA as the beliefs, thoughts and attitudes may interplay between the researcher and the participants. As suggested by Heidegger, the researcher's prior conceptions should interact with the experiential encounters during the study (Peat, Rodriguez and Smith 2019).

The dual role of the researcher as a healthcare professional and a research student may impact the participant's contribution in the interviews. This influence was minimised in this doctoral research as the participants and the research student did not encounter each other prior to the research activity. This is due to the fact that the research student works as a hospital pharmacist in the aseptic preparation of parenteral medicinal products, which provides limited direct contact with patients. However, this still offered a shared frame of reference with the participants, which was beneficial in ensuring a shared understanding. In accordance to the interpretivist philosophical worldview, a shared understanding is essential to the development of knowledge (Bunnis and Kelly 2010). Throughout this doctoral research, the student acknowledged her own beliefs, perceptions and experiences to enhance the participants' interpretations and understand their experiences.

2.7. Bias

Bias is an inherent error which results in distortion in the study outcomes compromising the quality of research (Polit and Beck 2014). The goal of the researcher is to minimise bias through the use of rigorous research methods (Sica 2006). The most common categories of bias are described in Table 2.21 together with measures adopted in this doctoral research to mitigate them.

Table 2.21: Common categories of bias and measures adopted in this doctoral research to minimise bias (Sica 2006, Bowling 2009)

Bias	**Description**	**Measures taken by this research to minimise bias**
Design bias	Results from studies with incoherent methods, sampling techniques and analysis leading to a difference between the observed and the true value	• Study was designed in collaboration with an experienced research team • Detailed description of the method, sampling techniques and analysis of this doctoral research is provided in the thesis
Selection bias	Influences both the recruitment process of the participants and the inclusion criteria. This occurs when the characteristics of the sample differ from those of the wider population of interest	• The inclusion criteria of participants in Phase II and III was established in a protocol prior initiation of the studies • Purposive sampling in Phase II was applied to all patients initiating treatment with FOLFOX/XELOX in the single oncology centre available in Malta • Participants in Phase III were nominated by patients involved in Phase II using snowball sampling
Data collection bias	Occurs when researcher's personal beliefs influence the way information or data is collected	• Interview guide developed iteratively based on the adapted conceptual PLEM model and tested in a pilot study • Neutrality of interviewer explained prior each interview
Acquiescence response set bias	Refers to the fact that participants more frequently endorse a statement than oppose it	• Interview guide consisted of open questions throughout rather than closed-ended questions with an obvious right answer
Interviewer bias	May occur subconsciously or even consciously when the interviewer leads the participants to reply in a particular way	• All interviews were conducted by the research student, hence by the same interviewer • Training in qualitative interviewing was undertaken by the interviewer to ensure appropriate knowledge and skill to perform the role
Reporting bias	Failure of the participants to reveal the requested information	• Participants were assured of anonymity and confidentiality whilst encouraging them to provide an honest response • Minimised by prolonged engagement allowing trust to be built between interviewer and participants

Evaluation apprehension	Refers to the anxiety experienced by participants when asked to answer questions and they answer as expected by interviewer	• Participants were assured of anonymity and confidentiality whilst encouraged to provide an honest response • Minimised by prolonged engagement • Patients were given a diary to document any experiences that deem important during their treatment journey
Attention bias	Due to awareness of the participants' involvement in the study, they tend to give more favourable responses to perform better due to attention received	• Minimised by use of the interview guide
Social desirability bias	May be exerted by a small pervasive effect as participants wish to present themselves at their best	• Minimised by providing clear statements of the purpose of the research
Mood bias	Participants with negative emotions may underestimate their degree of functioning, level of social activity and support	• If participants felt depressed or tired, they were allowed to postpone the interview
Recall bias	Relates to the participants' selective memories in remembering past experiences and behaviour	• Prospective study design was adopted to reduce this bias • Interviews occurred within 12 weeks for patients and 24 weeks for significant others • Patients were given a diary to document any experiences that they deemed important during their treatment journey
Loss to follow-up bias and Withdrawal bias	Participants who leave the study differ significantly from those that remain	• In view of a longitudinal study design, a cancer type (colorectal cancer) offering a good prognosis was studied to minimise drop-out due to death • Attempts were made to contact participants who stopped their treatment to enquire about their interest to participate in a final interview. Reason for withdrawal was noted if disclosed by participant
Analysis bias	In data analysis, the researcher may naturally look for data that confirms personal experience, overlooking data inconsistent with personal beliefs	• All transcripts were analysed by two independent researchers • Application of reflexivity to guard against personal bias

2.8. Research governance

Governance is defined by Shaw, Boynton and Greenhalgh (2005 p.497 in Zubrick 2016) as "the system of administration and supervision through which research is managed, participants and staff are protected and accountability is assured." As shown in Figure 2.7, this incorporates both the ethics and integrity components of the research (Schroeder, Cathfield and Edwards 2020). It is based on codes of practice, professional standards and law at national and international level together with norms and values (Shaw, Boynton and Greenhalgh 2005). Since the research was conducted by the doctoral student based in a Scottish University (Robert Gordon University), with fieldwork conducted in Malta, the doctoral research had to be authorised by the Robert Gordon University's research ethics committee under its internal supervision as well as the clinical governance of the hospital and ethics review board in Malta.

Figure 2.7: Constituents of ethical research
© 2019 Law, Schroeder, Chatfield (Schroeder, Cathfield and Edwards 2020)

Biomedical ethics are based on four principles namely autonomy, non-maleficence, beneficence and justice (Beauchamp and Childress 2013). Each principle is discussed below in relation to this doctoral research:

- Autonomy

In this doctoral research, a signed informed consent was obtained from each participant in order to take part in the study. The requirement of informed consent stems from the ethical principle of autonomy; whereby the subjective needs of the participants are put first prior to those of the society and welfare (Schroeder, Cathfield and Edwards 2020). In accordance to the International Conference on Harmonisation for Good Clinical Practice (1996 E6 point 1.28), informed consent is defined as ”a process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject’s decision to participate.” An ethically valid informed consent relies on three critical aspects, namely voluntarism, information disclosure and competence. In addition, the process of informed consent must not be considered as a one-time event, but as an ongoing process for a longitudinal study. By providing the consent upon initiation of the study, this does not oblige participants to actively take part for the whole duration of the study. Hence the participant has the right to withdraw from the study at any time (Gupta 2013). In view that this was a longitudinal study and involved several interviews, it was important that the research student reviewed the patient’s willingness to continue his/her participation, with informed consent verbally recorded prior to each interview. It was ensured that all participants had the opportunity to reflect on their ability to participate and were informed of their right to withdraw at any time without affecting the patient’s care.

- Non-maleficence

This ethical principle obligates the researcher to refrain from causing any harm to participants. Participants were allowed to terminate the interviews at any time and even if they felt tired during the interview it was postponed. If emotional distress was experienced by the participants or the research student, the necessary assistance was provided from the clinical psychologist who works in the same oncology and palliative care setting.

- Beneficence

During the research study, the patient may report symptoms indicating toxicity or adverse events from the treatment. In such a case, if the patient mentioned that such adverse effects were not reported to the healthcare professionals, then the research student discusses the issue with the respective patient's oncologist and/or colorectal nurse navigator in order to safeguard the patient's health and safety.

- Justice

In the doctoral research, justice was ensured by treating all participants with dignity and by the same approach. The study design was also in compliance with the relevant policies and legislation.

2.9. Data storage

Throughout the research process, materials pertaining to the study were stored in accordance to the Standard Operating Procedures of the School of Pharmacy and Life Sciences and the governance policy of Robert Gordon University (Robert Gordon University 2020).

Measures were taken to ensure participant anonymity. These include:

- Assignment of unique participant reference code for each participant at the first interview rather than the patients’ real identity in audio-recording, transcribing and reporting
- Diaries labelled by the participant reference code
- Transcriptions of all the interviews done by the research student who also conducted these interviews
- Only anonymised transcripts were distributed amongst members of the research team for data analysis

In addition, data protection measures were adhered to for the storage of the collected data. All signed consent forms, demographic sheets and diaries were stored in a locked drawer accessible only by the research student. Audio-recorded and soft-copy information were stored on a password protected notebook. Any electronic or hard-copy data will be destroyed after a minimum retention period of 3 years after publication of research data has elapsed (Robert Gordon University 2020).

2.10. Summary of the research approaches employed in the doctoral research

This doctoral research was conducted in three phases: systematic review of the literature (Phase I – Chapter 3), longitudinal qualitative study with patients (Phase II – Chapter 4) and with significant others (Phase III – Chapter 5). The research designs, philosophical worldviews and methods that were employed for each phase of this research are schematically outlined in Figure 2.8.

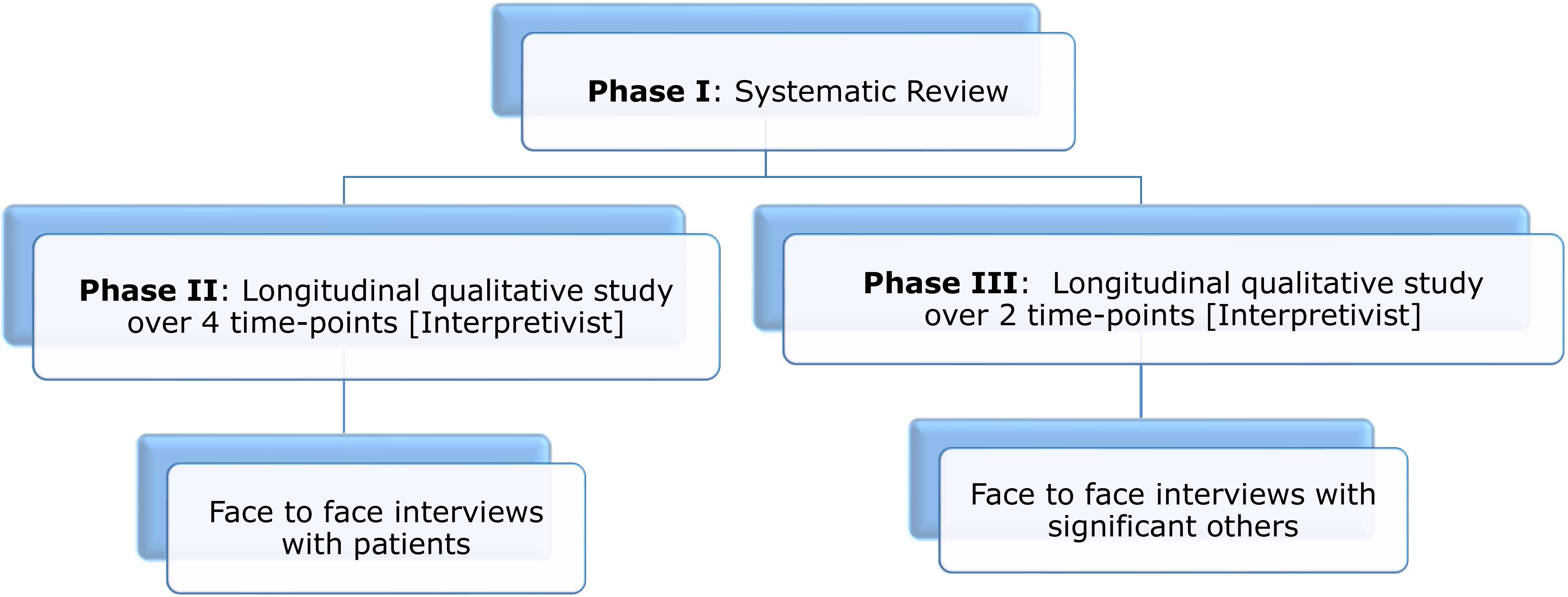

Figure 2.8: Summary of the research approaches used for this doctoral research

Chapter 3

Patients' lived experiences with antineoplastic medicines for the management of malignant solid tumours: A Systematic Review

3. Introduction to the chapter

This chapter provides a detailed account of a systematic review of the literature on patients' lived experiences with antineoplastic medicines. It describes the aim, method, findings, discussion and conclusion.

3.1. Rationale for systematic review

In recent years, there have been an increasing number of publications in the field of cancer. A PubMed search limited to systematic reviews in the field of oncology yielded around 26,000 citations over a 5-year period between 2013 and 2017 (Kelley and Kelley 2018). Most of the published systematic reviews focused on effectiveness and safety of cancer treatment, cell biology and supportive care interventions (Cabral, De Graca Derengowski Fonseca and Mota 2018, Goldkuhle et al. 2018). To date, there has been no systematic review focusing on the patients' lived experiences with antineoplastic medicines prescribed for the management of malignant solid tumours.
This systematic review is necessary to reveal the patients' beliefs, practice and burden related to the use antineoplastic medicines allowing healthcare professionals to better understand and interact with patients; thereby improving quality of cancer care.

3.2. Systematic Review aim and questions

The aim of this systematic review is to critically appraise, synthesise and present the available evidence of patients' lived experiences with antineoplastic medicines prescribed for the management of malignant solid tumours.

In relation to the patients' treatment journey with antineoplastic medicines for the management of malignant solid tumours, this systematic review sought to answer the following specific review questions:

1. What is the definition of the patients' lived experience with medicine?
2. What are the medicine-related beliefs of cancer patients?
3. What is the medicine-taking practice of cancer patients?
4. What is the medicine-related burden experienced by cancer patients?

3.3. Method

3.3.1. Protocol development and registration

A systematic review protocol was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) standards (Moher et al. 2015). The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) with registration number CRD42016048457 (Brincat et al. 2016 - Appendix 3.1), to improve transparency and prevent unplanned duplication of work.

3.3.2. Inclusion and exclusion criteria

The inclusion criteria were based on the following:

- *Population* - patients aged ≥18 years diagnosed with malignant solid tumours
- Phenomenon *of interest* - the patients' lived experience of medicine focusing on their medicine-related beliefs, practice and burden
- *Context* - receiving treatment with antineoplastic medicines

Only full-text publications that met the inclusion criteria and reported all the three aspects of medicine-related beliefs, practice and burden from the patient's perspectives were included in the systematic review. All types of study designs (qualitative, quantitative and mixed methods) were considered.

Studies were excluded if reported in non-English language or examining the patients' experience with antineoplastic medicines in experimental studies or with a palliative intent at end-of-life. Grey literature including conference abstracts were also excluded due to potential limited quality.

3.3.3. Search strategy

The systematic literature search was conducted in October 2016 in six electronic databases, namely Cochrane Database of Systematic Reviews, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, International Pharmaceutical Abstracts, Medline and PsycArticles. The area of focus of these databases is outlined in Table 3.1. A manual search within the reference list of included studies was performed to further identify potentially relevant publications.

Table 3.1: Area of focus of databases

Database	Date of inception	Area of focus
Cochrane Database of Systematic Reviews	1989	High quality randomised controlled trials, systematic reviews and protocols related to healthcare practice (The Cochrane Collaboration 2023)
CINAHL	1937	More than 500 journals based on nursing and allied health, biomedicine and health sciences (EBSCO 2023a)
EMBASE	1947	More than 8000 journals in biomedicine (Elsevier 2023)
International pharmaceutical abstracts	1970	Around 800 journals on drug therapy and other pharmaceutical information such as ethical and legal issues (EBSCO 2023b)
MEDLINE	1966	More than 5000 journals in biomedicine and different areas of health such as life sciences, behavioural sciences and bioengineering (National library of medicine, 2022)
PsycArticles	1894	More than 110 journals in social and behavioural sciences (American Psychological Association 2023)

A list of search terms was created based on terms captured in the PLEM conceptual model (Mohammed, Moles and Chen 2016). Concept mapping was utilised as a brainstorming technique by the research team to identify synonyms to the terms included in the search strategy. The search was performed using Medical Subject Headings (MeSH) and other appropriate subject headings and text words as applicable. Boolean operators together with truncations and wildcards were used to expand the search. The list of search terms is outlined in Table 3.2, exemplified by the search string as applied to Medline. The search string was then adapted to meet the specifications of the other different databases.

Table 3.2: Search string applied to Medline

Patient* OR People OR Consumer* OR Person* OR Individual* OR Client* OR User* OR Care recipient* OR Laype* OR Layman OR Laywoman OR Laymen OR Laywomen OR Survivor*
AND
tumour*OR tumor* OR Malignan* OR carcinoma OR Lymphoma OR Sarcoma OR Cancer OR Oncl* OR Neoplas*
AND
Cytotox* OR Antineoplas* OR Anti-neoplas*OR Anticancer OR Anti-cancer OR Chemo* OR Anticarcinogen* OR Anti-carcinogenic OR Drug* OR Pharm* OR Medication* OR Treat* OR Therap* OR Medicin* OR Agent
AND
Liv* experience* OR Life experience* OR Experience*
AND
Burden OR Routine OR Complex* OR Management OR Hassle OR Stress OR Access* OR Cost* OR Financ* OR Challeng* OR Side-effect* OR Side effect* OR Adverse effect* OR Undesirable effect* OR Adverse drug reaction* OR Adverse reaction OR Adverse event OR Adverse drug event* OR Barrier*
AND
Belief* OR Prefer* OR Expect* OR Adapt* OR Satisf* OR Attitude* OR View* OR Opinion* OR Concern* OR Motivat* OR Knowledge OR Emotion* OR Need* OR Trust OR Cop* OR Perce* OR Perspective* OR Famil* OR Relative* OR Healthcare professional* OR Health care professional* OR Health professional* OR Care* OR Healthcare provider* OR Health care provider* OR Health personnel OR Peer* OR Friend*
AND
Practice OR practise OR Behaviour* OR Behavior* OR Aware* OR cessation OR Withdr* OR Discontinu* OR Halt* OR Stop* OR Decision* OR Choice* OR Plan* OR Modif* OR Alter* OR Chang* OR Accept* OR Understand* OR Dependen* OR Complian* OR Adheren* OR Negotiat* OR Noncomplian* OR Non-complian* OR Nonadheren* OR Non-adheren* OR Journey* OR Trajector* OR Educat* OR Independen* OR Communicat*

3.3.4. Study selection

Screening was performed following a sequential assessment of titles, followed by abstracts and then full papers. A random sample of 10% of titles and abstracts in addition to all full-text publications were reviewed independently by the research student and another member of the research team (AB and AW). Any disagreement was resolved by consensus. This enhanced reliability of the screening process.

3.3.5. Quality assessment

Quality assessment of the included studies was performed using Critical appraisal skills programme (CASP) tool (CASP 2022 - Appendix 3.2). This was carried out independently by the research student and another member of the research team (AB and AW). Any disagreements were resolved by consensus or referred to a third reviewer if necessary.

3.3.6. Data extraction

Data extraction forms were developed by the research student to incorporate specific information pertinent to the systematic review aim and questions. These included publication details such as primary author and publication year, aim and objective(s), setting, sample size, study design, method and salient findings. Extracted data relevant to the medicines-related belief, practice and burden were mapped in accordance to the themes of the conceptual PLEM model (Mohammed, Moles and Chen 2016). Data extracted from qualitative studies was substantiated with quotations in order to maintain contextualisation. For quantitative studies, a narrative description was made to the numerical data. Data was extracted independently by two reviewers (AB and AW or DS or LW), with any disagreements resolved by consensus or referred to a third reviewer to resolve any inconsistencies if necessary.

3.3.7. Data synthesis

The research findings were analysed using a narrative synthesis. Popay et al. (2006, p.5) describes narrative synthesis as 'an approach to the systematic review and synthesis of findings from multiple studies that relies primarily on the use of words and text to summarise and explain the findings of the synthesis.' This analysis was deemed appropriate due to heterogeneity in the reported data. In view that only two quantitative studies were identified focusing on a different antineoplastic medicine, a meta-analysis of the quantitative data was not deemed appropriate. Proposed sub-themes were put forward by the research student and the rest of the research team through an iterative process.

3.4. Results

3.4.1. Results of the study selection process

The databases search yielded 31001 studies, which decreased to 29760 studies following electronic removal of duplicates. Screening of titles excluded 22738 studies which were not relevant to the patients’ experience. Of 7022 abstracts screened, 6949 were excluded and the remaining 73 studies underwent full-text assessment. The manual search yielded another 3 studies and underwent full-text assessment. A total of ten studies fulfilled the inclusion criteria and were included in the systematic review. Of these, eight were qualitative studies whilst two studies followed quantitative methodology. The screening and selection process is summarised in Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) Flow diagram in Figure 3.1.

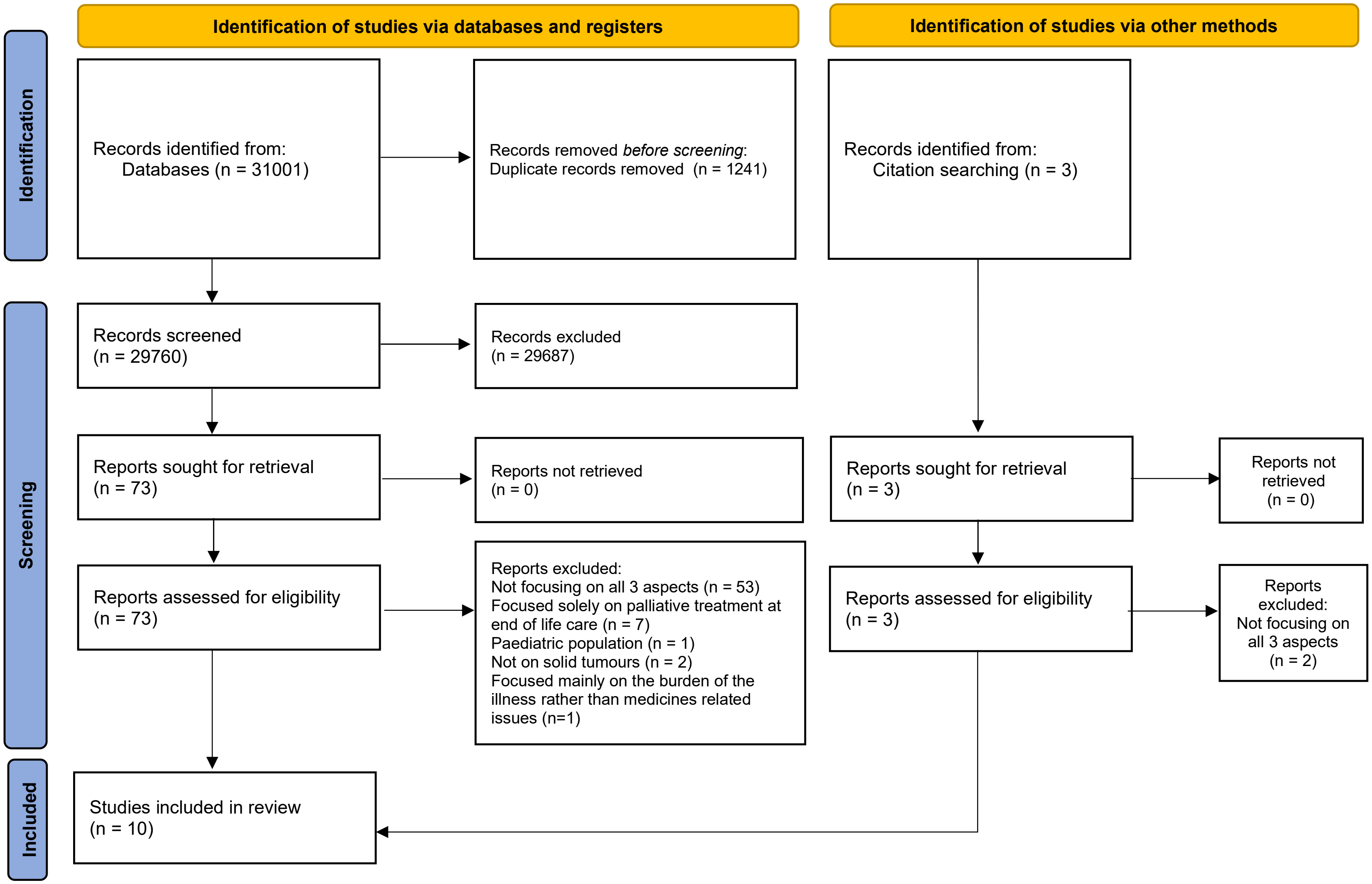

Figure 3.1: PRISMA Flow diagram detailing the screening and selection process (Page et al. 2021)

3.4.2. Characteristics of included studies

The characteristics of the ten included studies are summarised in Table 3.3.The aims and the key findings of each study are included in Table 3.4. The included studies were published between 2005 and 2016, with most being conducted in Europe (n=6), followed by America (n=3) and Asia (n=1). Sample sizes ranged from 1 to 92 participants, reaching a total of 304 patients.

Four studies included solely female participants in the sample population. The majority of the studies involved patients diagnosed from a single cancer type, namely breast cancer (n=3), lung cancer (n=2) and colorectal cancer (n=1). The remaining four studies involved patients with different cancers. There were four studies that focused on specific antineoplastic medicines, namely capecitabine (n=2), erlotinib (n=1) and adjuvant fluorouracil, epirubicin and cyclophosphamide treatment protocol (n=1). Out of the ten included studies, three studies did not state the time point when the interview was conducted with respect to the patient's treatment journey. Six studies collected data during the patient's treatment phase whilst one study took a retrospective look at patients who had completed antineoplastic treatment within the previous year.

Out of eight qualitative studies, the majority (n=6) followed a cross-sectional study design, with the exception of two longitudinal studies in America (Yokoyama dos Anjos and Zago 2005, Bell 2009). All quantitative studies (n=2) were conducted by the same research team in the Netherlands and followed a prospective observational cohort study focusing on erlotinib (Timmers et al. 2015) and capecitabine (Timmers et al. 2016).

Table 3.3: Information on the studies included in the systematic review

Study [First author, year]	Country	Setting	Number of patients	Cancer type	Study design	Data collection	Data analysis
Qualitative studies							
Yokoyama dos Anjos et al., 2005	Brazil	Oncology hospital and patient's home	1	Breast cancer	Qualitative ethnographic case study	• Semi-structured interviews • Observation • Patient's field diary	Interpretative anthropology
Bergkvist et al., 2006	Sweden	Gynaecology and oncology hospital	9	Gynaecology cancer (n=4) Breast cancer (n=1) Sarcoma (n=2) Teratoma (n=2)	Qualitative study	• Semi-structured interviews	Content analysis
Browall et al., 2006	Sweden	2 Oncology hospitals and patient's home	20	Breast cancer	Qualitative study	• Narrative interviews with one open question	Content analysis
Bell, 2009	Canada	Cancer support group at oncology hospital	8	Colorectal cancer	Ethnography	• Semi-structured interviews • Observation	Thematic analysis
Regnier Denois et al., 2011	France	2 Oncology hospitals	42	Breast cancer (n=32) Colon cancer (n=10)	Qualitative study	• Observation • Focus group or individual interviews	Content analysis
Gerber et al., 2012	United States of America (USA)	2 Oncology hospitals	47	Lung cancer	Qualitative study	• Focus group	Thematic content analysis
Gassmann et al., 2016	Switzerland	Oncology hospital	6	Lung cancer (n=2) Colon cancer (n=3) Prostate cancer (n=1)	Grounded theory	• Open interviews	Constant comparison coding and categorising

Komatsu et al., 2016	Japan	Oncology hospital	17	Breast cancer	Grounded theory	- Semi-structured interviews	Transcripts analysis by first coding and then labelling the meanings. Core categories emerged by connecting categories and subcategories
Quantitative studies							
Timmers et al., 2015,	Netherlands	12 hospitals	62	Lung cancer	Prospective observational cohort study	• Patients' reported questionnaires • Patient's medical file • Medication event monitoring system (MEMS) • Blood samples	Mann–Whitney test, Fisher exact test
Timmers et al., 2016	Netherlands	10 hospitals	92	Colorectal cancer (n=66) Breast cancer (n=16) Pancreatic cancer (n=4) Other type (oesophageal, head and neck and unknown origin, n=6)	Prospective observational cohort study	• Patients' reported questionnaires • Pill count, pharmacy data and patients' medical file (PPP method) • Medication Adherence Report Scale • Blood samples	X^2-test, Fisher's exact test, Logistic regression

Table 3.4: Aims and key findings of the included studies		
Study	**Stated aim(s)**	**Key findings**
Qualitative studies		
Yokoyama dos Anjos et al., 2005	To understand the meaning of chemotherapy from the patient's point of view	Six unities of meaning were identified: 1. discovery of cancer and search for assistance 2. knowledge about cancer 3. trajectory of chemotherapy 4. networks of support 5. lack of control of one's life 6. uncertainty of the treatment and expectation on the future The patient summarised her experience with chemotherapy as "the loss of the control over one's life." The study emphasised the need for nursing care to follow up the patient throughout the whole process and identified patient's resources to resume control of her life.
Bergkvist et al., 2006	To acquire a deeper understanding of cancer patients' symptom experiences with focus on nausea and vomiting during chemotherapy treatment and the consequences these have on daily life	Five main categories were identified: 1. before cancer diagnosis 2. being ill-consequences on daily life 3. going through chemotherapy treatment 4. coping with treatment 5. after treatment - looking forward to a normal life The study described the experience of receiving chemotherapy as a process that evolved over time. The findings suggest that experiences of nausea and vomiting during chemotherapy treatment have a profound effect on the cancer experience and thus may influence future decisions relating to new treatment.
Browall et al., 2006	To describe the experience of postmenopausal women with breast cancer who undergo adjuvant chemotherapy treatment	Four themes were identified: 1. the fear of the unknown 2. affects on body and mind 3. to get by 4. a transformed life The participants described feelings of imbalance in their relationships due to lack of support from those close to them. Support provided by healthcare professionals was received both positively and negatively; with most of the participants revealing variations in healthcare professionals' attitude, knowledge and empathy. Women who decided not to work during treatment felt pressure from society and healthcare professionals to get back to work as soon as possible. The participants expressed a feeling of not being afraid of dying but wanted more time to prepare themselves.

Bell, 2009	To explore patients' perceptions of adjuvant chemotherapy	Three themes were identified: 1. hurting the good cells & really hurting cancer cells 2. getting a "full dose" 3. oral vs intravenous chemotherapy A cultural model of chemotherapy was discussed where the value of suffering and pain were stressed as means of monitoring treatment effectiveness and providing a possibility of cure. This study showed the implications on anxiety levels experienced by the patients and the risk of recurrence.
Regnier Denois et al., 2011	To describe and understand existing practice for capecitabine and to evaluate the perceptions and descriptions of patients and oncologist about the prescription of capecitabine	Three key aspects were identified: 1. analysis of medical practices 2. patients' adherence with dose and schema for oral chemotherapy 3. information, communication and evaluation of side effects Adherence, which in this study was defined as being against not taking their treatment, seemed satisfactory. Results showed a wide diversity in the prescribers' practices, who often made decisions based on their experience of practice guidelines for intravenous chemotherapies. Although patients did not show any deliberate non-adherence, they revealed poor observance of the dose schedule. The study identified the patients' inability to recognise and report important signs of harmful toxicity.
Gerber et al., 2012	To gain insight into patients' perceptions of maintenance chemotherapy for advanced non-small cell lung cancer	Five themes were identified: 1. survival benefits, disease control and "buying time" 2. the importance of "doing something" 3. quality of life concerns 4. the role of provider opinion/preference 5. the importance of logistics
Gassmann et al., 2016	To explore the experiences of patients undergoing oral chemotherapy and investigate the impact of oral chemotherapy on their daily life	A core phenomenon of feeling responsible was identified, influenced by four factors: 1. context and intervening conditions 2. consequences 3. action and interaction strategies 4. causal conditions Participants reported physical and emotional reluctance towards oral chemotherapy as well as toxic side effects. Feeling responsible emerged as a core phenomenon with influences from context and intervening conditions. All participants aimed to adhere to treatment despite being a challenging task with a complex treatment regimen. Belief in the effectiveness of treatment was a strengthening factor. Participants struggled between the necessity of adhering to oral chemotherapy and the practicality as well as emotional difficulties of daily life. Hence patients developed coping strategies during the treatment journey. Oral chemotherapy was found to be omnipresent by determining the participants' thoughts and daily life.

Komatsu et al., 2016	To explore the experiences of patients with breast cancer who had received chemotherapy to understand how they perceived the impact of the treatment on their daily lives	Three categories were identified: 1. Distress 2. Personal safety net: confidence in control over life 3. My precious life Patients created personal safety nets for physical, emotional and social contexts during chemotherapy. The safety nets made participants feel more confident and in control of their lives and were willing to take a positive approach towards making their lives meaningful. In anticipation of side effects of chemotherapy, participants "hibernated" and consumed minimal amount of energy. They also created a protective inner space in which they were able to tolerate fear and anxiety and exert self-control. In maintaining their daily routines, patients felt more confident to balance their lives and illness.
Quantitative studies		
Timmers et al., 2015	To assess adherence to erlotinib treatment and evaluate experiences of patients as well as the relationship between medicine adherence, erlotinib exposure and symptoms	According to the Belief about Medicines Questionnaire (BMQ), 40% (n=25) of patients were classified as “accepting” treatment with erlotinib. Most patients (55%, n=34) considered their treatment with erlotinib to be of high necessity and high concern. Data revealed a mean adherence of 96.8% ± 4.0. Over one-third of patients had an adherence rate <95%. At 1 month, 21% of patients did not always correctly take erlotinib without food. Associated risk factors were older age, suboptimal adherence, ocular symptoms and stomatitis (all $p < 0.05$). After 1 month of treatment, fatigue (91%) and rash (86%) were the most common symptoms reported. AUCss of erlotinib was higher in patients with rash and patients with moderate–severe anorexia (both $p < 0.05$).
Timmers et al., 2016	To get insight into patients’ experiences with the use of capecitabine in daily practice and the various aspects that govern adherence	Most patients had an adherence rate of ≥95 and ≤105%. Symptoms were frequently reported and the dosing regimen was adjusted by the physician at least once in 62% of patients (n=57). According to BMQ, 50% (n=46) of patients were classified as “accepting” capecitabine. These patients perceived their medicine with a high necessity and low concern prior to initiation of treatment. 44% (n=40) patients who had started their treatment with capecitabine considered their treatment to be of high necessity and high concern. According to the Brief Illness Perception Questionnaire (IPQ), patients believed that treatment with capecitabine would help them control their illness. This is evidenced by the mean value which improved from baseline (7.8±1.8) to cycle 5 (8.0±1.6).

3.4.3. Quality assessment of the included studies

The quality assessments of qualitative and quantitative studies included in the systematic review are reported in Table 3.5 and Table 3.6 respectively.

The overall quality of the included studies deemed acceptable, with none of the studies being excluded from the systematic review. The strengths of the included studies were that almost all studies postulated a clear research aim (n=9), attained ethical approval (n=9) and followed an appropriate research design (n=9). The key limitations of qualitative studies were related to poor description of the recruitment strategy (n=3) and poor reflection on the relationship between the researcher and recruited patients (n=3). For the quantitative studies, the key weaknesses were lack of details with regards the recruitment of patients (n=2) and the duration of the follow-up period (n=2).

Table 3.5: Quality assessment of qualitative studies (CASP 2022)

Study	1	2	3	4	5	6	7	8	9	10
Yokoyama dos Anjos et al., 2005	Yes	Yes	Yes	No	Yes	No	Yes	Can't tell	Can't tell	Can't tell
Bergkvist et al., 2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Browall et al., 2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Bell, 2009	Can't tell	Yes	Can't tell	No	Yes	Can't tell	Yes	Yes	Yes	Yes
Regnier Denois et al., 2011	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Gerber et al., 2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Gassmann et al., 2016	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes
Komatsu et al., 2016	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes

CASP tool quality indicators
1. Was there a clear statement of the aims of the research?
2. Is a qualitative methodology appropriate?
3. Was the research design appropriate to address the aims of the research?
4. Was the recruitment strategy appropriate to the aims of the research?
5. Was the data collected in a way that addressed the research issue?
6. Has the relationship between researcher and participants been adequately considered?
7. Have ethical issues been taken into consideration?
8. Was the data analysis sufficiently rigorous?
9. Is there a clear statement of findings?
10. How valuable is the research?

Table 3.6: Quality assessment of quantitative studies (CASP 2022)

Study	1	2	3	4	5a	5b	6a	6b	7	8	9	10	11	12
Timmers et al., 2015	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Can't tell	Adherence and patients' experiences	Precise	Yes	Yes	Yes	Yes
Timmers et al., 2016	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	No	Adherence and patients' experiences	Precise	Yes	Yes	Yes	Yes

CASP tool quality indicators
1. Did the study address a clearly focused issue?
2. Was the cohort recruited in an acceptable way?
3. Was the exposure accurately measured to minimise bias?
4. Was the outcome accurately measured to minimise bias?
5a. Have the authors identified all important confounding factors?
5b. Have they taken account of the confounding factors in the design and/or analysis?
6a. Was the follow up of subjects complete enough?
6b. Was the follow up of subject long enough?
7. What are the results of this study?
8. How precise are the results?
9. Do you believe the results?
10. Can the results be applied to the local population?
11. Do the results of this study fit with other available evidence?
12. what are the implications of this study for practice?

3.4.4. Adapted PLEM model to oncology setting

Figure 3.2 illustrates a model of the patients' lived experience with antineoplastic medicines for malignant solid tumours. Nine themes and 26 sub-themes were produced under the superordinate themes of medicine-related belief, medicine-taking practice and medicine-related burden. Therefore, this permitted the development of an adapted PLEM model specific to the use of antineoplastic medicines in the oncology setting (Figure 3.2) based on the original PLEM model of Mohammed, Moles and Chen (2016). The results of this systematic review are discussed in relation to the research questions and in line with adapted PLEM model. A summary of the individual study findings in relation to each research question in this systematic review is found in Appendix 3.3.

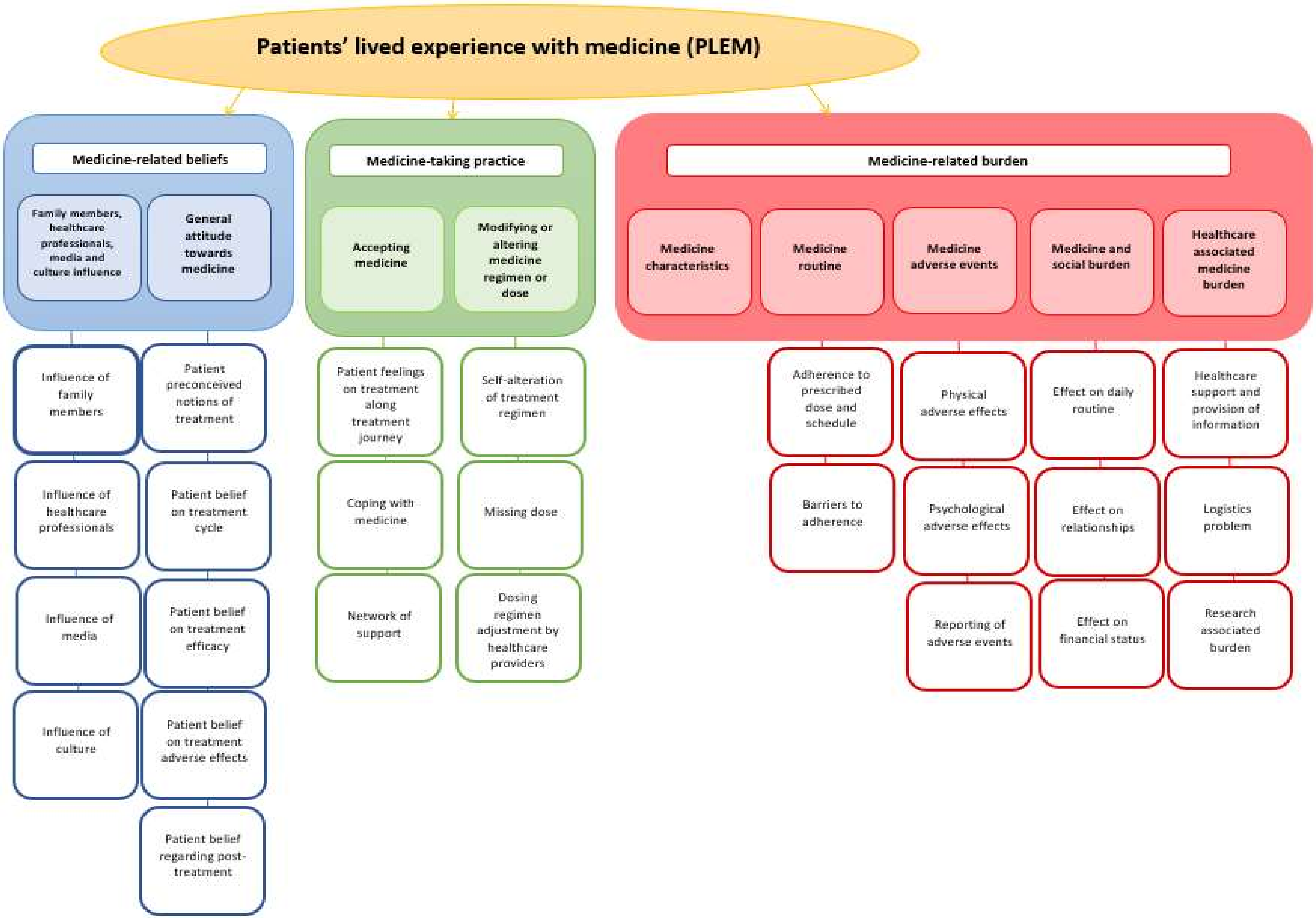

Figure 3.2: An adapted model of PLEM for patients with solid tumours receiving antineoplastic medicines

3.4.5. Definition of PLEM

All ten included studies evaluated the patients' lived experience with antineoplastic medicines but failed to provide a standard definition of PLEM. Attempts to at least define part of the phrase were not evident.

3.4.6. Medicine-related beliefs

Within this theme, two sub-themes were identified as highlighted in Figure 3.2.

a) Family members, healthcare professionals, media and culture influences

Family members showed to be highly influential on patients' beliefs regarding cancer and its treatment (Yokoyama dos Anjos and Zago 2005, Gerber et al. 2012, Gassman et al. 2016). As treatment with antineoplastic medicines was perceived by patients as an opportunity for survival, patients felt obliged towards their families to accept treatment even if this meant to consist of suffering and sacrificing their normal lifestyle (Gerber et al. 2012, Gassman et al. 2016).

> *Yes, I just thought that if something comes back again and I say no, then I have to look my family and friends in the eye and say I could have prevented it, perhaps. Now, if something comes back again, I can say I did everything I could …* (Gassman et al 2016)

Trust in healthcare professionals proved to be a critical factor for patients to accept and adhere to treatment with antineoplastic medicines (Yokoyama dos Anjos and Zago 2005, Gerber et al. 2012).

> *… if my doctors assured me this was a good move, this was a good move for me, I feel confident enough in [my doctor] to follow his advice.* (Gerber et al 2012)

Media was found to be another influence on patients' beliefs on cancer and its treatment. Newly diagnosed patients with cancer obtained a false picture about cancer and its treatment, thus provoking unnecessary anxiety (Yokoyama dos Anjos and Zago 2005, Bergkvist and Wengstrom 2006). Similarly, experiences shared within support groups tend to remain uncontested; with other patients accepting them as simple statements of facts or as hypothesis (Browall, Gaston-Johansson and Danielson 2006, Bell 2009).

> *… then I have to vomit—like the things I have seen on TV or been told, that you will vomit and feel very sick.* (Bergkvist and Wengstrom 2006)

Antineoplastic medicines were considered as means to achieve cure and prolong survival (Yokoyama dos Anjos and Zago 2005, Bell 2009). Instantaneously, such treatment was uniquely considered both culturally and medically *"as the source of suffering"* (Bell 2009). Suffering embraced both a personal meaning and a value for each patient. This was evident in the Latin-American culture where cancer was considered as a consequence of immoral behaviour (Yokoyama dos Anjos and Zago 2005). As a result, patients may be silenced to report any symptom suggestive of cancer or adverse effects of treatment, with the risk of presenting at a late stage (Yokoyama dos Anjos and Zago 2005, Bell 2009).

b) *General attitude of the patient towards medicine*

Prior to initiation of antineoplastic medicines, patients already had pre-conceived notions and expectations about their treatment. A common impression amongst patients was that antineoplastic treatment "*hurt the good cells and really hurting the cancer cells*" (Bell 2009). Treatment with antineoplastic medicines is a highly feared form of treatment that is commonly considered to be as bad or worse than the experience of cancer itself (Browall, Gaston-Johansson and Danielson 2006, Bell 2009). This may be due to the expected adverse effects of treatment on patients' aesthetics and constant feeling of sickness (Yokoyama dos Anjos and Zago 2005, Browall, Gaston-Johansson and Danielson 2006, Bell 2009).

> *This thing about being sick I had known for a long time. But people say: those who receive chemotherapy do not stand it, because it weakens your organism very much … I expected that I'd throw up a lot …* (Yokoyama dos Anjos and Zago 2005)

With regards to the administration of antineoplastic treatment in cycles, patients perceived the off-treatment period as "treatment break" (Gerber et al. 2012) and provided an opportunity for recovery from adverse effects (Gerber et al. 2012, Gassmann, Kolbe and Brenner 2016).

> *If the break allowed me to feel good enough that I could iron, go to the grocery store, go have a cup of coffee at Starbucks with friends, then I'd like to have that break*. (Gerber et al. 2012)

Patients believed that treatment efficacy may be related to its maximum tolerated dose with the outcome being reflected in decreased tumour markers (Reigner Denois et al. 2011, Gassman et al. 2016). Other patients who were receiving maintenance treatment with antineoplastic medicines interpreted this as actively "*doing something*" or as "*buying time*" by controlling their illness (Gerber et al. 2012). This instilled "hope" by giving them a greater opportunity to be selected as candidates for clinical trials of future cancer treatments (Gerber et al. 2012).

> *Naturally I had huge hopes, … in a new medication. Actually, I'm convinced there's a little something positive in the fact that the doubling of the [tumor marker] took a longer time, which means that it maybe really did work a bit. Without [name of the medication] I'd maybe be gone already …* (Gassman et al. 2016)

> *You know, it's just a big decision to make, but if it's more promising or if there's any way it prolongs life, of course I want to do whichever. That's what gives us a better chance …* (Gerber et al. 2012)

Patients who received oral antineoplastic medicines generally perceived their cancer to be a mild and non-aggressive type. They regarded the oral formulation 'as a diluted potency' of the parenteral (Bell, 2009).

> *well, mine* [cancer] *wasn't that bad because I only got capecitabine* [an oral chemotherapy agent]*, if you have intravenous it must be worse* (Bell, 2009)

The occurrence of adverse effects was considered by patients as a measure of effectiveness of treatment. Hence being the price to pay to achieve cure (Yokoyama dos Anjos and Zago 2005, Browall, Gaston-Johansson and Danielson 2006, Bell 2009). As a result, the fear of discontinuation of treatment with antineoplastic medicines or dose reduction resulted in patients refraining from reporting adverse effects (Reigner Denois et al. 2011).

> *Victoria wonders whether her chemo is actually effective because she is not experiencing many side effects and she has heard that the more side effects you have, the better it is working.* (Bell, 2009)

When thinking about their future following completion of treatment with antineoplastic medicines, patients wondered if further treatment would be required. This led to questioning their coping ability to proceed with further unplanned sessions of antineoplastic medicines (Yokoyama dos Anjos and Zago 2005, Browall 2006, Bergkvist and Wengstrom 2006, Komatsu et al. 2016).

> *But I can't think about if I were to find out that the cancer had spread, (and if I were to need more treatment) - how would I then manage to go through chemotherapy again, now that I know about everything, now that I have all the answers.* (Bergkvist and Wengstrom 2006)

Perceiving life through the lens of a cancer survivor resulted in re-evaluation of the patients' perception of the real value of life. Patients looked forward towards living a normal life even though this could mean experiencing persistent adverse effects or live in fear of cancer recurrence (Komatsu et al. 2016).

> *Nothing is worth it if I am not alive ...*[c] *Before I underwent treatment, I used to stay up all night, and I worked hard, even when I felt tired, but because I have experienced a serious illness, I no longer do it*. (Komatsu et al. 2016)

Quantitative data obtained from The Beliefs about Medicines Questionnaire showed that most patients accepting treatment with capecitabine (50%, n=46) and erlotinib (55%, n=34) had positive beliefs about the necessity of the medicine (Timmers et al. 2015, Timmers et al. 2016). The use of erlotinib raised strong concerns to patient about the potential adverse effects and the severity of the illness (Timmers et al. 2015). Also the Brief Illness Perception Questionnaire showed that patients had comparable perceptions about the extent to which treatment can control their cancer (erlotinib 7.8±1.8; capecitabine 6.4±2.3) (Timmers et al. 2015, Timmers et al. 2016).

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[c] … indicates that there were other spoken words without substantial importance as part of the quotation that was removed.

3.4.7. Medicine-taking practice

Within this theme, two sub-themes were identified as highlighted in Figure 3.2.

a) Accepting medicine

Upon disclosure of cancer diagnosis, the patients' attention rapidly shifted to the available treatment options and hence, their chance of survival. In fact, patients were willing to know the intention of treatment being offered so as to evaluate their situation and decide whether to proceed with treatment or otherwise (Yokoyama dos Anjos and Zago 2005, Bergkvist and Wengstrom 2006, Browall 2006, Gerber et al. 2012, Gassmann, Kolbe and Brenner 2016).

> *If this disease has no cure you can tell me, because in this case I do not wish any treatment… He told me that that depends on the case: if the disease is already too advanced, it is not worth to treat!* (Yokoyama dos Anjos and Zago, 2005)

Feelings expressed by patients at initiation of treatment with antineoplastic medicines included hope (Yokoyama dos Anjos and Zago 2005, Gerber et al. 2012), anxiety, stress and fear (Bergkvist and Wengstrom 2006, Browall, Gaston-Johansson and Danielson 2006, Gassmann, Kolbe and Brenner 2016).

> *When I found out that I was going to have chemotherapy my whole world came apart. It was the worst thing I could imagine.* (Browall, Gaston-Johansson and Danielson 2006)

The feelings of repression and fear towards cancer were overcome by the acceptance of treatment as patients metaphorised their treatment with antineoplastic medicines as a "*fight*" against cancer (Yokoyama dos Anjos and Zago 2005). This revived their strength in beating their helpless situation (Browall, Gaston-Johansson and Danielson 2006, Gassmann, Kolbe and Brenner 2016). Strategies were adopted by patients to ensure adherence with treatment particularly with oral antineoplastic medicines. These included the use of constant reminders (Gassmann, Kolbe and Brenner 2016, Reigner Denois et al. 2011), following the same routine (Gassmann, Kolbe and Brenner 2016) or engaging family members to provide them with medicine or remind them to take treatment (Reigner Denois et al. 2011). In addition, patients sought for various sources of support throughout the treatment trajectory. These included family members (Yokoyama dos Anjos and Zago 2005, Browall, Gaston-Johansson and Danielson 2006, Bergkvist and Wengstrom 2006, Gassmann, Kolbe and Brenner 2016, Komatsu et al. 2016), friends (Yokoyama dos Anjos and Zago 2005), support groups (Yokoyama dos Anjos and Zago 2005, Browall, Gaston-Johansson and Danielson 2006, Bell 2009) and religious or spiritual groups (Yokoyama dos Anjos and Zago 2005).

> *I've got a friend who helped a lot in my fight, she gave me strength. She comes here, brings medicines, teaches me things… She is the one who took care of me, very close. I went to the doctor because of her. She supports me a lot. She's really my friend!* (Yokoyama dos Anjos and Zago 2005)

b) Modifying or altering medicine regimen or dose

The majority of patients were highly adherent to treatment with most claiming never to miss a dose (Reigner Denois et al. 2011, Gassmann, Kolbe and Brenner 2016), taking them exactly as prescribed and striving to receive "*100% dose*" (Bell 2009). Patients missed treatment doses unintentionally often due to changes in their daily routine such as being on vacation or "*visiting friends and outing in town"*" (Reigner Denois et al. 2011). However, instances were described by patients when they self-altered their prescribed treatment regimen resulting in either under or overdosing. Underdosing may be deliberately done by skipping a dose to minimise the severity of unbearable adverse effects such as gastrointestinal symptoms. However, overdosing occurred in instances when some patients consumed the remaining forgotten tablets at the end of the cycle or like when a patient admitted that "he did not always respect the break between cycles" (Reigner Denois et al. 2011).

Delays in antineoplastic treatment schedule and dose reductions by healthcare professionals due to complications of treatment or occurrence of adverse effects instilled fear in patients due to risks of cancer "*grow*[ing] *faster*" (Bell 2009) and recurrence (Bell 2009, Reigner Denois et al. 2011). In view of this, some patients still begged to continue receiving their treatment with antineoplastic medicines "*Please just give it to me*" (Bell 2009).

Quantitative data showed that patients had high adherence to oral antineoplastic medicines (96.8% for erlotinib and 99.3% for capecitabine) (Timmers et al. 2015, Timmers et al. 2016). A patient was estimated to take "*more than 105% of the prescribed dose*" according to the pill count method (Timmers et al. 2016). Most patients (>70% for capecitabine; >60% for erlotinib) claimed to use a reminder method to adhere to treatment regimen (Timmers et al. 2015, Timmers et al. 2016). Despite this, patients who experienced unintentional adherence with capecitabine claimed to 'Forget to take pills' as their commonest reported reason (12%, 20% and 26% at cycles 1, 3 and 5 respectively) (Timmers et al. 2016). As treatment progressed, more patients were increasingly not strictly adhering to the correct intake of medicine with respect to food (13% for cycle 1 to 24% at cycle 5 for capecitabine; 21% after 1 month of treatment with erlotinib) (Timmers et al. 2015, Timmers et al. 2016).

Dosing regimen adjustment was a common experience for patients, with 62% patients (n=57) experiencing at least one variation in comparison to the initial dosing regimen of capecitabine. These variations were decreased (30%, n=28) or increased dose (13%, n =12), delayed next treatment cycle (35%, n=32) or reduced number of treatment cycles (21%, n=19) (Timmers et al. 2016). Around 40% of patients experienced discontinuation of treatment (37%, n=35 for capecitabine; 42%, n=26 patients for erlotinib) mainly due to occurrence of adverse effect (20%, n=7 for capecitabine; 31%, n=8 for erlotinib) and progression of illness (11%, n=4 for capecitabine; 69%, n=18 for erlotinib) (Timmers et al. 2015, Timmers et al. 2016).

3.4.8. Medicine-related burden

Within this theme, five sub-themes were identified as highlighted in Figure 3.2.

a) Medicine characteristics

Medicine characteristics that adversely influenced the patients' experience were the treatment dosage form (Bell 2009), colour of the parenteral infusion (Bergkvist and Wengstrom 2006) and tablet size (Gassmann, Kolbe and Brenner 2016).

> *Every time it was as if they got stuck in my throat* (Gassmann, Kolbe and Brenner 2016)

Those patients who received antineoplastic treatment parenterally watched nurses wearing the personal protective wear. This appalling experience made the patients recall about the serious effects they would ultimately be facing from treatment (Bergkvist and Wengstrom 2006). Additionally, they felt "*chained*" to the infusion line (Bergkvist and Wengstrom 2006).

b) Medicine routine

Patients were "*feeling responsible*" (Gassmann, Kolbe and Brenner 2016) to regularly take their oral antineoplastic medicines at the right dosage and time; this being the only task that was not delegated to others. They "*invested all their energy in* ensuring adherence" with regards time and dosage to feel "*actively engaged in fighting"* against cancer (Gassmann, Kolbe and Brenner 2016). Barriers to adherence to the prescribed treatment plan included uncertainty in the correct number of pills, missing the timing as result of disruption of daily routine and running out of pills (Gassmann, Kolbe and Brenner 2016).

c) Medicine adverse events

The adverse effects of treatments manifested in various physical and psychological effects that ranged from mild to life-threatening severity. These included fatigue, nausea and vomiting (Bergkvist and Wengstrom 2006, Komatsu et al. 2016), peripheral neuropathy (Komatsu et al. 2016, Gassmann, Kolbe and Brenner 2016), alopecia and neutropenic infections (Bergkvist and Wengstrom 2006). Psychological adverse effects experienced by patients included emotional distress (Bergkvist and Wengstrom 2006, Gassmann, Kolbe and Brenner 2016, Browall, Gaston-Johansson and Danielson 2006, Komatsu et al. 2016) and mild cognitive impairment described as "empty head" and "fog" (Komatsu et al. 2016) which adversely affected their concentration (Gassmann, Kolbe and Brenner 2016, Browall, Gaston-Johansson and Danielson 2006, Komatsu et al. 2016). Their experience to deal with these adverse events was considered to be one of the most challenging aspects of living with antineoplastic medicines.

> *Very strange and when you say you have cancer, and then you have surgery and, well, then you feel a little bad right afterwards for a while, but it wasn't so complicated, and then you get sick from the chemotherapy, then you get actually sick …* (Browall, Gaston-Johansson and Danielson 2006)

The aspect of "suffering" (Bell 2009) is so ingrained with the experience of antineoplastic medicines that patients did not recognise or underestimated the occurrence of adverse effect of treatment. This affected the timeliness of reporting of adverse effects to healthcare professionals (Yokoyama dos Anjos and Zago 2005, Bell 2009, Reigner Denois et al. 2011, Gassmann, Kolbe and Brenner 2016), with patients waiting a few weeks until their next scheduled appointment with their healthcare professional (Reigner Denois et al. 2011, Gassmann, Kolbe and Brenner 2016). Other issues were shyness to discuss specific intimate adverse effects such as vaginal dryness or feeling uncomfortable to repeat the same adverse effects in each appointment or fearing the possibility of change in treatment regimen potentially adversely affecting their survival (Yokoyama dos Anjos and Zago 2005, Reigner Denois et al. 2011, Gassmann, Kolbe and Brenner 2016) (Browall, Gaston-Johansson and Danielson 2006, Gassmann, Kolbe and Brenner 2016). Others resorted to self-care by resorting to complementary medicine such as phototherapy, homeopathy and hypnotism or home remedies (Browall, Gaston-Johansson and Danielson 2006, Reigner Denois et al. 2011, Gassmann, Kolbe and Brenner 2016).

Quantitative studies reported that rash (86.4%), fatigue (82.6%) and cough (75%) were the most common patient-reported symptoms after 2 months of treatment with erlotinib (Timmers et al. 2015). Similarly, patients complained of hand and foot syndrome (94.5%), fatigue (91.1%) and flatulence (67.9%) after around 4 months of treatment with capecitabine (Timmers *et al*. 2016). At the same time, patients claimed to be calmer and more peaceful as treatment progressed (mean value of the mental component of SF-12 Health Survey improved from 47.1±7.5 at baseline to 50.4±5.4 at cycle 5) (Timmers et al. 2016).

d) Medicine and social burden

Patients felt that treatment with antineoplastic medicines dominated their life with treatment with antineoplastic medicines being their sole focus, adversely affecting their quality of life. Patients described their life revolving in accordance to the treatment outcome.

> *I stopped playing with the orchestra in November of last year. That also has something to do with (name of medication); I got shaky and it had a few other side effects than with (intravenous) chemo.* (Gassmann, Kolbe and Brenner 2016)

> *And then there was the constant worry that the lab tests wouldn't be good so that everything would have to be postponed, and my whole life was about this …* (Browall, Gaston-Johansson and Danielson 2006)

Patients experienced social isolation secondary to changes in relationship with family members and friends as a result of adverse effects, complex treatment regimen and social stigma (Browall, Gaston-Johansson and Danielson 2006, Bergkvist and Wengstrom 2006, Gassmann, Kolbe and Brenner 2016, Komatsu et al. 2016).

> *I used to work every day, so I met people and talked to them. But my everyday life was suddenly shut down. I was confined to my house. I was depressed, lonely, and tearful …* (Komatsu et al. 2016)

Patients described this illness as a challenging experience even for the family as the latter needed to support the patient even if they themselves were still coming to terms with the illness. The family offer paramount support to cancer patients (Bergkvist and Wengstrom 2006, Browall, Gaston-Johansson and Danielson 2006, Komatsu et al. 2016, Gassmann, Kolbe and Brenner 2016), with the role of the spouse often considered as a "lifeline" (Browall, Gaston-Johansson and Danielson 2006).

> *It was naturally, it was enormous dramatic and traumatic for the family, meanwhile, it was insane.* (Browall, Gaston-Johansson and Danielson 2006)

> *My family has become much…closer to me, I have to say; in a way they have helped me very, very much …* (Bergkvist and Wengstrom 2006).

Patients' attendance to support groups was an event they looked forward to; whereby the sharing of inner feeling with other patients with cancer promote positive, strength and induce feeling of unity (Yokoyama dos Anjos and Zago 2005, Browall, Gaston-Johansson and Danielson 2006).

> *There are days when you meet good people in there! I was crying. Then, he calmed me down, talked to me, you know. With me! Then, one feels better, starts to talk and feels better!* (Yokoyama dos Anjos and Zago 2005)

The patients' work and finance were impacted by their treatment with antineoplastic medicines, with the frequency and intensity of adverse effects identified as the contributory factors in discontinuing their work. (Yokoyama dos Anjos and Zago 2005, Browall, Gaston-Johansson and Danielson 2006). Patients remarked feeling pressured from society and healthcare professionals to return to work as early as possible. Those patients who returned to work, particularly in leading roles, agreed that returning to work was much harder than anticipated and instilled inner worry (Browall, Gaston-Johansson and Danielson 2006). Patients were concerned that their employer was expecting the same amount of work to pre-diagnosis and that their work environment could pose health-risk factors due to weakened immune systems as a result of antineoplastic medicines. Contrastingly, the patients who continued to attend to work used it as a coping measure to detach themselves from the illness itself (Yokoyama dos Anjos and Zago 2005, Browall, Gaston-Johansson and Danielson 2006).

> *But then I noticed, and when I came back and started to work full-time my boss came to me and said that this position I had applied for had gone to someone else because I had to think of my illness* (Browall, Gaston-Johansson and Danielson 2006)
>
> *…because when I'm working I don't see the time passing. Finishing the chemotherapy, everything will go better* (Yokoyama dos Anjos and Zago 2005)

e) Healthcare associated medicine burden

Patients obtained the necessary support from the healthcare system but often experienced challenges in relation to the complexity of the healthcare system and the resultant relationships (healthcare professional-patient relationships and patient-patient relationships). Patients with cancer sought for empathy, respect as well as professionalism of healthcare professionals (Browall, Gaston-Johansson and Danielson 2006, Bergkvist and Wengstrom 2006, Reigner Denois et al. 2011).

> *Well the important thing is of course how they care for you, and not that it has to be so incredibly professional so that, that … Empathy is alpha and omega …* (Browall, Gaston-Johansson and Danielson 2006)

Patients remarked that they felt overwhelmed with the information provided about their diagnosis and treatment. Sometimes they felt that healthcare professionals were placing a lot of responsibility at their end by letting them decide on the information they want to receive (Bergkvist and Wengstrom 2006, Reigner Denois et al. 2011, Gassmann, Kolbe and Brenner 2016).

Difficulties related to logistics were raised by patients, particularly those who commuted frequently to hospital to receive parenteral treatment. These include transportation, distance to hospital for multiple visits, hospital waiting time, commitment and financial burden of the caregiver by accompanying them to treatment. These subsequently resulted in reduced patients' enthusiasm when prescribed with long-term maintenance treatment with antineoplastic medicines (Bergkvist and Wengstrom 2006, Gerber et al 2012).

> *I live alone as well, and every time I come for chemo or transfusions I have to have someone bring me. So that would—if I had to come real frequently that would put a hardship on.* (Gerber et al 2012)

Whilst the use of oral antineoplastic medicines spared patients from the frequent experiences of such burden, they remarked that the lack of regular professional support made them feel insecure in self-administration of antineoplastic medicines (Bergkvist and Wengstrom 2006, Gassmann, Kolbe and Brenner 2016).

Given the ongoing oncology research, patients questioned the lack of availability of new treatment options (Gerber et al. 2012). A patient was surprised that his treatment consisted of fluorouracil, a standard antineoplastic medicine that has been used for the past 20 years (Bell 2009.

> *Surely we can do better than that!* (Bell 2009)

3.5. Discussion

3.5.1. Summary of key findings

A number of important key findings were generated from this systematic review with regards to the patients’ lived experiences with antineoplastic medicines for the management of malignant solid tumours. A limited number of studies of acceptable overall quality explored the patients’ lived experiences with medicines incorporating the beliefs, practice and burden with regards the use of antineoplastic medicines.

The studies included in this systematic review did not provide a standard definition of the patients' lived experiences with medicine. Patients’ beliefs about antineoplastic medicines were mainly negative, particularly in relation to the anticipated adverse effects of vomiting and alopecia due to the uncertainty with regards to the efficacy of treatment. These beliefs stemmed from various sources mainly family members, healthcare professionals, media and culture. Studies showed that the use of antineoplastic medicines for the treatment of malignant tumours is highly metaphorised to wartime, with commonly used phrases like “fighting”, “suffering”, “hurting”, “buying time” and “assault”. This further emphasises patients’ perception of a daunting treatment journey.

With regards to medicine-taking practice, patients aspired to take oral treatment precisely as prescribed, at the exact dose and timing of administration, to make sure that they attained the maximum benefit. Patients raised high concerns about any delays or reduction in doses, as they perceived potential increased risk of cancer recurrence. Given that patients often associated adverse effects to be a sign of effective treatment, they were cautious in their self-assessment of severity of the adverse effects. This resulted in delayed reporting of adverse effects to healthcare professionals, with a detrimental risk to patient safety.

Whilst treatment with antineoplastic medicines was considered as hope by some patients, others remarked that the treatment was worse than the illness itself. This may be due to the burden experienced by patients as a result of treatment such as physical, psychological and financial impacts. Some patients refused to attend to social activities to make sure that they took their medicines at the exact time. The development of personalised coping strategies such as reminder methods together with a network of support were critical for the patients to face the medicine-related burden.

3.5.2. Interpretation of findings

This systematic review described the literature available about the patients' lived experience with antineoplastic medicines for the treatment of malignant solid tumours. The number of studies available was limited. Collectively the studies offered an extensive account of the patients' perspectives in terms of the beliefs, practice and burden with the use of different antineoplastic treatment. Findings of this systematic review revealed that PLEM is a highly subjective and complex concept, with a lot of considerations.

Contradictory findings were evident amongst patients' beliefs about antineoplastic medicines in this systematic review, with attempts to make sense of their illness and treatment. As cancer was perceived as a life-threatening illness (Lewandowska et al. 2020), some patients perceived antineoplastic medicines as hope of cure from illness. In fact, patients in the included studies made use of war metaphors when referring to the treatment with antineoplastic medicines in cancer. This further stressed the patients' perception of its difficulty (Passik et al. 2001, Hauser and Schwarz et al. 2020). The influence of media and culture might have ingrained patients' misconceptions and fears further; by prefiguring association of suffering. Findings from this systematic review calls for healthcare professionals to address patients' beliefs on antineoplastic medicines, with the intent to educate them and address misconceptions. Studies should be conducted on patients who refused to initiate or discontinue treatment with antineoplastic medicines so to understand their beliefs, perceptions and attitudes towards treatment.

Oncology is one of the few areas of medicine where the use of parenteral medicines persisted despite the introduction of oral medicines (O'Neill and Twelves 2002). This systematic review described patients' experiences with both oral and parenteral antineoplastic medicines. Patients associated the use of oral formulations to treat mild forms of cancers compared parenteral administration of medicines (Bell 2009). The rationale for breaks between cycles was rarely understood by patients, giving rise to various interpretations. Patients associated these breaks with periods of relief and freedom from constraints to the medicine plan or as burdensome periods with worsening of adverse effects and fear of recurrence. This emphasised the importance of educating patients and encouraging them to take more active role in their cancer treatment (Reigner Denois et al. 2011). Informed decision-making is even more important in patients who are offered oral treatment options, as this calls for an autonomous behaviour in terms of adherence as well as identification and self-management of adverse effects.

Patients receiving antineoplastic medicines reported a myriad of physical and psychological effects. As a result, treatment with antineoplastic medicines was claimed to transform and even dominate the patient's social and family life. Besides the support provided by family members, peers, support groups and healthcare professionals, the patients identified the need to develop their own coping skills (Komatsu et al. 2016). Studies emphasised the importance of the provision of holistic care to vulnerable patients, taking into consideration their physical, psychological, social and spiritual well-being. Furthermore, development and implementation of educational and motivational strategies shall be explored to address issues particularly treatment burden.

Patients are experts by experience as they provide a unique perspective on their disease and required care. The understanding of the patients' experience with the antineoplastic medicines sheds light on the patients’ needs and support services needed during this journey. This will ultimately lead to better health outcomes and improved quality of healthcare services.

3.5.3. Comparison of the adapted PLEM model to the original PLEM model

None of the published studies included in this systematic review made use of the PLEM model or presented a standard definition of PLEM. As elicited by this systematic review, this may be due to the fact that PLEM is a highly subjective and complex concept taking into consideration various aspects in relation to medicines use. Given that the findings generated from this systematic review about antineoplastic medicines fitted into the conceptual PLEM model (Mohammed, Moles and Chen 2016) originally developed for medicines used for acute and chronic conditions, indicated that this model was likely to be transferrable to the oncology setting with minimal modifications.

As shown in Table 3.7, which compares the original PLEM model to the adapted model for the oncology setting, findings from the studies included in this systematic review supported nine out of the ten themes. Specific amendments to the original conceptual model of Mohammed, Moles and Chen (2016) included:

- the removal of the theme *medicine-related burden magnitude and coping skills* with regards to medicine-related beliefs
- the inclusion of media and culture within the theme *family, peers and healthcare professionals*
- the inclusion of sub-themes within the model to promote readers' comprehension
- the term medicine was used throughout this systematic review to ensure consistency

Table 3.7: Comparison of original PLEM model to adapted PLEM model to oncology setting

Original PLEM model (Mohammed, Moles and Chen 2016)	Adapted PLEM model to oncology setting
Medication related beliefs	
Family, peers and healthcare providers	Family members, healthcare professionals, media and culture influence
Medication related burden magnitude and coping skills	x
General attitude	General attitude towards medicine
Medication taking practice	
Accepting medicine	Accepting medicine
Modifying or altering medicine	Modifying or altering medicine regimen or dose
Medication related burden	
Medication routines	Medicine routine
Medication characteristics	Medicine characteristics
Medication adverse event	Medicine adverse events
Medication and social burden	Medicine and social burden
Healthcare and medication	Healthcare associated medicine burden

x – this sub-theme was not included

3.5.4. Strengths and weaknesses of the systematic review

This systematic review has several strengths. A protocol for this systematic review was developed in accordance with PRISMA-P (Moher et al. 2009) and registered with PROSPERO. A systematic and extensive search strategy was employed in six databases starting from their respective date of inception to consider all relevant literature. A random sample of 10% of the retrieved titles and abstracts, the quality assessment and data extraction of all the included studies were performed by two independent reviewers. These steps improved reliability and enhanced methodological rigour.

This systematic review has its limitations and so the findings should be interpreted with caution. The restriction of the search to publications in the English language might have limited the inclusion of other potentially relevant papers published in other languages. Various confounding factors arising from the individual studies such as patient characteristics including cancer type and antineoplastic treatment regimen and time-points in the treatment journey may have affected the findings. Variations in healthcare system in different countries and cultures may have increased complexity of the results. This systematic review relied on secondary data and combined data from studies with different research designs and of variable quality resulting in a potential element of bias. In the absence of a standard definition of PLEM, the conceptual PLEM model (Mohammed, Moles and Chen 2016) composed of three inter-related themes was adopted.

The inclusion criteria were restricted to studies which considered all the three themes (medicine-related belief, practice and burden).

3.6. Implications for next phase of research

The systematic review identified limited literature in exploring PLEM in terms of beliefs, practice and burden to antineoplastic medicines. It became evident from this systematic review that patients tend to undergo a continuous process of reinterpretations of their situation during the treatment journey. Given that the majority of qualitative studies were cross-sectional studies, the systematic review could not illustrate the changes in patients' beliefs, practice and burden longitudinally along the treatment journey with antineoplastic medicines. This may also indicate the patients' specific needs at particular timepoints during the treatment journey may not have been adequately addressed.

The next phase of research attempted to address these gaps by performing a primary longitudinal qualitative study in Malta which focus on the exploration of patients' lived experience with antineoplastic medicines at different time-points during the treatment journey (Chapter 4). The adapted conceptual PLEM model was used as a theoretical underpinning for evaluation of the patients' experience with treatment.

In view that the systematic review revealed that patients relied heavily on support provided from other individuals, a parallel longitudinal qualitative study was conducted to study significant others perception of the patients' lived experience during treatment with antineoplastic medicines
(Chapter 5).

Chapter 4

Patients’ lived experience with antineoplastic medicines: a longitudinal study from the perspective of patients

(Phase II)

4. Introduction to the chapter

This chapter provides a detailed description of a longitudinal qualitative study of the patients' lived experience with antineoplastic medicines during and after the treatment journey. Antineoplastic medicines are the mainstay of treatment for patients with colorectal cancer as neo-adjuvant, adjuvant or palliation (Aschele, Bergamo and Lonardi 2009, Weeks et al. 2012). Despite this, no published literature has employed a longitudinal qualitative methodology to provide an in-depth exploration of the beliefs, practice and burden regarding the use of antineoplastic medicines in colorectal cancer along the treatment journey. Within this chapter, the research aim and objectives of this phase of research are stated, followed by an overview of the method, a comprehensive account of findings and discussion.

4.1. Research aim and objectives

The aim of this phase of the research (Phase II) was to explore longitudinally the patients' lived experiences with antineoplastic medicines for colorectal cancer during the treatment journey and beyond.

The specific research objectives of this longitudinal study in the context of treatment with antineoplastic medicines for colorectal cancer were to:

- Explore the patients' beliefs and knowledge of antineoplastic medicines
- Explore the patients' medicine taking practice of antineoplastic medicines
- Explore the burden experienced by patients with colorectal cancer during treatment with antineoplastic medicines and beyond

4.2. Method

4.2.1. Study design

A longitudinal qualitative phenomenological study was conducted on 16 patients using four serial semi-structured interviews at regular intervals over 36 weeks. The semi-structured interviews were based on the PLEM conceptual model adapted to the oncology setting published by Brincat et al. (2020) and discussed in Chapter 3. Given that little was known about this topic, the qualitative approach was chosen to explore the patients' beliefs and knowledge, medicine-taking practice and burden of antineoplastic medicines. This was considered as the most appropriate approach with regards to the research aim and objectives, with justification provided in Chapter 2.

4.2.2. Setting

The study took place at Sir Anthony Mamo Oncology Centre, the only oncology hospital within the public healthcare system in Malta with 113 beds catering for almost 1,400 new cases annually (Micallef 2015). Of these, around 260 persons are diagnosed with colorectal cancer every year (Ministry for Health 2021[b]).

The first three interviews with the patients (interviews 1, 2 and 3 were undertaken at Sir Anthony Mamo Oncology Centre. The last interview (interview 4) took place either at Sir Anthony Mamo Oncology Centre or at the patients' home, depending on the patient's preference.

4.2.3. Inclusion and exclusion criteria

Patients aged ≥18 years diagnosed with colorectal cancer who received either FOLFOX or XELOX for the first time as part of either 12 or 8 treatment cycles respectively were included in the study implying all were naïve to antineoplastic medicines. They also had to be fully aware of their diagnosis and treatment following consultation with their oncologist. This was evidenced by the signed patient's declaration form of informed consent available in the patient's medical records.

Patients were excluded from the study if they had a history of past treatment with antineoplastic medicines or were unable to communicate in English or Maltese.

Participation in the follow-up interviews proceeded even if there had been modifications to the FOLFOX or XELOX treatment protocol, for instance addition of immunotherapy. Patients were excluded from the study if their treatment with antineoplastic medicines was discontinued.

4.2.4. Recruitment of participants

The sampling frame included all patients within the national oncology centre meeting the inclusion and exclusion criteria between October 2018 and September 2019. All patients receiving antineoplastic medicines for colorectal cancer were recorded by the nursing staff. A list of the contact details (name, identification number and date of appointment to receive the first treatment cycle) of all patients who were eligible to participate in the study was collated by the research student. Though the research student had access to such data as part of her day-to-day work, permission to make use of this data for the study was granted by the Data Protection Office of the hospital. Purposive sampling strategy was used, as described in Chapter 2, to select patients with a diversity in demographic characteristics (age, gender, marital status) undergoing treatment with antineoplastic medicines for colorectal cancer with either curative or palliative intent.

4.2.5. Development of data generation tool

The semi-structured interview guide was developed in both Maltese and English. It was underpinned by the conceptual PLEM model adapted for the oncology setting. The draft interview guide was submitted for critical review to a panel of experts of three healthcare professionals with special interest in oncology, psychology and qualitative research methods. They ensured questions were understandable and met the research objectives. Minor modifications were recommended to question sequencing and wording. The final semi-structured interview guide was piloted on four patients recruited under identical conditions to the main study. As no major changes to the interview guide were necessary following the pilot study, the data generated was incorporated in the actual study. The final interview guide is presented in Table 4.1.

In addition, patients were also invited to keep a diary (Appendix 4.1) to record any event that they deemed as important. The patient diary was developed by adapting the capecitabine treatment diary developed by Faithfull and Deery (2004) and the chemotherapy side effects worksheet developed by the American Cancer Society (2018). Though the patient diary was kept simple and generic, only three participants filled it in. Those patients who filled in the diary used it as an aide memoire to ensure they mentioned specific episodes in the interview.

Table 4.1: The interview guide for the patients

PLEM major themes from original model (Mohammed, Moles and Chen 2016)	**PLEM themes from the adapted model*** (Brincat et al. 2020)	**Interview questions**
Medicine-related beliefs	Family members, healthcare professionals, media and culture influence	What does the term 'chemotherapy' mean to you? Can you describe the thoughts and feelings you experienced when you were informed that you will be starting treatment with chemotherapy? What do you think has shaped your thoughts and feelings around chemotherapy?
	General attitude towards medicine	What do you think the benefits of chemotherapy will be?
		What are your main concerns about starting chemotherapy?
Medicine taking practice	Accepting medicine	Have you been explained how you shall be receiving the chemotherapy?
		Do you have a network of support (family members, friends, support groups)? How do they help you?
Medicine-related burden	Medicine characteristics	Are there any aspects of chemotherapy such as the pharmaceutical form (intravenous or oral formulation), colour or size of the tablet, infusion time that might affect you?
	Medicine routine	Do you envisage any problems to follow the treatment schedule as prescribed?
	Medicine adverse events	Do you know when to report side effects to the doctor or other healthcare professionals?
	Medicine social burden	Do you feel that chemotherapy will have an impact on your daily life?
	Healthcare associated medicine burden	What are your experiences with the healthcare system?

*Questions pertaining to theme 'Modifying or altering medicine regimen or dose' as part of 'Medicine taking practice' was not included in this interview guide as the patients were interviewed at initiation of their treatment with antineoplastic medicines.

4.2.6. Amendments to the data generation tool for follow-up interviews

The semi-structured interview guide was used at different time points, with minor amendments made to the structure of the questions to reflect the time of interview as outlined in Table 4.2. The use of the interview guide ensured that all patients were given the opportunity to elaborate on the same open-ended questions at different time-points.

Table 4.2: Amendments carried out on the interview guide

PLEM major themes from original model (Mohammed, Moles and Chen 2016)	**PLEM themes from the adapted model** (Brincat et al. 2020)	**Interview questions**
Medicine taking practice	Accepting medicine	Were you explained how you shall be receiving the chemotherapy and any supportive medicines? How would you describe your experience of taking chemotherapy? Can you tell me how do you follow your treatment schedule for oral and/or intravenous chemotherapy? Do you have a network of support (family members, friends, support groups)? How do they help you?
	Modifying or altering medicine regimen or dose	Have you ever experienced any dosing adjustment in the treatment by the doctor?

4.2.7. Data generation

The data generation process followed in this study is portrayed in Figure 4.1.

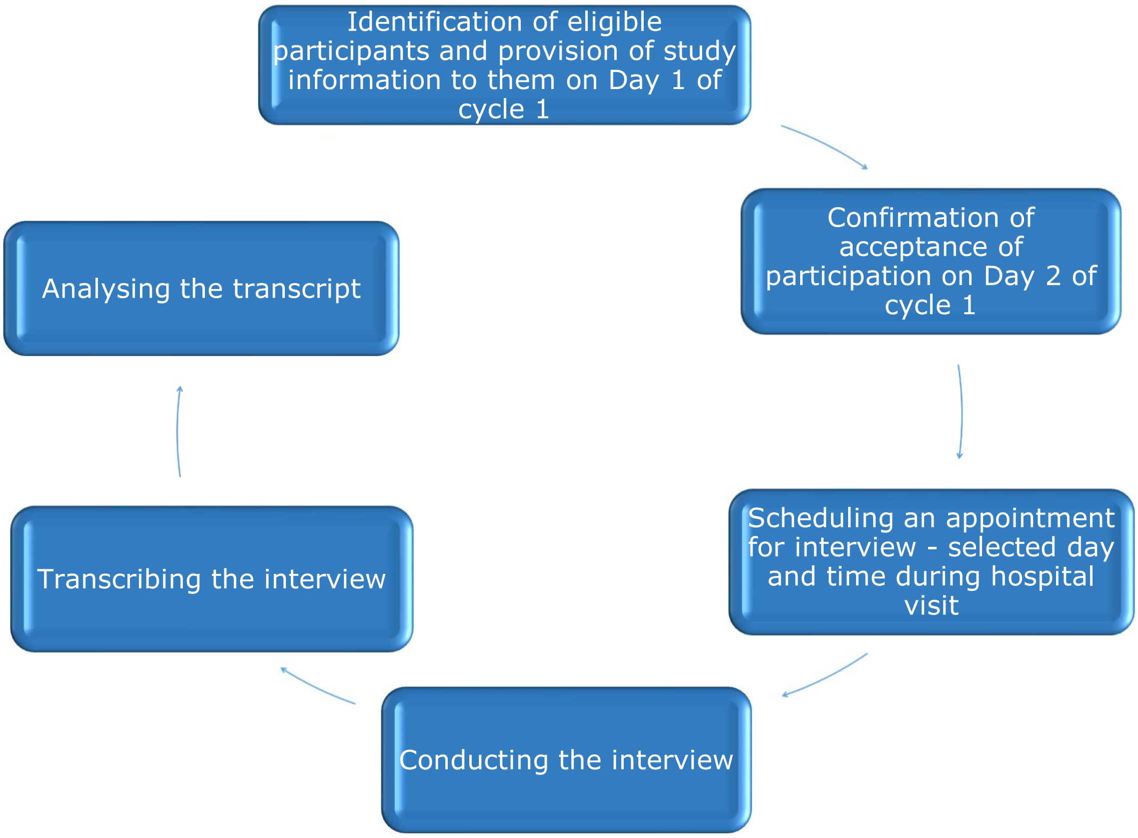

Figure 4.1: Data generation process

Each potential participant was approached by the research student to participate in this study and a detailed explanation about the study was provided using the participant information leaflet (Appendix 4.2). If the patient was interested in participating, an appointment was organised at a time convenient for the patient.

Prior to commencing each interview, patients were reinformed about the aim and objectives of the study as outlined in the participant information leaflet. They were also reminded that their participation was voluntary with all the information disclosed being treated as confidential. Additionally unique participant codes were used to protect the patient’s identity. Patients were also advised that if the information disclosed was suggestive of risk of harm to self or if they become visibly distressed, then the interview would be terminated and their oncologist would be informed accordingly.

Considering the sensitivity of the research topic, participants were able to receive individualised psychological counselling by the hospital's psychologist upon request. A signed informed consent (Appendix 4.3) was obtained from each participant prior to the first interview and verbally re-affirmed prior to each interview.

Interviews were intended to last approximately 40 minutes and were digitally audio recorded using a portable voice recorder to allow all data to be captured fully. These semi-structured interviews were conducted face-to-face in the presence of the patient and interviewer. Patients were allowed to participate in whichever language they felt more comfortable, Maltese or English, to aid better expression of their experiences and views. Efforts were made to reduce interviewer bias by having the same interviewer for all interviews and using an interview guide as described in Chapter 2.

For subsequent interviews, patients who participated in interview 1 at initiation of treatment were approached by the research student to continue their participation in this study. If patients were interested to continue their participation, appointments for subsequent interviews were made by phone two weeks in advance. The follow-up interviews were conducted every 12 weeks from initiation of treatment (interview 1), as follows:

- mid-treatment with antineoplastic medicines at cycle 6 of FOLFOX or cycle 4 of XELOX (interview 2)
- upon completion of antineoplastic medicines at cycle 12 of FOLFOX or cycle 8 of XELOX (interview 3)
- 12 weeks after completion of antineoplastic medicines (interview 4)

All interviews were transcribed verbatim by the research student in a denaturalised approach onto a securely stored, password protected document. A 10% sample of transcripts were randomly selected using randomizer.org and cross-checked by a person independent to the study to ensure accuracy of transcription.

4.2.8. Data analysis

Data analysis was carried out in the original language of the transcripts using Interpretative Phenomenology Analysis. The steps outlined by Smith, Flowers and Larkin (2009) were followed as described in detail in Chapter 2 and summarised in Figure 4.2. An idiographic stance was adopted by first understanding the lived experience of each patient at individual level prior to analysing the similarities and differences to the group of participants. Also, all transcripts at interview 1 were analysed prior to moving onto the subsequent interviews. Transcripts of participants who did not complete interviews at all timepoints were still included in the analysis. Analysis of each transcript was conducted independently by the research student (AB) and a member of the research team who is also a Maltese native speaker (PVB), to promote confirmability. Any disagreements were resolved through discussion and documented to ensure an audit trail which strengthened dependability.

Figure 4.2: Stages of interpretative phenomenological analysis (Smith, Flowers and Larkin 2009)

In summary, each transcript was read multiple times to allow the researcher to immerse in the data. This then followed a line-by-line analysis, which led to initial noting and identification of preliminary codes. Any interpretations were noted as memos. All codes generated during analysis of the transcripts were collated in a table in electronic document using Microsoft Excel®. Codes were then organised into themes with common meanings. Regular meetings were held with the research team to discuss, review, and refine the initial themes into a final list of themes and sub-themes. A narrative account was then written with similar experiences grouped together. Interpretation of the themes and sub-themes were substantiated using illustrative quotations. Quotations in the Maltese language were translated into the English language by the research student, followed by reverse-translation by another member of the research team (PVB or AT) to ensure the precise contextual meaning of the original quotation. The translation has been kept as literal as possible, except where minor modifications were necessary to preserve the conversational style. A longitudinal presentation was developed for each theme to highlight the identified key point(s) at each time-point during the treatment journey. Besides, a visual representation was developed to portray the changes in the relative importance of the sub-themes throughout the treatment journey.

4.2.9. Research governance

Ethical approval (Appendix 4.4 and 4.5) was obtained from:

- Ethics Research Committee, School of Pharmacy and Life Sciences, Robert Gordon University, Aberdeen UK (Approval reference S131)
- Health Ethics Committee, Ministry for Health, Malta (HEC reference number 12/18)

Governance approval for access to patient's records and conducting the study at the oncology centre (Appendix 4.6) was sought from:

- Chief Executive Officer of Sir Anthony Mamo Oncology Centre
- Data Protection Office
- Quality Assurance Office
- Chair of Oncology and Haematology Department
- Oncology Consultants

All approvals were in place prior to recruitment of participants and conduction of interviews. The General Data Protection Regulation (Regulation (EU) 2016/679) of the European Union, in conjunction with the Data Protection Act 2018 (UK) and the Data Protection Act 2018 (CAP 586) (Malta) were adhered to.

4.3. Results

4.3.1. Participant demographics

A total of 19 patients were approached and 16 patients were recruited since 3 patients refused to participate in the longitudinal study in view of the long term commitment. Interviews took place between October 2018 and March 2020. These lasted an average of 55 ± 10 minutes.

From a total of 16 patients agreeing to participate in the longitudinal study, ten patients completed the final interview (interview 4) at 36 weeks. A total of 54 transcripts were analysed for this longitudinal study. An overview of the completed interviews is shown in Table 4.3 with reasons for participants' attrition documented. Due to the outbreak of the Covid-19 pandemic in Malta on the 7th March 2020 and a subsequent visitors' ban for all hospitals, it was not possible to conduct the final three face to face interviews of the study.

Table 4.3: Overview of the interviews conducted

Patients	**Interviews**			
	1	**2**	**3**	**4**
P001	√	√	√	√
P002	√	√	√	√
P003	√	√	√	√
P004	√	√	√	√
P005	√	√	√	√
P006	√	√	√	√
P007	√	√	Discontinued antineoplastic treatment	Discontinued antineoplastic treatment
P008	√	√	√	√
P009	√	√	Discontinued antineoplastic treatment	Discontinued antineoplastic treatment
P010	√	√	√	Deceased
P011	√	√	√	√
P012	√	√	√	√
P013	√	√	Withdrawn	Withdrawn
P014	√	√	√	√
P015	√	√	√	COVID suspension
P016	√	√	COVID suspension	COVID suspension
Total	**16**	**16**	**12**	**10**

√ Interview completed

Most participants were females (n=10, 63%) with a mean age of 62 ± 10.89 years (range 38-78 years). All patients except one received FOLFOX; with 9 patients (56%) receiving antineoplastic medicines as adjuvant treatment. Most patients (n=9, 56%) received treatment with curative intent. Demographic characteristics of patients are outlined in Table 4.4.

Table 4.4: Demographic characteristics of patients

Participant	Gender	Age (years)	Prior treatment	Antineoplastic treatment planned	Intent of treatment	Educational level	Employment	Marital status	Lives (with)
P001	Male	68	Surgery	FOLFOX	Curative	Secondary	Pensioner	Single	Sister
P002	Male	46	-	FOLFOX	Palliative	Secondary	Unemployed	Single	Parents
P003	Female	69	Surgery	FOLFOX	Curative	Primary	Housewife	Married	Spouse
P004	Female	61	Surgery	FOLFOX	Curative	Secondary	Full-time (stopped for treatment)	Divorced	Children
P005	Female	78	-	FOLFOX	Palliative	Primary	Pensioner	Single	Alone
P006	Female	61	-	FOLFOX	Curative	Secondary	Full-time (stopped for treatment)	Married	Spouse
P007	Male	38	Surgery	XELOX	Palliative	Postgraduate	Full-time	Married	Spouse
P008	Female	53	-	FOLFOX	Curative	Secondary	Full-time (stopped for treatment)	Single	Alone
P009	Female	67	Surgery	FOLFOX	Curative	Secondary	Pensioner	Married	Spouse
P010	Male	65	Surgery	FOLFOX	Palliative	Secondary	Pensioner	Married	Spouse
P011	Female	48	-	FOLFOX	Palliative	Secondary	Full-time (stopped for treatment)	Separated	Children
P012	Female	71	Surgery + stoma	FOLFOX	Curative	Primary	Pensioner	Married	Spouse
P013	Female	71	-	FOLFOX	Palliative	Secondary	Housewife	Married	Spouse
P014	Female	63	Surgery + stoma	FOLFOX	Curative	Secondary	Housewife	Married	Spouse
P015	Male	73	-	FOLFOX	Curative	Secondary	Pensioner	Married	Spouse
P016	Male	59	Surgery	FOLFOX	Palliative	Secondary	Full time (self-employed)	Married	Spouse

4.3.2. Themes

Five themes and 15 sub-themes were generated from the analysis of interviews with the patients to describe their experience with antineoplastic medicines. These are summarised in Table 4.5.

Table 4.5: Themes and sub-themes identified from the interviews

Themes	Sub-themes
Perceptions and knowledge of the illness and treatment	Perceptions about illness and treatment
	Knowledge about illness and treatment
	Influences on attitudes and knowledge about illness and treatment
The healthcare system in relation to the illness and treatment	Experiences of patients of cancer services as part of the healthcare system
	Healthcare professionals' communication with patients
	Recommendations for services
Patient's involvement in treatment decision-making and their experience of medicine-taking	Influences on acceptance of treatment
	Experiences of administration of antineoplastic medicines and other medicines
Medicine and illness-related impact on patients	Impact of physical effects on patients
	Impact of psychological effects on patients
	Social consequences for patients
	Implications on financial status
	Seeking refuge in spirituality and religion
Personal support structure	Establishing a support network
	Self-regulation as a coping strategy

4.3.2.1. Theme 1: Perceptions and knowledge of the illness and treatment

4.3.2.1.1. Sub-theme: Perceptions about illness and treatment

Perception of illness and its presentation

At the start of treatment, all patients lacked experience of living with colorectal cancer together with the use of antineoplastic treatment. Hence, their comments were mainly based on their perceptions of the illness and its treatment. As treatment progressed and as reflected in subsequent interviews (interviews 2, 3 and 4), all patients gained knowledge through their own personal experience, information given and from others' experiences; this altered the balance between their perception and knowledge which shifted more towards knowledge.

Irrespective of when interviewed, most patients perceived cancer as a serious illness with a potential fatal outcome resulting in fear and anxiety.

> *I know a lot of people who take the news of cancer and treatment with chemo really badly due to its associated stigma, which is then worsened by fear and anxiety … if you're diagnosed with cancer, then you have a death sentence. Unfortunately, this is a common remark made by the public.* [P006-1]
>
> *[After receiving a cancer diagnosis]*[d] *It is a period in one's life where you feel that the world has stopped and feel unable to make any long-term plans.* [P001-4]

At initiation of treatment, most patients expected cancer to present with serious symptoms such as rectal bleeding. However, later they themselves realised that they experienced non-specific symptoms such as altered bowel habits, persistent abdominal pain and vomiting. This occasionally led to misdiagnosis, with the diagnosis of colorectal cancer being confirmed later upon conducting further investigations. Patients claimed that this situation resulted in a lack of preparedness for them to face the truth of the actual diagnosis and hence this led to a greater shock and distress.

> *That was a shock … My family doctor had already assured me that it was highly suggestive of trapped wind.* [P010-1]

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[d] [] indicates words that were not spoken by the participants but have been included by the research student for clarity and to aid contextualisation.

As treatment progressed, some patients questioned the invisibility of the illness. They expected that colorectal cancer would have an impact on their physical appearance; characterised by them looking sick, thin, frail and depressed. Patients also considered that this misperception even applied to individuals around them.

> *At face value, one cannot notice that they have encountered a sick man. So it's very strange for someone else to consider me as a sick person unless I tell them. People portray a sick individual as a thin weak person. On the other hand, my weight is fine and I'm still always laughing … this is how the image deceives you.* [P007-2]

Some patients expressed their concern about the high prevalence of cancer. In fact, most of them knew someone with cancer.

> *This* [Cancer] *has become common. It has become common like the flu … almost everyone you speak to, knows someone who has it.* [P001-3]

Perception of treatment of colorectal cancer

When patients were advised to start treatment with FOLFOX or XELOX, they felt *"devastated"* [P013-1]. This initial shock worsened upon being informed of the need to receive 12 cycles of treatment with FOLFOX or 8 cycles of XELOX, with some patients assuming that the more treatment cycles, the more advanced the illness and the worse the prognosis.

> *I think that the more cycles I require, the more aggressive it* [the cancer] *is … Hopefully I'll soon be making progress.* [P013-1]

At the last cycles of treatment, patients realised their misconception and that in reality the number of cycles were pre-set in line with evidence-based research.

> *Having a six-month treatment seemed a very long journey for me. At first, I thought that the high number of cycles reflected the severity of my illness. But now I noticed that I was wrong.* [P002-4]

Treatment of cancer with antineoplastic medicines brought "*fear of the unknown"* [P014-1] due to the general view of the high toxicity profile of treatment. However, patients were still motivated to embark on treatment with the belief that benefit of achieving cure would outweigh the risks.

> *Nothing beats the cure from cancer! … not even the worst adverse effect I may experience.* [P016-1]

Another misconception held particularly at the start of treatment by a few patients was that their small body frame would make them unable to tolerate the effects of treatment. The patient's own experience made them realise their false perception as treatment progressed.

> *Initially I was afraid, as this type of treatment was new to my body. I have a small body frame so I was more afraid that such a long treatment would be too much for me.* [P014-3]

Prior to initiation of treatment, all patients assumed that all antineoplastic medicines caused alopecia and that their physical activity and independence would be adversely affected due to treatment-associated fatigue.

> *I thought about my hair … I was really worried that I would experience hair loss and become bald.* [P009-1]

As treatment progressed most patients realised their misconception about alopecia and fatigue. Though some patients claimed to experience hair thinning during treatment, they were pleased to observe improvement in hair volume and texture following completion of treatment. Similarly, as treatment progressed most patients did not experience debilitating fatigue, as expected prior to onset of treatment.

> *I did not experience hair loss with chemo and my hair remained in a good condition. I think now I have more hair volume and it became thicker*. [P012-4]

> *At the beginning of the treatment I was concerned about fatigue as I used to hear my friend who received chemotherapy complaining of lethargy. Thankfully it did not affect me so badly.* [P003-4]

Along the treatment journey, a few patients realised that there were different modalities of treatment and these depended on the cancer stage. They also understood that there were several antineoplastic medicines and treatment regimens that led to different adverse effect profiles.

> *I know a friend of mine with cancer who had undergone only surgery ... However, I met another patient here who told me that he did not undergo surgery but received only chemotherapy. I think that if no surgery was done, this inferred a bad cancer stage. A friend of mine is now receiving concurrent chemotherapy with radiotherapy and receives treatment on a day care basis. [P016-2]*

Perceptions of the treatment journey

The treatment journey with antineoplastic medicines was initially perceived as challenging and long, with one of the patients comparing it to "*climbing up a hill"* [P002-1]. Some patients felt a sense of personal achievement at a later stage, in being able to overcome the challenges and making it through the first half of the treatment journey. A few patients assumed that they would not be experiencing any new issues with subsequent cycles, having made it through the first few cycles without experiencing their perceived serious complications, mainly alopecia and debilitating fatigue. At cycle 6 of FOLFOX, a participant described that he "*reached the summit and will now be walking back down the slope, as the remaining number of cycles are decreasing"* [P002-2]. With every treatment cycle, some patients' initial fear about the use of antineoplastic medicines was subsiding. Their outlook on treatment generally turned more positive and their ability to cope with the treatment improved.

> *Along the cycles, I was visually noticing improvement in myself and also feeling physically better. Even the investigations showed this. Hence I'm feeling more positive.* [P014-2]

At completion of treatment, a few others were querying whether their current weak body would still be able to tolerate other long treatment courses of antineoplastic medicines including second line treatment.

> *If the oncologist prescribes chemo again for me, I don't think it will consist of another dozen as I don't think my body would tolerate further chemo? It can be 3 or 6 cycles … or none at all?!* [P002-3]

As patients approached the end of the treatment journey with antineoplastic medicines, most patients together with their families hoped and sought a return to their former daily routine. These patients had huge yearning for normality.

> *I tell myself that healthcare professionals are providing me with the necessary care to be cured … I'm looking forward to finish the treatment to regain my health and resume my routine and continue from where I left. My physical strength is adversely affected with chemotherapy.* [P012-3]

At initiation of treatment, all patients expected a complete cure from cancer and hoped for a long-term survival. At the end of treatment, some patients were still hoping that complete cure can be achieved whilst others had different perceptions and hopes in relation to the recurrence of cancer following treatment with antineoplastic medicines. Some patients realised that they had to live with cancer, similar to other chronic conditions. Likewise, their illness could still be controlled with the use of long term treatments.

> *I see chemotherapy as the cure of an illness. As from the start of treatment I felt that chemotherapy will cure me. It gives me hope*. [P012-4]

> *I was reading that recurrence of colorectal cancer within the first 5 years is rare, though it can happen after the 5 year period. So then I understood why we were advised to keep the port-a-cath for 10 years!* [P004-3]

When some patients had their treatment changed from first-line to second-line treatment with antineoplastic medicines, they realised that cure was unlikely to be achievable. A patient presumed that his second-line treatment was more potent in comparison to FOLFOX as the new treatment regimen consisted of 8 cycles instead of 12 cycles. The fact that the dose had to be decreased because of episodes of nausea emphasised this patient's initial thought.

> *This time the oncologist suggested 8 cycles of chemo to be taken at the day ward as I think it is more potent. In fact, its first cycle made me feel terrible and they had to lower the dose in its second cycle so as to be milder. Though I was still in my first cycle, I had to take anti-nausea tablets regularly at home.* [P002-4]

4.3.2.1.2. Sub-theme: Knowledge about illness and treatment

Knowledge about the illness

Unlike the start of the treatment journey where patients mainly had perceptions about illness, their knowledge was noted to increase along the treatment journey with some patients gaining knowledge through healthcare professionals.

> *When they first told me that it's cancer, they did not tell me where it is. I enquired whether it is in the lungs due to cigarette smoking but was informed that it was in the colon. I repeated to question whether this was related to cigarette smoking. However, to my surprise, I was told that cigarette smoking had nothing to do with it*. [P010-3]

> *The doctor told me to repeat the colonoscopy after 3 years as a screening test … then he asked me whether I have any children or siblings? He urged me to encourage them be tested too as the illness might be related to our genes*. [P001-3]

Knowledge about treatment of colorectal cancer

Prior to initiation of treatment with antineoplastic medicines, it is apparent that patients consented to treatment without having all the required knowledge. Some patients who started treatment with FOLFOX or XELOX were still not aware of the route and method of administration of treatment as well as the dosing of treatment which they were to receive. Very few patients expected that antineoplastic medicines would emit radiation.

> *I had no idea of what the treatment involved … but the procedure how to take the medicines was explained to me [by the oncologist] … I know that I need to take 2 tablets [capecitabine] but I do not know exactly the schedule of treatment or how they work.* [P007-1]
>
> *What does it contain? Radiation? Does it emit any form of radiation?* [P014-1]

Patients found difficulty with understanding the various stages of cancer and the respective management. Some patients were not aware that they would require antineoplastic medicines after undergoing successful surgery.

> *The fact that the polyp was surgically removed, I thought that no further treatment was required. Then when I attended the last follow-up, the consultant told me … to better receive chemotherapy … I wasn't expecting this!* [P004-1]

As treatment progressed, the patients understood better the rationale behind the use of antineoplastic medicines.

> *From what was explained to me [by the surgeon and oncologist], my surgery was successful but a gland taken during the surgery was found to contain cancer. So, I learnt that this chemo is necessary to destroy any remaining traces of cancer and lowers the risk of cancer coming back in the future.* [P003-2]

As from initiation of treatment, most patients showed a poor level of health literacy, with none of the patients recalling at least the name of the treatment protocol provided. They referred to treatment as "chemotherapy" throughout. This low level of health literacy could also lead to patient safety issues; for example, a patient, who was allergic to teicoplanin, was shocked to realise that she was receiving oxaliplatin as she confused the two because of the similarity in names.

> *What does this bag contain?!* [Oxaliplatin] *Because there's a drug which I am allergic to, it is written on my bracelet, look.* [There was written Teicoplanin, an antibiotic] *That's ok then … as both words end similarly -plat(n)in!* [P008-1]

During the administration of the antineoplastic medicines at cycle 1, almost none of the patients knew that they may also need supportive medicines at home.

> *No one mentioned anything about medicines that I may be taking at home till now.* [P004-1]

Patients' knowledge of receiving concurrent antineoplastic treatment and supportive medicines improved along the treatment journey. However, patients were still unable to distinguish between the infusion bags containing antineoplastic medicines and those with supportive medicines even though infusion bags were labelled. Patients appeared to prefer to be informed of the treatment they received during its administration. This enhanced their understanding of treatment and contextualised what had been explained to them by their consultant or during the information session.

> *I always have to enquire with the nurses what medicine is being administered. Prior to attaching the bags, they ask me to confirm my personal details. When they give me the tablets, they just tell me 'You have the tablets here.' I prefer to be provided with further details at these instance as I will be understanding better what is happening.* [P003-2]

Their lack of knowledge at initiation of treatment also applied to drug-food interactions, with a few patients not reporting any concurrent consumption of herbal medicines and vitamins or food allergies. They were unaware of the implications of withholding such information from the healthcare professionals.

> *My wife read that ginger is beneficial to combat cancer but I don't like it. Ginger with food is awful for me! So, she bought me pills containing ginger to mask the taste. I've started ginger pills and Vitamin C to prevent me from catching a cold. Being herbal treatment, there's no need to tell the doctor.* [P016-1]

Patients also showed lack of knowledge about the irreversibility of adverse effects such as peripheral neuropathy.

> *The fact that I'm experiencing irreversible side effects, it is a shock! It is like you're curing one area but at the same time, other areas are getting damaged. It is like you're being dissolved from the inside. Whilst curing one thing, you're damaging the others!* [P004-4]

Patients were also surprised with the complications arising following completion of treatment such as new onset of pain and cataracts, describing the treatment journey to '*opening a Pandora's box*' [P004-4].

Knowledge about patients' rights and charter

Throughout the treatment journey, knowledge of the patient's charter relating to service provision and outlining patients' rights and responsibilities was noted to be lacking amongst almost all patients. In fact, a few patients were annoyed when healthcare professionals asked them routine questions such as consent to blood transfusions as they did not understand the rationale behind the questions.

> *Do I have any rights as a patient?! I'm not aware of any. No one has ever spoken to me about them.* [P003-3]

> *That's why I told him that I don't want to know anything except to give me the best possible care. The oncologist then asked me whether I would like to receive blood transfusion? What type of questions are these? … Certainly, I would like to receive blood!* [P006-3]

Knowledge about cancer research

Patients did not mention anything about cancer research at initiation of treatment. As treatment progressed, some patients acknowledged the importance of research in the development of new cancer treatments and considered themselves as its ultimate beneficiaries. The patients showed their willingness to know about the availability of treatment options under research. They considered that treatment was still not optimal and that more research was still needed.

> *Researchers are doing their utmost to understand and find solution to this illness. Scientists can guide us as otherwise we cannot find the cause of cancer. [P008-3]*

> *I don't think the public is aware of what is happening in terms of research. I think researchers have been trying to cure it because the disease has been with us for quite a long time.* [P005-4]

4.3.2.1.3. Sub-theme: Influences on attitudes and knowledge about illness and treatment

Influence of the patients' own experience

The patients' previous experience of comorbidities and chronic treatment such as diabetes, made them familiar with the healthcare system and allowed them to better understand the importance of investigations to monitor their illness. This made them accept treatment for cancer more willingly.

> *Regular testing is essential whilst receiving treatment. From my experience with diabetes and kidney transplant, I know that you may be feeling physically fine, but blood tests can show otherwise.* [P002-1]

Following completion of treatment with FOLFOX, some patients required a change in treatment of antineoplastic medicines (second-line treatment). The patients' own experience of the first-line treatment with FOLFOX affected their outlook towards the second-line treatment. Patients were often shocked to start a new set of treatment cycles, because this reflected that the original planned treatment outcome was not achieved. These patients feared a new unknown; yet their previous experience helped them embrace what lay ahead of them.

> *The news to begin this new treatment* [second-line treatment – parenteral irinotecan] *was given to me by the oncologist. It was a shock for me. It seemed that the first one did not exert its full effect. But there's nothing I can do, except to hope that this new treatment is effective … Now I have an idea of what to expect during the treatment journey.* [P002-4]

Influence of family members' and friends' experience with cancer

Most patients reported that they either had a family member or a close friend who previously experienced cancer and its treatment and during the interviews along the treatment journey, there was a continual reference to these individuals including those who had passed away. Witnessing these experiences of others dealing with cancer influenced the patients' own perspective and patients who knew cancer survivors realised that living with cancer and treatment is achievable. However the news of persons who died from cancer brought patients back to reality, by stressing that the ultimate risk of the illness was fatality.

> *I have a friend who was diagnosed with breast cancer 7 years ago and also received chemotherapy as she could not be operated … she describes that she still experiences tingling sensation in her feet. Then I question myself whether I would be experiencing these effects for such a long time?!* [P012-1]

> *As soon as I was informed I was receiving chemo, I was shocked. I recalled the memory of two of my wife's friends who experienced bad effects from the chemo they received for breast cancer. Unfortunately, both passed away. Other than that, I didn't know what chemo was all about.* [P015-*2]*

The patient who lacked personal experiences of cancer was feeling lost not knowing what to expect. She felt the need to speak to other cancer patients to find the courage to initiate her own treatment with antineoplastic medicines.

> *I am the first case of cancer in my family ... I would have preferred meeting another patient to get the real experience of it all.*
> [P004-1]

Influence of healthcare professionals

Contact with healthcare professionals mainly consisted of the nurse-led information session prior to initiation of antineoplastic treatment, communication with oncologists during their initial hospital visit and nurse-navigators as required.

The nurse-led information session provided non-specific general information about different antineoplastic treatment regimens and medicines resulting in patients being afraid that they would experience adverse effects such as alopecia, debilitating fatigue, drowsiness and swallowing difficulties. Since the antineoplastic treatment with FOLFOX or XELOX generally produced mild symptoms, the lack of specificity and unnecessary information given produced unwarranted fear and anxiety amongst the patients interviewed. The information session also highlighted lifestyle changes and precautionary measures which needed to be implemented by patients whilst taking antineoplastic medicines. Patients understood these precautionary measures but seemed to take the implementation in their stride.

> *The information session was needed to provide us with knowledge but at the same time caused a lot of fear.* [P001-2]
>
> *I had to find a solution as I wasn't ready to abandon my pets. So I did some infrastructural changes at home to accommodate my pets … I was advised by nurses to use gloves to get things out of the fridge or freezer … I must use an electric shaver to remove body hair, ammonia-free hair dye and alcohol-free mouthwash.* [P008-1]

As from initiation of treatment, the communication approach and skills of healthcare professionals influenced the patients' attitude towards their treatment. One-to-one individual sessions with the medical team made patients feel respected and integrated as part of their own treatment journey.

> *I got the information I needed from my meeting with the oncologist … he calmly explained to me everything and listened to my queries. This is really all important to me, that as a patient I'm informed about chemotherapy, what happens and everything … this is very very important for me … how it works, what important side effects to look out for etc.*' [P007-2]

Influence of other patients' experiences

Patients were very willing to discuss the illness and treatment with other patients, particularly during their visit to hospital. The sharing of personal positive experiences and stories between patients during hospital visits was a strong means of encouragement for patients. One of these patients tried to encourage herself and others by repeating the phrase – *"there is nothing to be afraid of."* [P008-1] As treatment progressed, patients were observing other patients in the ward to evaluate whether they were experiencing the same adverse effects and assessed the degree of severity of these effects.

> *Last time, I was sharing the room with a lady in her 12th cycle. She was feeling terribly tired, sleeping most of the time. However she was also having problems with swallowing … thank God I'm not experiencing any of the sort … but I don't know if these happen to me in the future, as I'm still receiving the 6th one.* [P013-2]

> *Looking at other patients who successfully surpassed this difficult period in life motivates me to move forward. I do no longer feel alone when I witness stories of real persons here.* [P011-3]

Influence of media

As from the first interview with patients, almost all claimed not to refer to the internet to search for further information. In fact, only one Maltese patient claimed to use the internet, with searches mainly focused on the illness but not on the treatment.

> *I am the first case of cancer in my family; hence this experience is all new to me. I can only imagine what may happen from what I read online.* [P004-1]

Some patients relied on their significant other to search on their behalf and provide them with the necessary patient-specific information.

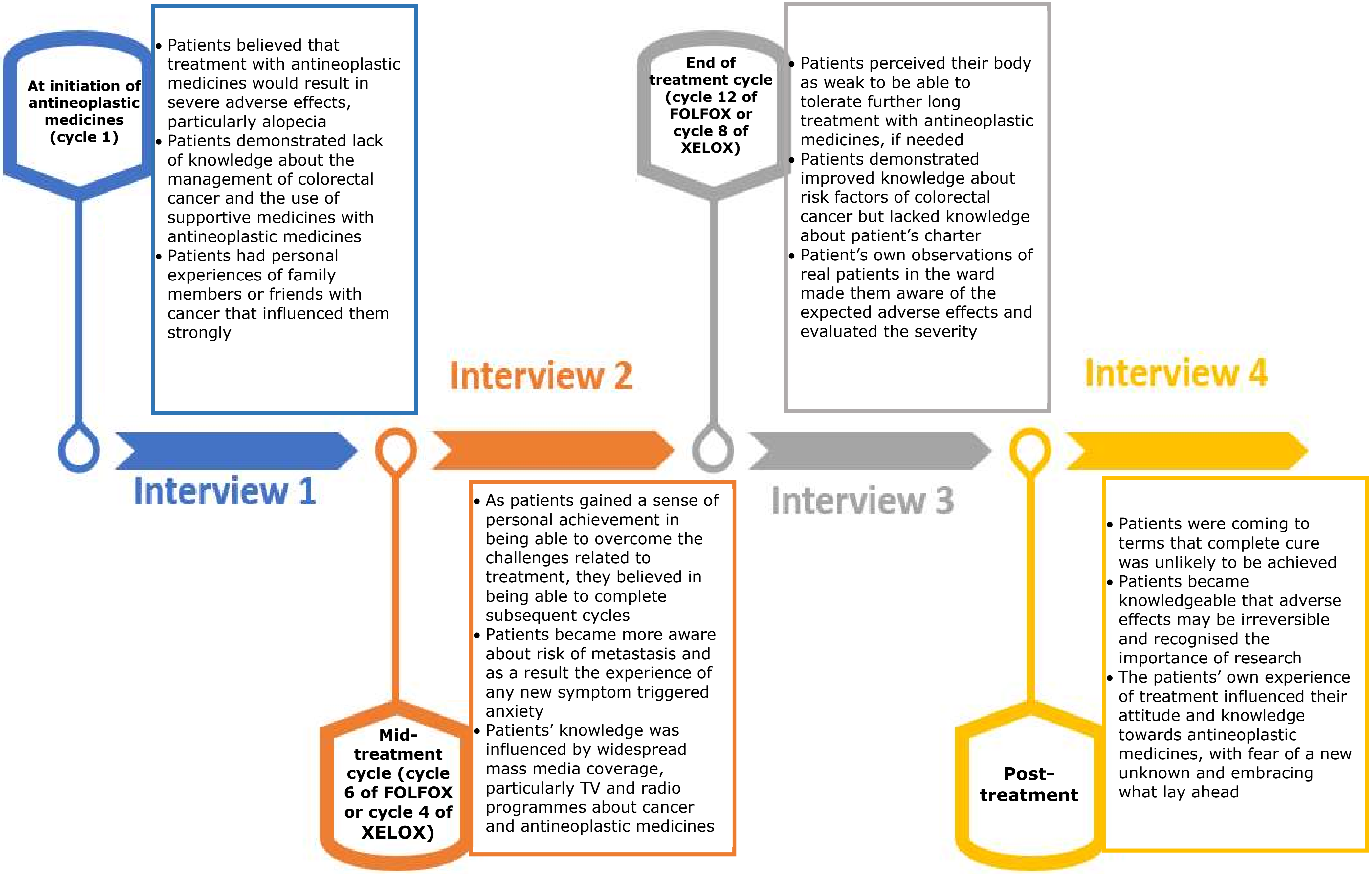
> *My husband searches the internet and then afterwards he provides me with the information that I require*. [P003-2]

Patients reported that the continuous mass media coverage about cancer and its management affected them negatively and kept reminding them about their own situation. They noted that patients with cancer were portrayed as vulnerable and that adverse effects of alopecia and debilitating fatigue were emphasised. Patients going through the cancer experience realised that their individual journey was different from that being portrayed by the media. A few patients remarked that sometimes media lacked sensitivity towards patients currently going through the cancer journey, with this subject becoming highly sensationalised.

> *In the media you hear about this* [cancer and treatment] *all the time. Sometimes I get so fed up, that I switch the station so that I don't continue to follow the discussion. This subject is brought up almost every*

> *day and now even on the news … For someone going through the journey like me, this makes it much more difficult.* [P001-3]
>
> *They mention chemotherapy and cancer on TV all the time … When hearing a lot about cases of deaths, then you start feeling bad and start questioning the reason behind treatment use.* [P010-2]

Figure 4.3 highlights the longitudinal presentation of key points of Theme 1 at four specific time-points during the patients' treatment journey.



- Patients believed that treatment with antineoplastic medicines would result in severe adverse effects, particularly alopecia
- Patients demonstrated lack of knowledge about the management of colorectal cancer and the use of supportive medicines with antineoplastic medicines
- Patients had personal experiences of family members or friends with cancer that influenced them strongly

- As patients gained a sense of personal achievement in being able to overcome the challenges related to treatment, they believed in being able to complete subsequent cycles
- Patients became more aware about risk of metastasis and as a result the experience of any new symptom triggered anxiety
- Patients' knowledge was influenced by widespread mass media coverage, particularly TV and radio programmes about cancer and antineoplastic medicines

- Patients perceived their body as weak to be able to tolerate further long treatment with antineoplastic medicines, if needed
- Patients demonstrated improved knowledge about risk factors of colorectal cancer but lacked knowledge about patient's charter
- Patient's own observations of real patients in the ward made them aware of the expected adverse effects and evaluated the severity

- Patients were coming to terms that complete cure was unlikely to be achieved
- Patients became knowledgeable that adverse effects may be irreversible and recognised the importance of research
- The patients' own experience of treatment influenced their attitude and knowledge towards antineoplastic medicines, with fear of a new unknown and embracing what lay ahead

Figure 4.3: The longitudinal presentation of key points identified in the theme Perceptions and knowledge of the treatment and illness

4.3.2.2. Theme 2: The healthcare system in relation to the illness and treatment

4.3.2.2.1. Sub-theme: Experiences of patients with cancer services as part of the healthcare system

Patients' experiences of services related to diagnosis

Patients' initial encounter with cancer services was at the point of diagnosis. Whilst some patients were symptomatic at presentation, others were identified through the screening programme. The latter were grateful for being enrolled in the screening programme as they recognised the importance of early diagnosis and treatment long before being symptomatic.

> *It was odd, I could not open by my bowels for 4 days so decided to go to the community pharmacist. She gave me Movicol sachets for 2 days but this still had no effect. So then I decided to go to emergency department, … blood tests and X-ray were normal so I was discharged with a three-day treatment of Movicol. On the third day, I suffered from severe abdominal pain and vomited twice, phoned the ambulance and was rushed to hospital … Following surgery, I was informed that I would be referred to the oncology centre.* [P012-1]
>
> *Through the screening programme, I was diagnosed with this cancer at its early stage. Hence being spared the need of being given aggressive treatment … The screening programme saved my life!* [P004-1]

It was during the treatment journey that most patients realised the importance of participating in the national colorectal screening programme. Those patients who refused previous invitations regretted this and attributed it to their poor knowledge about screening programmes.

> *Both my wife and I refused to do the screening test after receiving the invite. At that time, I thought that it is useless to perform the test since I did not notice any blood-stained stools. Now I realise how ignorant I was!* [P010-2]

Patients' experiences of cancer services beyond the oncology centre

To reduce the delay for surgery, some patients were referred to the acute hospital in Gozo. This was a burden since the patients together with their significant others were required to commute between the two islands by ferry and identify suitable accommodation for their family members. Subsequent follow-up visits were also in Gozo. Along the treatment journey, most patients suggested that healthcare services should be provided closer to their home, with follow-up visits in Malta.

> *I had to go to Gozo for surgery and even for the follow-up visits. If possible, I would have done the surgery in Malta. It was a hassle for me and all the family, moreover since we have a phobia of travelling by sea. It would have been much better if at least the surgeon holds a clinic in Malta for follow-up visits.* [P001-3]

Patients who experienced outreach programmes along the treatment journey had praise for such services being offered. These services included the stoma nurses who visited patients at their home to counsel them and also nurses who administered parenteral medicines such as subcutaneous low molecular weight heparin.

> *For the first few weeks, two nurses were coming to my house, one in the morning and one in the evening to assist me in changing the stoma bag. That was helpful until I learnt to do it on my own.* [P002-4]

> *I was started on injections to be administered in the abdomen* [enoxaparin subcutaneous injections] *… Nurses came to my house to teach me and my wife how to administer them. She also observed my wife a few times to ensure she had the correct administration technique … it was a good service.* [P016-2]

Irrespective of when interviewed with respect to the treatment cycle, patients who made use of the free transport service offered by the hospital complained about receiving an inadequate service as it was not on time. As a result, patients had to find alternative means of transport to arrive to hospital appointments on time or use this service only to get back home. Also, patients were advised against using public transport for health reasons and had to rely on their support network to bring them to hospital. However parking within hospital grounds was limited, further compounding to their problem with transport.

> *You get nervous when you arrive late or too early for hospital appointments when using the government-funded transport services. Then the driver calmly explained to me how they work, and I better understood the situation. Then I arranged for my sister to take me to hospital and used the transport to get back home. The driver was so helpful that he helped me down to the van*. [P008-4]

> *Parking is a nightmare. I cannot park anywhere not even when I come here for blood tests. You need to come early in the morning to secure a parking space. If this was not a problem, I could use my own transport even when admitted and leave the car on site for 3 days. [P010-2]*

Quality and timeliness of cancer services within the healthcare system

A critical aspect of the patients' experiences with cancer services all along the treatment journey was the timeliness of services. At initiation of treatment patients were particularly concerned regarding delay in diagnosis. A few complained that there was a delay sometimes of months when referred to the acute hospital by their general practitioners for further investigations. Others criticised the lack of implementation of cross-checks to prevent the loss to follow up of positive screening test results.

> *I still have some pending hospital appointments for further investigations regarding anaemia following referral requests from my general practitioner …* [P003-1]

> *I did not receive the result of the screening test. After 4.5 months, I remembered and phoned to follow this up … To make things worse, I was told by the surgeon that if I presented 6 months earlier my situation would have been different, this made me even more frustrated. This was a shock as this was the result of negligence! …we are referring to CANCER not a cut to your finger.* [P009-1]

Other patients complained about the delay between the diagnosis and initiation of treatment with antineoplastic medicines. They were concerned about the high risk of metastases due to the delay. No further complaints were highlighted by patients in terms of timeliness of services until completion of treatment.

> *It took me a month and two days to start chemotherapy. Since I did not have surgery, I'm getting more worried that it took me quite a while to start this treatment.* [P002-1]

Once the patients enrolled at the oncology services, a system of fast track appointments was started resulting in reduced waiting times. Patients considered this very positively.

> *I received a colonoscopy appointment within a few days. Then I was quickly referred to the oncology centre.* [P009-1]

However, when patients were referred to other services following completion of treatment, delays were being experienced again. As the fast-track service stopped, a few patients re-experienced a long waiting time for hospital appointments.

> *The doctor here referred me to both the gynaecology and ophthalmology departments at the acute hospital. I waited for a long time to receive appointments even though I'm a cancer patient and the doctor requested*

> *an urgent appointment. They still gave me a late appointment, so don't really give priority to us, cancer patients*. [P004-4]

Along the treatment journey, patients appreciated that there was a specific oncology centre which catered for their needs and this made them feel part of a community.

> *The good thing here is that everyone has the same problem … not like in Mater Dei* [acute general hospital] *you are in a ward with patients with different illnesses … here everyone is in the same boat*. [P001-3]

Since patients had multiple appointments at hospital, they were positive about the introduction of text message mobile reminders of hospital appointments.

> *Whenever I have a hospital appointment, I receive a message on my mobile. This is helpful to remember!* [P005-3]

Patients identified gaps in the communication system within the healthcare service along the treatment journey. Issues included appointments being received late and diagnostic notifications not received by patients. Patients stressed the implications of such errors on their health such as delayed diagnosis as well as psychological distress. Patients felt that they could not rely on the efficiency of the healthcare system and that they must take ownership of their health. They must chase up staff regarding the necessary appointments.

> *I think that these hard copy forms between the different departments … result in lack of traceability … If it had not been for the persistence of my husband, I would still be waiting for this appointment.* [P003-1]

A major shortcoming of the oncology services identified was the absence of a designated symptom control unit. Though patients were given a chemotherapy alert card to be prioritised at the acute hospital emergency department, this did not help. Patients described their psychological distress at being left waiting for hours in the same room with other sick persons, with the risk of contracting infections. Moreover, patients complained of being reviewed by emergency medical team and not by their oncology specialists.

> *It was futile to show the chemo alert card to the receptionist to give me priority access! I started screaming hysterically with worry and fear… as I was surrounded by people who were unwell. It's ridiculous that I always stay at home not to avoid meeting any sick persons and then I had to stay there [emergency department waiting room] surrounded by all those patients – coughing and sneezing!* [P006-2]

Another issue was that the patients' oncology notes were not accessible to the emergency medical team but were exclusively available to the oncology services. Patients expressed concern about the lack of confidence in oncology related practice such as use of port-a-cath. Besides, patients were admitted to hospital under the care of general medicine.

> *When I had abdominal pain and was admitted at Mater Dei [acute hospital], they could have admitted me here [oncology ward]. … there's a whole difference with what they say about the card in the information session and what happened in reality!* [P002-3]
>
> *When I go to emergency department, the doctors get confused and cautious on how they would be controlling my pain etc … I don't blame them as the doctors here [oncology centre] are trained to provide care in such illness and also know all my history. That's why the services here should increase such as provision of emergency services with patients being directly admitted here ….* [P011-3]

Despite patients' praise for having a quarterly review by both the oncology and the surgical teams, some patients criticised the lack of communication amongst both teams following their independent medical reviews. Patients stressed the importance of sharing information between department by centralising data to improve communication.

> *I had two separate outpatients' reviews, one from the oncology medical team and the other from the surgeon. It's good to be monitored but the problem is that they don't communicate with each other, everyone working in their own silo.* [P004-4]
>
> *There's no one IT system that collates all the information from all the different departments within the hospital for ease of reference.* [P003-3]

Moreover, some patients felt that the healthcare professionals had fulfilled their duty towards them until completion of treatment. Most patients complained that after completion of treatment with antineoplastic medicines they experienced a gradual decrease of support from healthcare professionals within the oncology centre. This resulted in them feeling left to cope on their own.

> *When I finished the last chemo, they just followed the procedure of the previous cycles. At that time, I didn't feel alone … but then I realised that the treatment was completed and I was back home. I didn't know exactly what to expect … No one has ever phoned me after I finished chemo … then after 3 months I had an outpatient's appointment at the oncology centre.* [P006-4]

Patients reported that as from initiation of treatment they were advised not to seek medical assistance outside of the oncology team. Despite this, at initiation of treatment some patients still updated their general practitioner or other medical specialists about their cancer treatment. After completion of treatment, patients described that the support from the oncology centre completely stopped and they had to resort for private consultations with healthcare professionals and had to resume their contact with the general practitioner.

> *I was informed at the information session that my general practitioner cannot provide me with any assistance any longer.* [P004-1]

> *I disclosed everything about this [diagnosis of cancer and treatment with FOLFOX] to the nephrologist who has been following me for years now … where he informed me that I might suffer from additional complications due to the transplanted kidney.* [P002-1]

> *The pharmacy is round the corner where I live. I have been living here [in the same house] for the last 46 years. They are like my second family. As they know about my situation, sometimes the pharmacist even phones to check on me. If I encounter any problem from now onwards, I can always phone them.* [P012-4]

The effect of hospital environment on the patients' experience

During the interviews, patients highlighted that the hospital physical environment was an integral part of their experience in the healthcare system. With patients' repeated admissions, the oncology centre became their second home. All patients praised the serene and calm environment of the ward.

> *The ward was nicely decorated with lights and a nativity scene for Christmas. It offered a peaceful environment.* [P014-2]

Irrespective of the stage in the treatment journey, some patients complained about sharing rooms as they considered this as limiting their privacy. Other patients felt lonely in a single room due to lack of contact with other patients with whom they can share their experiences. Though recommendations were put forward by some patients to organise activities in the tearoom, this was not accepted by the ward management.

> *I prefer a room on my own as it is more private and also spares me from the anxiety of getting to know the patient next to me. Despite this, I don't find a problem if I must share the room with a nice person like X … but once I had a bad experience where the lady with whom I was sharing the room was experiencing problems with her stoma and was not able to keep our shared bathroom clean! I was not comfortable at all … and risked contracting an infection*. [P009-2]

> *I used to get lonely, so I used the tablet and listened to music. I wish they organised an activity in the tearoom … I used to have my breakfast there with other patients, and I enjoyed it. We laughed together which distracted us from our worries …* [P006-4]

Whilst patients appreciated the provision of catering services during their hospital admissions, they unanimously complained about the lack of appetising meals.

> *Food is so bad that it is worse than the treatment itself. Food always smells the same … really bad smell … Thank God I have my sister who prepares and brings me food to eat whilst I'm here.* [P011-2]

The patients' experience of holistic care

Along the treatment journey, patients encountered various healthcare professionals. Apart from the oncologist, patients were reviewed by the nurse navigator, nutritionist, dental hygienist, psychologist and/or social worker depending on the patient's needs. As treatment progressed, patients highlighted the need of having a multidisciplinary team, though sometimes (particularly at the beginning of the treatment journey) this led to patients' confusion over the different healthcare professionals' specific roles.

> *I've already met a lot of healthcare workers here [oncology centre], the oncologist, phlebotomist, Aurora nurses [practice nurses] and the nurse navigator [colorectal nurse navigator] amongst others. Sometimes I get confused who they are and whom to approach in case of problems.* [P005-1]

All patients highly praised the support provided by the nurse navigators during the treatment period. They were highly accessible whilst the patients wereat home and gave individualised care. They provided information about the illness itself, treatment administration and adverse effects as well as referring patients to other healthcare professionals according to their immediate needs. They acted as a primary link between patients and oncologists and offered practical solutions to their problems.

> *The nurse navigator accompanied me along the process, even to the first meeting with the oncologist. She gave me her contact number in case I had any queries.* [P013-2]

Some patients considered that ward nurses did not offer much information and they mainly focused on treatment administration.

> *The ward nurses provide you with the necessary medication and if you ask them regarding that medication, they reply to you in few words in a hurry and walk out. As a nurse, they spend minimal time talking to us except when checking the parameters.* [P003-1]

Overall patients remarked that healthcare professionals treated them with professionalism and kindness. The friendly greeting by healthcare professionals made patients feel comfortable and well cared for. Patients felt respected as an individual when addressed by name. They appreciated that healthcare professionals gave them individual attention. Furthermore, patients described how ward nurses enquired about any changes in the patients' moods. This emphasised the continuity of care along the treatment journey with a personalised approach. All patients appreciated the support shown by the hospital staff through flexible scheduling of appointments. Most patients reported an overall positive experience at the oncology service throughout the treatment journey. Patients were grateful to healthcare professionals for making this difficult process bearable.

> *I received a phone call from the nurses as I was 20 minutes late for my appointment to receive this treatment ... they were waiting for me and welcomed me with great love and escorted me to my room.* [P002-2]
>
> *Yesterday the nurses immediately noticed that I wasn't feeling emotionally well as they know my character by now. They queried why I was listening to that type of music and why I was in bed so early. I was glad that they observed the change in my behaviour.* [P006-3]
>
> I*t* [Oncology centre] *has become my second home … truly I'll miss them. Though I'm not going to miss the treatment, but I'll miss their support and love they showed us as patients! Though you're just a number here you're not just a number for the staff. They know us by name not by bed number. This is highly important for us … THANK YOU isn't sufficient to ever show our appreciation to all of them*. [P014-3]

Comparatively throughout the 6-month treatment journey, the negative experiences reported by patients were only a few. Disagreements between the healthcare professionals and patients on the ward stemmed particularly from lack of awareness of hospital policies.

> *I feel hesitant to press the assistance button next to my bed. Earlier today, I pressed it as I thought there was a problem with the infusion pump. I'm new to all of this! The nurse came and with a harsh voice told me that they had other patients that needed assistance and there was no need to press it more than once! I expected her to acknowledge that I'm new to the system and explain this in a calm manner.* [P004-1]
>
> *A nurse was shouting at me not to enter their staff room with the infusion set. I was only speaking to her from the corridor. It isn't the appropriate way to speak to a patient!* [P014-3]

4.3.2.2.2. Sub-theme: Healthcare professionals’ communication with patients

Communication with healthcare professionals

The patients’ first interaction was a one-to-one session with the consultant. Patients described that they were provided with adequate amount of information, specific to their needs.

> *The consultant explained everything to me in clear simple words and in great detail. In fact, he explained that they [healthcare professionals] do not force chemotherapy treatment on patients. … first the surgery was done, then I was referred to an oncologist for consideration of further treatment* [P001-1]
>
> *I got the information I needed from the meetings with the oncologist … this is very important to me …* [P007-2]

As treatment progressed, most patients highly rated the time spent by healthcare professionals to actively listen to their concerns and were grateful to have their questions answered. This conveyed respect and strengthened their trust in the healthcare professionals. Only a few patients had suspicion that healthcare professionals were withholding the truth about their actual prognosis. Consequently, patients were continuously trying to gain further knowledge by asking the same specific questions to different healthcare professionals. Conflicting information between healthcare professionals undermined patients’ trust. In view of this, they commonly sought additional information from other healthcare professionals to judge whether the information was credible prior to making their own decision.

> *I still clearly remember the consultant at Gozo Hospital [surgeon] telling me that my body can withstand treatment with chemotherapy, so she was recommending a strong treatment with chemotherapy … When I visited the consultant here [oncologist at SAMOC] and repeated this, she told me that this is irrelevant and explained that FOLFOX is the ideal treatment in such circumstances with a specific dose for me … This confused me.* [P004-2]

Most patients prioritised the need for empathy.

> *My consultant is a bit arrogant, in fact I talk the bare minimum with her. Once I asked her about my chances to live and she aggressively replied that she’s not God to know! I speak more with the senior doctor, who is more approachable.* [P010-3]

Patients remarked that information on the supportive medicines was initially provided by the oncology medical team upon discharge with reinforcement of information by the hospital pharmacist upon collection.

> *The pharmacist explained to me the indication and to be taken as required. I was advised that there was no need to take them exactly on time unlike antibiotics without any effect on food intake.* [P012-2]

As the current healthcare system lacked communication between different departments, patients experienced appointments on different days, physically required to attend departments to organise their appointments. A coordinated discharge plan was recommended by some patients whereby their appointments may be booked through an integrated IT system and medicines may be dispensed to them whilst waiting in the discharge lounge. This would create an opportunity for patients to have a medication review considering their chronic medicines.

> *If those medicines given to me for home had to be delivered to us by the pharmacist in the ward, that would be better. They can also explain to us better. It's a pity that we must go down to the pharmacy after being discharged to collect a 3-day supply of medicines after being confined in the ward for 3 days!'* [P012-4]

> *Due to my heart problems, I wonder whether another 'safe' medicine may be used to prevent nausea … prefer to discuss this with healthcare professional whilst having a review of all my medicines.* [P003-2]

Additionally, some patients expected that the case summary should include all the detailed information of what has happened during their admission, what is expected or any necessary advice for in-between cycles.

> *In the ward the nurses were not informed about what was being communicated with me in-between cycles. Again, there is a disconnect between the oncologist and the ward, particularly upon discharge.* [P003-3]

Most patients who started second-line treatment with antineoplastic medicines complained that they did not receive any supplementary information about this treatment from healthcare professionals except from the oncologist who informed them about the need to change treatment. These patients relied mainly on their own experience gathered from their first set of treatment cycles with antineoplastic medicines and from bedside information provided by the nurse navigator, upon patient's request. Additionally, they felt that another information session was essential as they did not know what to expect from their new treatment.

> *For the doctors this is just another treatment ... I was not invited to another information session of Aurora so I have to remember the information given to me the first time. Besides the oncologist's explanation, I preferred to have someone explaining this treatment in detail* [P011-4]
>
> *Though I've restarted another 8 cycles of another chemo … they didn't explain what it entails, and I don't want to read anything. I wasn't invited to attend again that information session by the Aurora … I think I have enough experience from the previous cycles.* [P002-4]

Communicating information using different means

All patients were referred to a voluntary nurse-led information session prior to starting of antineoplastic treatment. This covered the necessary information that patients required till the end of the treatment journey. Besides the learning experience, patients attending the group information session experienced various conflicting emotions such as anxiety to deal with the extensive effects that antineoplastic medicines can have and a sense of belonging by meeting other patients and their families in similar situation. Later, patients asked for improvements in the nurse-led information sessions by introducing a follow-up information session to reinforce the given information and answer their concerns about treatment. Additionally, patients recommended that during the session they should be given information on self-care enabling them to assess the severity of adverse effects when not in hospital and obtain advice on the use of supportive medicines.

> *If they had to do another information session at cycle 6, I would attend as there are still a lot of things to learn and also you would have built up your experience and can ask certain questions.* [P012-3]
>
> *Although extensive information was provided in the information session … guiding us on what to eat, what to avoid and any precautions necessary, but in the long run during the treatment cycles other information becomes essential. At the first cycle, you do not have any symptoms but after the 4th cycle it is a completely different scenario as I had to take more control of myself*. [P004-4]
>
> *I think that they gave us enough information … I found a lot of help from staff at the ward. Sometimes the more information that is given, the worse it is in terms of fear. The information session was good but instils fear at the same time. You are inexperienced at that time and hence such information could be interpreted differently by each patient.* [P001-4]

The information session was supplemented with information booklets. Despite this, some of the patients were advised by the oncologist to seek further cancer information from the Macmillan online cancer support, which is a voluntary organisation in UK. Though informed about it, none of the patients except for one patient described the need to search for further information. In fact, most patients disclosed their fear of having psychological repercussions from knowing the truth, accepting untruthful information or inability to understand all the information on the internet. This fear discouraged most patients from reading the illness-specific patient information booklets available in the ward.

> *I don't want to upset myself by searching for further information. If I need anything, I will ask the doctors or the nurses … not rely on whatever is written by Google! If I search online I wouldn't know whether the information I find applies to me.* [P006-3]

The effect of language and non-verbal cues

Healthcare professionals were described as becoming the patients' strongest allies in this difficult and vulnerable time of their lives. Patients felt that healthcare professionals were often the only ones who were able to understand their situation and offer a solution. However, at the start of treatment, they were highly sensitive to the words used by the healthcare professionals and carefully observed the non-verbal cues such as attitude and gestures of the healthcare professionals. These transmitted additional meanings to the spoken words, particularly on delivery of sensitive news such as prognosis.

> *I asked " … What is the chance that I live? What are the odds 50/50 or 60/40?" He replied that we are not in the business of odds and removed the eye contact. And his body language showed either he was not confident, or it was bad news for me ... so it gave me a bad feeling … If someone is lying, they do not look into your eyes.* [P016-1]

Patients stressed the importance of receiving simple reliable information delivered at the right time in a language that ensured a clear understanding without medical jargon. Patients referred to unique terms used by healthcare professionals in their explanations about cancer. These include the terms '*skin tag'* [P004-1] or '*tumour'* [P001-1] when referring to cancer, '*having roots'* [P015-1] for lymph node invasion, no sign of metastasis as '*no infiltration into any organ'* [P013-1], and palliative treatment as '*treatment provided to control and stabilise illness'* [P011-2].

> *This is the same as when they [healthcare professionals] tell you that you have a tumour. You still understand that they are referring to that … but I always refrain from saying that dreadful word …* [P001-2]

Right at the start and throughout their journey, some patients avoided the use of terms 'cancer' or 'chemo'. Instead, they used general terms such as 'the illness' or 'treatment' or 'this'.

> *I do not refer to it as chemo, I call it treatment! This is because, in my opinion, the word chemo has fearful connotations.* [P013-1]

Even though Maltese citizens are generally bilingual and speak both Maltese and English, many communicate effectively only in Maltese. In fact, patients acknowledged that they found difficulty in understanding and engaging in active communication with foreign healthcare professionals. In these instances, patients complained that they were barely receiving the basic healthcare service, let alone allowing for the development of healthcare professional-patient relationship. In fact, some patients resorted to the ward nurse to act as a language translator.

> *Though I was talking to the doctor, I wasn't sure whether he understood me correctly. I know how to speak some English but to make things worse, he was a foreigner and not from an English country*. [P008-3]

4.3.2.2.3. Sub-theme: Recommendations for services

During the first interview, patients did not provide any service recommendations. As treatment progressed, patients were building their personal experience in the healthcare services, identified areas of unmet needs and possibly were more forthcoming with making recommendations for services.

Need for improved awareness about available cancer services

Most patients complained about their lack of awareness of services available to patients during and after completion of treatment. When patients had any issues, they referred to the nurse navigator who would decide on the services to be accessed. Most patients requested to be provided with a list of services and method of referral to make use of services at their discretion in line with their needs.

> *We should be made aware of the available services … by being introduced to these services by meeting the healthcare professional offering the service … this will be more helpful for us [patients] to ask for a particular service.* [P014-2]

Recommendation of new services within the healthcare system

Though at initiation of treatment most patients did not feel the need for a psychologist, some patients later realised that it would have been useful to have psychological support soon after disclosure of the diagnosis. They claimed that they were unaware that such support was available. The only patient who got such help accessed this after her significant other actively sought external psychological support. The patient admitted that it was difficult to accept and seek psychological help due to stigma. Another patient described how he preferred to share his grief with a relative who was going through the same situation.

> *Learning about your own diagnosis* [of cancer] *is hard … I was much more anxious and in fear initially, with all my thoughts focussing about this thing [cancer] and its effects … made me feel more emotional. I'm getting better with time … looking back I think that the assistance of a psychologist could have been beneficial.* [P010-2]

> *I cried when I was alone as I was feeling sensitive to the words being told … I could not continue like this and had to ask for psychological help myself. No one in my family knows about it except my youngest daughter who arranged everything for me.* [P014-3]

An outreach service was also recommended to assess the patient's living situation to ensure that adequate support was available and provided upon patients' request or offered to those really in need.

> *It would be great if a healthcare professional came to our home and provided the necessary advice to ensure continuity of care. This should be offered particularly to those patients in need such as those living on their own with those carried out prior to the first treatment or mid-way*. [P003-3]

Throughout the treatment journey, patients showed appreciation of the opportunity of speaking with other patients. Consequently, they proposed the establishment of individual or peer educational and support sessions whilst receiving parenteral antineoplastic medicines in hospital. Additionally, most patients expressed the need to be supported by other fellow patients since they felt that the sharing of experiences between patients would be helpful. In fact, following completion of treatment, they asked for the preparation of recorded material and were even willing to share their own experiences for the compilation of a video.

> *Last time we met a group of patients in the tearoom and we stayed awake till around 10pm talking to each other. Whilst we're here it's a good thing to have educational sessions where we can meet with healthcare professionals to clarify or discuss certain issues.* [P010-2]

> *If another person who already received this chemo came over and narrated their experience with the illness and treatment, this would have been useful … even offer some practical tips.* [P008-3]

Patients remarked that the healthcare system did not cater for family members who were supporting the patient. Patients made recommendations on how the healthcare system can support their caregivers including education, skills-training and psychological support.

> *Though the focus here [oncology centre] is on us, the patients, I think that the family needs support as well, particularly related to psychological issues. They [family members] struggle a lot … their need of support is much greater than they even realise.* [P014-3]
>
> *I'm willing to record a video of myself narrating my journey … New patients may find this information useful and encourage themselves to continue with the treatment. I can give them my contact details as well to phone me in case they require further assistance.* [P008-4]

Because of the progressive nature of the illness together with effects of treatment, a few patients suffered from physical deterioration resulting in difficulties to perform basic essential activities of independent living. These patients requested permission to be allowed access to an informal personal carer particularly at night whilst during their hospital stays. However, such requests were declined on the premise that this was against hospital policy, thus patients recommended a revision of the hospital policy.

> *No rounds are done by nurses during the night … During the first few cycles, I was able to cope on my own but I'm terribly in need to have a relative all the time with me here during such a difficult period. I'm embarrassed to press the buzzer all the time … When I raised the concern, they informed me that this is allowed only for those who are on their death bed.* [P011-3]

Though patients were offered a call out service by the nurse navigators, they recommended a helpline or mobile application that offered support, information and help to patients and relatives in the community. This was expected to be of particular benefit after finishing their treatment as assistance would be mostly required whilst patients were at home on their own.

> *Having a WhatsApp group to post your queries may also be an option. We need to think of persons with different abilities as not everyone is familiar with technology.* [P008-3]

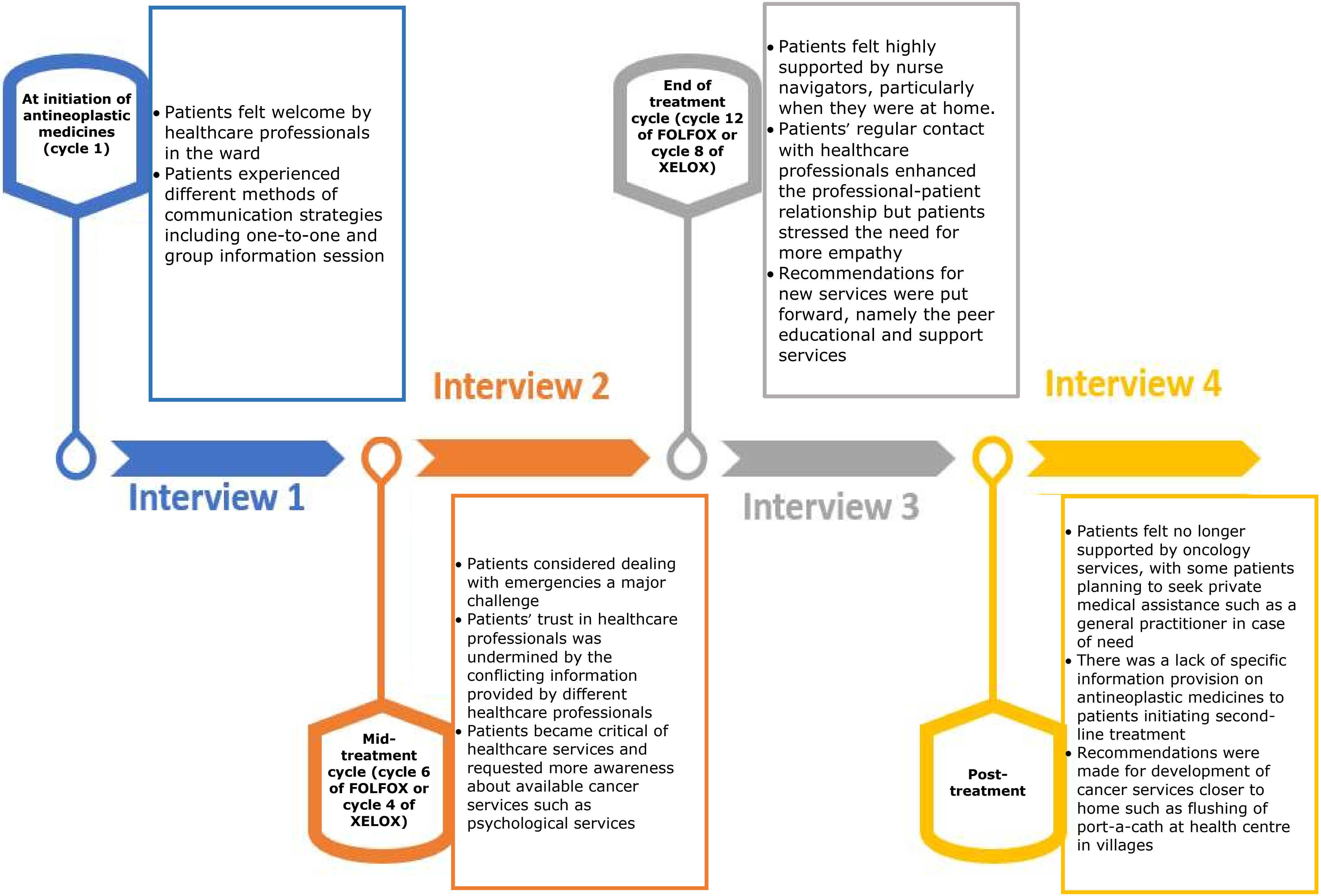
Following completion of antineoplastic treatment, some patients remained with port-a-cath in place requiring regular fortnightly flushing. This service was being offered at the oncology centre only on Sundays. A few patients suggested that this procedure could be carried out by trained healthcare professionals at the health centres in the villages.

> *At the last cycle, I was informed to go every alternate Sunday to Ward 2 to flush my port-a-cath. Upon asking whether this can be done at the health centre, the nurse told me that such service was not offered as there wasn't any trained nurses.* [P001-4]

Following completion of treatment, all patients felt confident to provide various recommendations to improve the healthcare service within the oncology setting. A few patients realised that when complaints were filed through the official channels, necessary actions were implemented to improve the service.

> *I was not allowed by the nurse-in charge to use my own sandwich toaster. After I complained with customer care, I heard that a sandwich toaster was bought for all the wards.* [P006-4]

Figure 4.4 highlights the longitudinal presentation of key points of Theme 2 at four specific time-points during the patients' treatment journey.



Interview 1

At initiation of antineoplastic medicines (cycle 1)

- Patients felt welcome by healthcare professionals in the ward
- Patients experienced different methods of communication strategies including one-to-one and group information session

Interview 2

Mid-treatment cycle (cycle 6 of FOLFOX or cycle 4 of XELOX)

- Patients considered dealing with emergencies a major challenge
- Patients’ trust in healthcare professionals was undermined by the conflicting information provided by different healthcare professionals
- Patients became critical of healthcare services and requested more awareness about available cancer services such as psychological services

Interview 3

End of treatment cycle (cycle 12 of FOLFOX or cycle 8 of XELOX)

- Patients felt highly supported by nurse navigators, particularly when they were at home.
- Patients’ regular contact with healthcare professionals enhanced the professional-patient relationship but patients stressed the need for more empathy
- Recommendations for new services were put forward, namely the peer educational and support services

Interview 4

Post-treatment

- Patients felt no longer supported by oncology services, with some patients planning to seek private medical assistance such as a general practitioner in case of need
- There was a lack of specific information provision on antineoplastic medicines to patients initiating second-line treatment
- Recommendations were made for development of cancer services closer to home such as flushing of port-a-cath at health centre in villages

Figure 4.4: The longitudinal presentation of key points identified in the theme The healthcare system in relation to the illness and treatment

4.3.2.3. Theme 3: Patient's involvement in treatment decision-making and their experience of medicine-taking

4.3.2.3.1. Sub-theme: Influences on acceptance of treatment

The healthcare professionals' recommendations

On initiation of treatment, the main influence on treatment acceptance was the oncologist. The latter explained the basic treatment strategy and associated information about FOLFOX or XELOX as well as any monitoring requirements of the treatment. Patients took this up without any questioning and almost all patients highlighted the fact that their only option was accepting or rejecting treatment. They considered the oncologist an expert in the field with superior knowledge and left the decision about treatment at the oncologist's discretion. Throughout the treatment journey, patients did not show any regrets in accepting treatment as patients were confident that the best treatment decision was taken.

> *I was not offered any options and was only informed about this treatment. No one told me anything … so you just need to receive treatment as is.* [P005-1]

> *I followed the oncologist's recommendation. The fact that I relied on healthcare professionals to take care of me implies there is nothing for me to worry about.* [P012-3]

Contrastingly, the youngest patient, who was also non-Maltese, was offered treatment options to choose from with a period in which to make a decision. He opted for a combination of oral and parenteral formulation of XELOX as he claimed that this option offered him the opportunity to stay at home and maintain his normal routine.

> *The doctor spoke to me about everything … He tried to help me so much. He gave me 2 options to see and explained the difference between the two. The second option was to take the tablets at home … I was given a week to think about the treatment options … Why I chose the tablets? Because of work … so that I may spend a lot of time at home, maybe working from home rather than staying in hospital.* [P007-1]

The risk-benefit outcome

All patients commented that hope of cure drove the patient to accept the treatment.

> *I'm on the edge to know how this is going to end, whether for better or worse? I accepted the treatment with the intention to be cured as otherwise no one would have accepted it if there is no hope to get physically better … Hence it is a requirement to take the treatment. I feel that I'm getting better.* [P005-3]

As the treatment progressed, patients assessed the risk-benefit of antineoplastic medicines. The benefits of treatment were assessed by receipt of positive results of investigations (such as downward trend of tumour markers and improved radiological results). These encouraged patients to continue with their treatment. Also, most patients identified their own measures to further evaluate effectiveness of treatment. These included improvements in symptoms such as weight gain, reduced abdominal pain or discontinuation of rectal bleeding. These were all compared to the risk of cancer growth and metastasis.

> *My weight prior to surgery was 95kg, then I lost 15kg within a week as I was nil by mouth for surgery. My weight was decreasing all along the journey. When I started chemo, I was deeply worried but lately I noticed that my weight has increased by 2 kilos. This really encouraged me!* [P015-2]

> *I've got to know that the level of that [tumour markers] is decreasing, so it shows that the treatment I'm taking is working. This is great news to me … as otherwise death [from cancer] was certain. [P010-2]*

As treatment progressed, a few patients became increasingly sceptical about achieving a cure and they understood that the treatment may be futile or even harmful with the occurrence of adverse effects. This led patients to increasingly question the intent and effectiveness of treatment.

> *I can't really know how to describe this experience, because there is uncertainty and one can't predict what can happen.* [P005-3]

Three months following completion of treatment, patients pondered on the real benefits of treatment with antineoplastic medicines and made comments that they would re-consider their acceptance of treatment if further treatment required in the light of persistent adverse effects such as peripheral neuropathy, oxaliplatin-induced permanent retinal damage and risk of recurrence.

> *After I completed the treatment, one problem after another keeps cropping up. This really shocked me as I'm suffering from blurred vision due to treatment … with the need to undergo cataract surgery. I think the treatment solved one area but caused more damage in other organs. I should have asked further about these effects … thinking twice about having this treatment again.* [P004-4]

Nonetheless, all patients who were recommended the second line treatment by their oncologist accepted to proceed with this treatment, even if this caused alopecia. Patients' life balance shifted towards the emphasis of living independently rather than physical effects affecting aesthetics. In fact, they decided against the wearing of wigs at initiation of second-line treatment.

> *Though the oncologist suggested treatment that causes hair loss, they suggested to wear a wig. For the time being I can cope without it. I am not young ... If I can carry out the housework independently, able to make some tea and wash myself without any help, I am willing to continue with treatment.* [P005-4]

Access to a safe and supportive environment

The fact that the oncologist informed patients that parenteral treatment would be administered in hospital encouraged them to accept treatment and consent. Patients considered that the hospital environment offered them a sense of security with surveillance by experienced healthcare professionals, giving them respite besides reduced cytotoxic exposure to their family. Despite being unaware of oral formulations at the start of treatment, some patients remarked that they would still have chosen the parenteral route of administration if given a choice.

> *If I was offered another form of treatment … I would not have chosen it. It is better to have healthcare professionals keeping an eye on you ... They [Nurses] do not even let us touch the [infusion] bag, let alone expose all my family to more of these things. Going through this experience is already enough for the family!* [P016-1]

Nonetheless, a few patients changed their mind as treatment progressed and showed interest in considering oral formulations if this option was made available as this could offer more quality time with their family. Their main concerns were then the lack of availability of oncology services in the community setting and reduced social contact with other patients.

> *In the case of a positive result from the CT, can they consider changing this treatment to oral now? If the oral treatment had been offered, I will seriously have considered it … though I will miss the friends I made here and be a bit lost about where to seek immediate help in case of need.* [P012-2]

Some patients who heard about the use of a chemotherapy portable infusion pump were sceptical regarding its use. In spite of improving the patients' comfort, the shift of the responsibility of treatment administration onto the patient and family was concerning. Moreover, they were concerned that direct supervision from healthcare professionals such as the regular blood pressure and temperature monitoring would not be available.

> *If it was for me, I would have received treatment through the pump at home but my husband would surely object as otherwise he would not take a break from caring for me. In this way [receiving treatment in hospital], he has his mind at rest that I'm being well cared for by experienced healthcare professionals in hospital.* [P009-2]

4.3.2.3.2. Sub-theme: Experiences of administration of antineoplastic medicines and other medicines

The experience of receiving treatment in oncology centre

The experience of antineoplastic medicines administration focused almost entirely on the parenteral administration of these medicines. Most female patients felt that their two-night admission for parenteral administration of FOLFOX treatment in the oncology centre provided space and time to focus on themselves and reflect on their current situation in a calm and well-cared environment.

> *I considered the time spent in hospital for treatment administration as a weekend break. I used to be admitted for treatment on Saturday and then be discharged on Monday morning. During that time, I disconnect from my daily routine and reflect on my own life.* [P006-4]

A patient who received his first treatment as an in-patient and the second-line treatment as an out-patient in the day ward described how his experience differed. Though he was pleased that he needed to spend less time in hospital for his treatment, he remarked that the day ward environment was not supportive to offer a personalised treatment approach in view of the high patient turnover.

> *The environment at the day ward is totally different from that of being an in-patient in the ward. I noticed that nurses are so overwhelmed with work here* [dayward at oncology centre] *due to the presence of many patients. In fact, nurses have minimal time to speak to us as patients and whenever I have a query, I phone nurse X [nurse of oncology in-patient ward].* [P002-4]

The process of administration of antineoplastic medicines

Contrasting to the initial patients' perception of the high risk of antineoplastic treatment, along the treatment journey patients commented that there was nothing so extraordinary in their administration. This was like administration of other medicines except for regular monitoring of parameters and safety measures taken by nurses during its administration. Patients praised the nurses' diligent behaviour in ensuring that the right treatment was administered to them. Nurses checked the patient's identification prior to starting a new infusion bag of treatment.

> *I feel safe as the treatment is based on my weight and height and reconstituted specifically for me. There's even the ID card number on it! And before they attach it to the line, they enquire my ID card number to ensure that that bag belongs to me.* [P015-1]

Patients described how the process of each cycle started from two days prior to the administration of antineoplastic medicines by taking baseline blood investigations. This step led to anxiety as patients waited to be notified about the blood results and were consequently unsure whether treatment with antineoplastic medicines would be administered as planned or postponed. This situation worsened along the treatment journey.

> *My blood pressure reading is always high when it is checked by the doctor prior to admission … The waiting for the news about the results of blood tests makes me anxious.* [P010-2]

The hospital allowed a level of flexibility for scheduled appointments to accommodate the patients' needs. However, most patients tried to make sure that their planned treatment schedule would be retained, so as to secure the full benefits from treatment.

> *I prefer to come here on weekends … I was invited for a wedding on the day when my 4th treatment cycle was due. Though the doctor offered to change the day of treatment, I decided not to attend the wedding. This would also allow me to continue the treatment routine as planned and not mix up the treatment regimen and routine* [P004-2]

The use of port-a-cath for administration of antineoplastic medicines

Most patients were referred for the port-a-cath insertion following the parenteral administration of the first cycle of antineoplastic medicines. All patients commented on the improved experience in medicine-taking following the insertion of port-a-cath when compared to the use of peripheral venous access, particularly due to improved mobility during treatment administration, prevention of damaging peripheral veins and frequent needle pricks. Patients recommended the use of port-a-cath to each other.

> *With the use of a port-a-cath, my experience of treatment administration has improved a lot. I took my first cycle through the peripheral line and could not move my hand … with the port-a-cath my mind is at rest that my veins are being preserved. And I can sleep well at night too.* [P012-2]

A patient refused this procedure due to aesthetic concerns linked to the port-a-cath device and she was concerned that the port-a-cath would be visible underneath her clothes in view of being very thin. As treatment progressed, she then became increasingly concerned about the potential risk of chemical phlebitis as nurses stressed the importance to be careful not to dislodge the cannula due to high risk of extravasation.

> *'What is worrying me is the port-a cath! As I think that I'm too thin and it will be aesthetically visible from my neck ... as a pipe popping out from the neck and going up! I heard everyone here praising it; I noted that only one patient was receiving treatment like me through her hand.'* [P014-1]

Some patients complained that despite having the port-a-cath, nurses in the acute hospital still made use of their peripheral venous access instead.

> *Whenever I came to emergency department nurses were reluctant to draw blood from the port-a-cath unlike nurses here [oncology centre]. This is possibly due to lack of training.* [P001-2]

As treatment progressed, some patients experienced problems with the use of the port-a-cath, mainly catheter induced thrombosis. The latter warranted an early removal of the port-a-cath and treatment with anti-coagulant medicines. Furthermore, these patients had to receive the remaining treatment cycles through peripheral veins.

> *I sensed that something was not right as I noticed protruding veins in my arm and my hand was becoming bluish in colour. So I went to the emergency department, where I was informed that I had a blockage secondary to port-a-cath and had to undergo surgical removal of the port-a-cath. As a result, I have to take 2 tablets of Xarelto® daily.* [P006-3]

After completion of treatment, patients were advised to keep the port-a-cath thus requiring regular maintenance every 2 weeks to ensure its patency. Patients were annoyed to learn this from other patients instead of the healthcare professionals prior to port-a-cath's insertion.

> *Last time there was a patient who told me that this [port-a-cath] has to be flushed every 3 weeks to remain open, as otherwise it gets blocked. I wasn't informed about flushing when I accepted it. I got to know later from other patients!* [P003-2]

The monitoring of treatment

The monitoring of parameters (blood pressure, temperature and blood glucose) formed an integral part of the medicine-taking experience, that could even result in modification or postponement of treatment. Along the treatment journey, patients learnt about monitoring through their own experience and including the potential of deranged blood tests affecting future treatment cycles. A few patients were not aware about any modifications of their treatment such as a change in treatment protocol or dose. Along their treatment journey, patients observed that weight was an important parameter however, they lacked knowledge that this was required for dose adjustment.

> *When I was due for the last treatment cycle 12, I was going to start a new treatment but it was postponed as the white cells were low so treatment had to be postponed by another 2 weeks … so the gap was of a month from the last treatment cycle.* [P010-3]

> *They increased my dose around two weeks ago as my husband noticed a change in the dose stated on the label of the bag and then when I enquired they told that it's due to the increase in my weight … I'm 60.2kg now as I was only 50kg … around 10kg change*! [P003-3]

The patients' experience with supportive medicines

Patients were given supportive medicines to control symptoms of the illness and adverse effects of treatment. Patients remarked that these oral medicines were administered as loose tablets in a plastic medication cup with a bed number written on it. The tablets were not dispensed in their original package and therefore patients could not check what they were given.

> *Nurses come and place the pills in front of you with advice not to forget about them … they don't explain what they are … I feel awkward asking them about their indications … when I ask they just reply quickly and rush out of the room … so do not know exactly what I'm taking.. I would prefer the nurse to calmly explain that I have two tablets for that and the other tablet for the other effect.* [P003-3]

Upon discharge, a 3-day supply of supportive medicines such as loperamide and metoclopramide were dispensed from the hospital pharmacy as per standard hospital procedure. At home, supportive medicines were taken only when necessary, with patients resorting to their own self-management skills to decide whether they needed to take these medicines to control their symptoms. Some patients refrained from taking supportive medicines despite being symptomatic.

> *… I refrain from consuming tablets as much as possible until pain becomes unbearable … even in terms of paracetamol. I wasn't sure whether I could take because of chemotherapy …* [P010-3]

Some patients complained that despite the increased need for supportive medicines along the treatment journey due to worsening of adverse effects, they were still entitled for the same amount of medicines supply from hospital. Patients stored their medicines in different places, mainly in the bedroom or the bathroom. Some patients were concerned about being over-stocked with these medicines, possibly leading to wastage. Almost all patients lacked knowledge on how to dispose of any expired medicines safely; with each patient deciding on their own method of disposal.

> *I throw the medicines in a bag inside the black bag … It's a good idea if there's a bin that collect unwanted medicines in the hospital pharmacy downstairs so that you may get them with you when coming to hospital for appointment.* [P014-2]

The concurrent intake of chronic medicines

The care plan of patients with cancer and concurrent comorbidities became more complex with time. As treatment progressed, patients experienced multiple symptoms making it difficult to assign their symptoms to a particular illness. Additionally, cancer took precedence over other chronic conditions with some patients disregarding their control of chronic conditions. In some cases, this was made worse as treatment with antineoplastic medicines resulted in disruption of control of their chronic conditions leading to modifications in their treatment regimen.

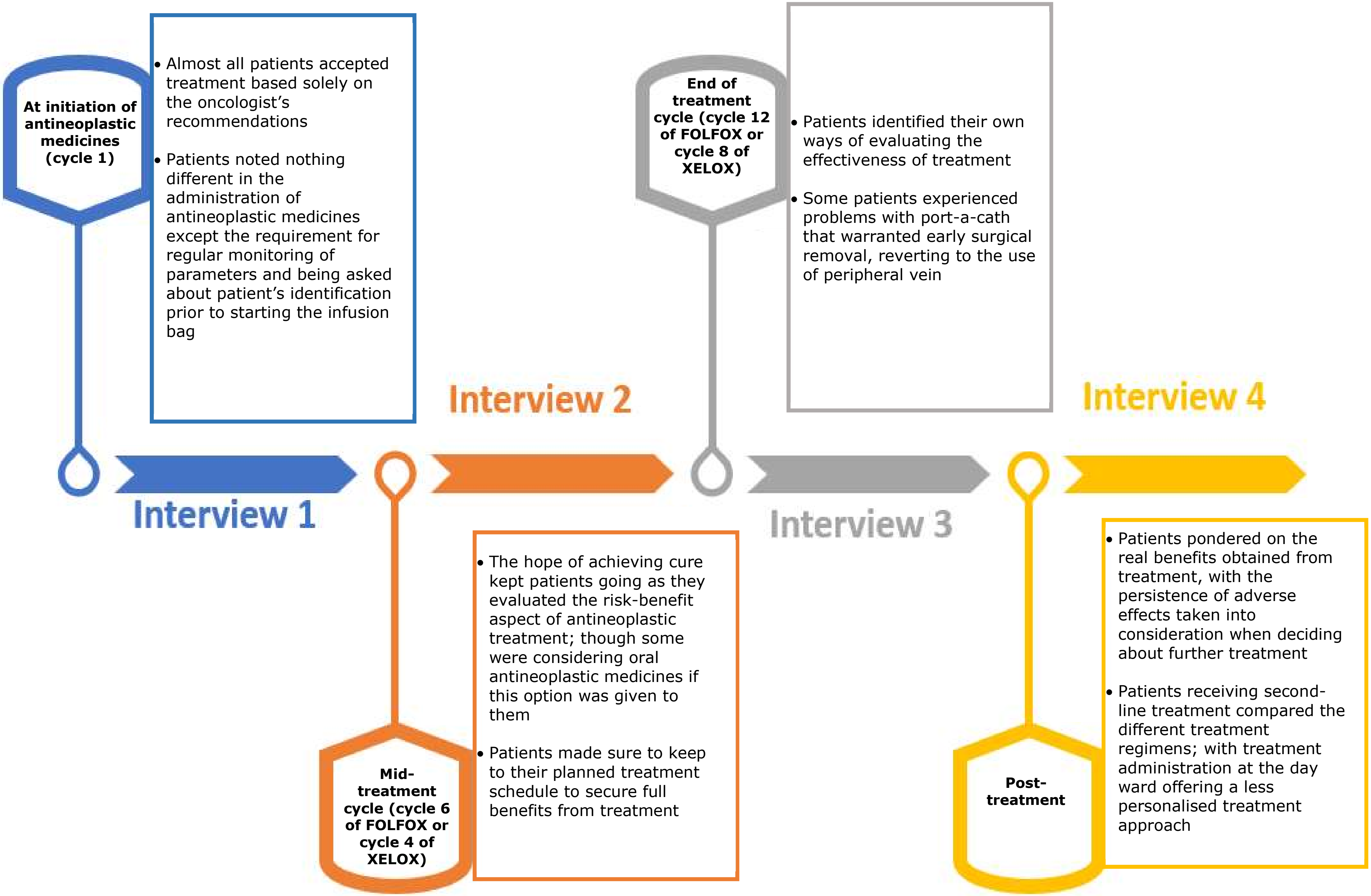
> *After each cycle* [with FOLFOX]*, I had to readjust the dose of insulin as my blood glucose was constantly high. Insulin dose had to be adjusted as the dose is not like anti-hypertensive pills always taking 1 tablet daily regularly …* [P015-3]

In line with hospital policy, patients were instructed to give over their medicines for chronic conditions to nurses. This made patients feel they were losing control over treatment management of chronic conditions and also complained about disruption of their medicine routine.

> *The nurses distribute medicines at 5am. I don't know what I'm taking at that time. It is not the usual time I take the tablets.* [P014-2]

> *I get the medicines for high blood pressure and kidney transplant from home and then I have to give all the bag with the medicines to the nurses upon admission. They can administer these medicines according to the treatment chart. I know how to take them but I do as instructed, not going to argue with them. [P002-3]*

Figure 4.5 highlights the longitudinal presentation of key points of Theme 3 at four specific time-points during the patients' treatment journey.



At initiation of antineoplastic medicines (cycle 1)

- Almost all patients accepted treatment based solely on the oncologist’s recommendations
- Patients noted nothing different in the administration of antineoplastic medicines except the requirement for regular monitoring of parameters and being asked about patient’s identification prior to starting the infusion bag

Mid-treatment cycle (cycle 6 of FOLFOX or cycle 4 of XELOX)

- The hope of achieving cure kept patients going as they evaluated the risk-benefit aspect of antineoplastic treatment; though some were considering oral antineoplastic medicines if this option was given to them
- Patients made sure to keep to their planned treatment schedule to secure full benefits from treatment

End of treatment cycle (cycle 12 of FOLFOX or cycle 8 of XELOX)

- Patients identified their own ways of evaluating the effectiveness of treatment
- Some patients experienced problems with port-a-cath that warranted early surgical removal, reverting to the use of peripheral vein

Post-treatment

- Patients pondered on the real benefits obtained from treatment, with the persistence of adverse effects taken into consideration when deciding about further treatment
- Patients receiving second-line treatment compared the different treatment regimens; with treatment administration at the day ward offering a less personalised treatment approach

Figure 4.5: The longitudinal presentation of key points identified in the theme Patient’s involvement in treatment decision-making and their experiences of medicine-taking

4.3.2.4. Theme 4: Medicine and illness-related impact on patients

4.3.2.4.1. Sub-theme: Impact of physical effects on patients

Physical effects experienced along the treatment journey

As early as the second day of the first treatment cycle, a few patients reported symptoms of altered taste, hoarseness, increased appetite, bleeding gums, diarrhoea and nausea. At this early stage, some patients even reported feeling physically healthier, with less pain compared to a few days prior to initiation of treatment.

> *Yesterday evening I noted bleeding gums, where I immediately recalled that they told us that we may suffer from sore throat or gums during the information session.* [P003-1]

> *Yesterday, though it was my first day of the first cycle of treatment, I felt less in pain than usual. Thank God, I'm feeling much better today. Now we'll see what happens.* [P011-1]

At initiation of treatment, some patients correlated adverse effects directly with the effectiveness of treatment.

> *I think that it is inevitable not to experience any side effects, more so if the treatment is really affecting the bad cells.* [P001-1]

Along the treatment journey, other patients believed that adverse effects worsened with the increase in the number of treatment cycles completed due to accumulation of antineoplastic medicines in the body.

> *With each cycle, chemicals are accumulating in my body … in the beginning of the treatment I didn't have any effects but these effects like tingling sensation developed later and are increasing after each cycle*. [P004-3]

At mid-treatment journey, common adverse effects experienced by almost all patients were change in weight, increased appetite, fatigue and peripheral neuropathy. Other adverse effects mentioned by a few patients included mouth ulcers, altered taste, diarrhoea, constipation and nausea. Uncommon adverse effects included intertrigo, dark spots in vision and hearing loss.

> *I noticed that I cannot hear properly … I have to check what I can do about it.* [P005-2]

> *I was seeing black spots in my vision and this really worried me. When I informed the doctor she referred me to ophthalmic department for review and I was diagnosed with dry eyes.* [P009-2]

When patients compared their adverse effects with the information initially received, the actual physical effects were not as bad as expected.

Till mid-treatment journey (cycle 6), most patients remarked that they were coping well with the physical effects experienced, which were described as mild.

> *Thank God I was not severely affected by the side effects … In comparison to all those side effects mentioned at the information session, I expected to be feeling much worse after receiving treatment.* [P010-2]

Due to the generalised effects of antineoplastic medicines, patients attributed any symptom to the antineoplastic and supportive medicines.

> *My appetite improved quite a lot, that I can't stop eating … clothes are not fitting me well. Hopefully once the treatment is over and I stop the steroid, I will return to my original self.* [P009-2]

With every treatment cycle, patients reported the same adverse effects particularly fatigue, peripheral neuropathy and nausea. The first few days following treatment administration were considered the worst, where they needed more time to rest during these days. Some elderly patients were worried that prolonged bed rest may result in being bedridden.

> *I start to feel differently once I leave hospital on Monday. There are moments where I need to sleep, especially in the afternoon. The day after I still feel tired. I hope this won't get worse; living the rest of my life confined in bed.* [P011-2]

> *This tingling sensation affected me badly … I used to walk three quarters of an hour everyday but nowadays I don't risk it as I lost strength in my lower limbs feeling unstable whilst walking. It has limited me a lot and hopefully I can restart again in the future …* [P015-2]

Every treatment cycle can be described as a unique experience. As treatment progressed (after cycle 6 of FOLFOX), the adverse effects experienced after each cycle were noted by patients to increase in their intensity and persist for a longer duration. Patients noted that they experienced adverse effects upon hospital discharge, with these effects lasting for around 7-10 days.

> *To tell you the truth, the tingling sensation has become part of my new life, I'm learning to live with them ... I'm not concerned about it [tingling] as I know the cause. I feel tired with heavy legs to walk, worsened by a sensation of a ball beneath my feet … I'm eating well as I have good appetite. However, regarding weight I've lost 9 kilos but I am still overweight*. [P012-3]

During the treatment journey, some patients experienced adverse effects that warranted hospital admission which included lower limb weakness, gastroenteritis, thrombosis and fever. Most of these patients did not seek immediate help (except for fever) as they were unable to evaluate the severity of their symptoms. They were concerned about these negative effects as they were perceived to outbalance the positive outcomes.

> *… a few days following the 11th cycle, I was admitted at hospital with fever, so during these last 15 days I avoided meeting persons to ensure that I would be fit for the last chemo cycle, so that I will be able to recover slowly.* [P012-3]

The mild pain and the reddish-brown discolouration of the skin due to chemical phlebitis faded completely with time. Improvement in taste was reported, with comments made that '*metallic taste decreased considerably*'. [P001-4] Patients noted that most adverse effects were reversed except for peripheral neuropathy and fatigue. Though being on '*the road of improvement*' [P001-4], they commented that they had not attained their health to pre-diagnosis. A few patients were startled to notice new symptoms such as generalised pain and cataracts during the three months following completion of treatment. They were not expecting to experience any new physical effects after cessation of treatment as the effects of antineoplastic medicine were expected to diminish with time.

> *Each day I'm getting better than the day before … However, I'm not yet feeling the same person I was before* [pre-diagnosis]. *Whilst receiving treatment, I was not suffering from any pain. However, after its completion, pain seems to be returning back … I expected medicine to disintegrate in my body with time, thereby after finishing this treatment I should be experiencing less side effects.* [P003-4]

Patients gauged improvement from treatment based on their engagement in physical activities. Those who continued to live independently despite suffering from adverse effects of treatment considered this as a great achievement.

> *At first my wife used to get me to hospital for treatment administration as they advised me that I might not be feeling well to do so. Since I continued to drive, I tried to come here for treatment with my car and leave it in the carpark. As soon as I'm finished, I drive myself back to open the shop. I tried it last cycle and it worked.* [P016-2]

Patients receiving the second-line treatment complained about the immediate occurrence of adverse effects upon its initiation, with effects including decreased appetite, altered taste and diarrhoea. In comparison to

FOLFOX, the effects experienced were worse in nature right at the start of the new treatment. As these patients were experiencing diarrhoea and therefore felt more lethargic, they felt constrained to stay at home. Consequently, the oncologists increased the treatment-free period to a 3-week gap to allow patients to achieve better recovery from the physical effects. In addition, these patients were advised about the possible occurrence of treatment-induced alopecia, whereby a few patients accepted it without major concern and cut their hair in preparation for this event.

> *It is a difficult time … and the adverse effects aren't pleasant ... I get diarrhoea and feel miserable and that's why I am reluctant to come to the next treatment cycle … I know what I will be experiencing. I know that I will suffer from the same effects like the previous two weeks.* [P011-4]

The impact of peripheral neuropathy

Looking back at the treatment journey, most patients considered peripheral neuropathy to be the worst adverse effect they experienced. Although peripheral neuropathy limited their independence, patients were not particularly concerned at the beginning of the treatment journey as this was an expected adverse effect of antineoplastic medicines. However, the persistence of peripheral neuropathy at a later stage of treatment worried patients due to its interference with some activities of daily living such as drying laundry or sewing. The initial mild tingling sensation, particularly upon touching cold surfaces was transformed to a continuous '*feeling of padded hands similar to a cushion*.' [P001-4] The description of this effect varied amongst patients, each experiencing a variable degree of severity. Along the treatment journey, patients had to learn to live with these symptoms and applied various coping strategies to improve their situation. These included wearing gloves or limb warmers and using lukewarm water to clean the house. Despite these mitigation measures, a few patients still complained of instances when experiencing loss of grip and lack of strength, with a patient describing how her bird ran free after losing control in holding the cage whilst cleaning it. The degree of severity and duration of this adverse effect was not explained by any healthcare professionals and concern about the persistence of peripheral neuropathy following completion of treatment led them to seek advice from healthcare professionals. Patients felt ignored when speaking with healthcare professionals about this chronic symptom as '*there is no remedy to control* *it*' [P014-4] and were later informed that it could persist for a year after cessation of antineoplastic medicines.

> *The numbness and tingling sensation of my hand got worse after 2 weeks of completion of chemo … sometimes also being so painful as to wake me during the night. I wear gloves, two pairs of socks but to no avail. When I reported this, the doctor told me that the tingling sensation on my feet may last at least one year.* [P012-4]

The impact of stoma

All patients with the stoma described drastic changes in their lives. Though stoma was constructed prior to initiation of treatment with antineoplastic medicines, patients spoke about it as from interview 2 onwards. Besides the aesthetic changes, having a stoma prevented them from meeting other persons as well as limited their physical activities due to risk of leakage and foul smell. Despite the training received about stoma care, they still experienced challenges to live with the stoma, particularly complicated with any changes in diet and treatment with antineoplastic medicines.

> *I felt badly when looking at myself in the bathroom … During the night I wake up around 3 times to change it … however it does not affect my sleeping pattern. You learn to know yourself.* [P014-2]

> *I find it difficult to walk long distances as I feel the stoma heavy when walking. I think I have been living with the stoma for the last 2 to 3 months, but I'm getting better.* [P002-4]

4.3.2.4.2. Sub-theme: Impact of psychological effects on patients

An interplay of positive and negative emotions

Most patients explained the shock they experienced on being diagnosed with cancer. The treatment journey with antineoplastic medicines was then a '*rollercoaster of emotions'* [P011-4]. Patients claimed to suffer from changes in their emotional status including fear, anxiety, irritability, sadness, uncertainty and hope as well as transient cognitive effects with loss of concentration. As treatment progressed, some patients felt sad and often cried. Some others became highly sensitive and empathised with other patients experiencing the same situation.

> *I was definitely affected emotionally as the* [cancer] *situation touches you somehow. Sometimes I get nervous and irritable more and more quickly just on small things. For instance, I hate it when neighbours are noisy when you are tired and want to sleep, though when this happened before it was tolerable.* [P007-2]

> *You feel a little bit more emotional and sometimes even shed tears for the other patients I meet in the ward. As I can easily understand their situation of uncertainty, I truly empathise with them*. [P001-3]

Prior to initiation of treatment, most patients made sure that they engaged in an activity they enjoyed most as if it was their last opportunity.

> *I really like eating red meat cooked as rare, but I cannot eat it anymore once I start this treatment. To be honest with you, last Saturday I went to my favourite restaurant with my family to eat this meat as if it would be my last time …* [P009-1]

Initiation of treatment with antineoplastic medicines brought with it intense emotions of fear and anxiety whilst concurrently offering hope for overcoming their life-threatening illness. As treatment progressed, the emotional distress persisted and most patients claimed that their thoughts constantly focussed on their treatment with cancer.

> *There were so many things going on initially that made it difficult for me to register everything in my mind. I was so anxious upon hearing the news in front of the oncologist, with my eyes staring blankly at her and saying 'yes' repeatedly. My anxiety remained sky high for the first few cycles. Though, I must admit that lately I am more in control of my emotions and coming for treatment with less fear and anxiety … the treatment has become part of my life so much so that I can't stop thinking about it.* [P010-2]

Increased familiarity with administration of treatment, receipt of positive results and experiencing mild adverse effects kindled positive emotions of hopefulness and feeling of coping amongst patients. Some patients looked forward to the next cycles with anticipation of completing the treatment journey.

> *Along the treatment, I was not feeling adversely bad. I was mostly affected physically such as heartburn … however I'm coping quite well. The positive results I'm receiving continue to keep me hopeful.* [P004-2]

As treatment progressed, the intensification of adverse effects led to patients' physical disability and aesthetic changes that evoked negative emotions of concern and despair.

> *I'm noticing this yellowish tinge on my skin … I hope that the liver is not affected. As I wake up, I wear make-up so that I feel and look better, otherwise I'm pale and weak*.' [P006-2]

> *When I'm in pain, I'm truly depressed with no urge to use my mobile or television. I feel frustrated with the whole world, crying and shouting that I'm helpless to continue combating the situation and tired of this situation! Then when I'm fine I will be cracking jokes again*. [P011-3]

As patients increased their reliance on family members and shifted their tasks onto them, they felt irritable and frustrated. Moreover, patients claimed that when they went to medical visits, they experienced a lack of concentration and felt overwhelmed with feelings of anxiety and fear, particularly of negative results.

> *I was always short-tempered but I've become more irritable. I think because I'm unable to carry out the things I used to do before myself and always depend on others. I don't like calling my husband all the time as he is not my servant. Moreover, it makes me feel useless.* [P003-3]

On completion of treatment, patients complained about resurging feelings of anxiety, irritability and uncertainty mainly attributed to an unknown future and a lack of control of the future. Moreover, patients were unsure about the effectiveness of treatment.

> *I'm hoping that it* [cancer] *has been completely eradicated with treatment. I will have to undergo that test with the camera* [CT scan] *to know what is happening inside my body. I will be anxious to know the result. I'm hoping for a positive result and expecting that all my sacrifice was not in vain.* [P015-3]

This journey with cancer and its treatment left an imprint on the patient's own character, as they realised that they could never be the same person they were prior to their diagnosis. All patients were grateful of being alive but were constantly reminded about their negative experiences by the persistence of adverse effects. Patients claimed that they changed their outlook towards life, developed a stronger character and learnt to adapt to different situations in life. Patients felt that having been through this experience enabled them to face any future challenges. In fact, a few described that they have become calmer and more rational when facing daily life problems. To feel better, patients kept reminding themselves that their situation could have been worse.

> … *from the emotional aspect, I am more sensitive occasionally crying more but also laughing more. Chemo has made me stronger in character, because of what I have gone through and all the experiences it had brought with it.* [P006-4]

Patients receiving second-line treatment experienced worsening of psychological effects. At this stage the hope of cure was clearly vanishing, and patients were losing their fighting spirit. In fact, one of the patients disclosed '*a feeling of always digging deeper in a solitude journey.'* [P011-4]

Though the patients were more accustomed to deal with bad news, they were still feeling depressed and distressed.

> *At first it was a shock let's face it. You do not expect to receive the bad results. But as time goes on, you learn to adapt and accept it. Hearing other patient's stories, you come to realise that you are not alone and there are others who are going through a similar experience. Now that I completed chemo, I hope not to receive more bad news, as I am tired of it.* [P005-4]

Reluctance to speak about diagnosis and treatment

Some patients experienced feeling of shame about their diagnosis of cancer and treatment. This made them reluctant to speak openly about it. Due to the connotation of cancer and its treatment with death or life nearing the end amongst the public, they did not want to feel pitied due to their diagnosis. At the first interview, most patients shared the news with a select group of individuals, namely their immediate family members, close friends, and employers. As time went on, patients spread the news more openly particularly when they received comments about their appearance.

> *I told only my family and close friends. It is not something that you have to tell everyone about.* [P010-1]

> *There are some whom I did not tell [about diagnosis of cancer] as I do not speak with everybody about my situation. With time, I'm telling more individuals about it. Till now, I told my close friends, work colleagues, family and my sister … and they try to help me out.* [P007-2]

> *I met a long time friend and he commented on me getting thinner.* I had no other option but to tell him about my illness. [P004-2]

During the treatment journey, the feeling of shame was also evident in relation to infectious diseases. A patient described how she was refusing visitors so as not to disclose information about her diagnosis with carbapenem-resistant Enterobacterales (CRE) and Methicillin-resistant *Staphylococcus aureus (MRSA)*.

> *At first, I took it badly when nurses informed me to stay in a single room and that they have to wear those things to visit me as I tested positive for that [MRSA and CRE screening] … It was really difficult to accept, in fact I did not tell persons other than my siblings to visit me here [oncology centre]. I don't want to share the news with other persons that I have an infection as everyone will abandon you.* [P008-3]

Some patients described that people reacted differently to the news of their diagnosis. They described individuals who were lost for words or provided words of advice though these were not convincing or became more keen to provide their support.

> *Persons with whom I had argued before made the step to talk and helped me when necessary.* [P008-4]
>
> *Whilst my family advise me to be courageous, I notice that they themselves do not have such courage*! [P002-2]

4.3.2.4.3. Sub-theme: Social consequences for patients

Consequences of voluntary social isolation

Patients were highly concerned of their risk of acquiring infections due to their weakened immune system. They prioritised their need to be cautious to mitigate this risk, particularly by reducing social contact. In view of this risk, patients re-evaluated their own social activities. At initiation of treatment most patients planned a complete ban on their social activities such as weddings, travel abroad and community events. The enforcement of cautionary measures led to social isolation and to psychological effects, with patients being concerned about the long-term impact of these.

> *I'll be spending a lot of my time at home with my husband with minimal contact with other persons due to risk of contracting other illnesses; I hope I do not feel lonely and depressed*. [P013-1]

With time, they slowly reduced their voluntary social ban. Whilst remaining cautious, all patients were hopeful that during the treatment journey they would engage in physical activities to keep themselves active, enhance their well-being and lift their spirits. They considered this would make up for the time lost in hospital. Most patients found alternative means of enjoying themselves and maintaining communication by using digital technology. Whilst still avoiding crowds, some patients prioritised family activities or met close friends. These included meeting friends in a field, keeping social distance to attend social events or staying at home with their spouse preparing their favourite meal.

> *I form part of the geriatric community of my hometown. At first, I was so afraid that I decided to stop attending completely. However, then I was lonely and decided to attend the monthly tombola event where I stay on a table on my own shouting the numbers. In this way, I did not lose all the social contact with my friends.* [P004-2]
>
> *Today with the technology such as mobile phones, I can keep contact with my daughters without them having to come visiting me at hospital. Since one of them is pregnant, I don't have to worry about their safety and be an additional burden to them.* [P010-2]

> *I still go out normally but avoid the crowds. I even attended my niece's wedding but stayed in a corner in the garden with my family. The most important thing is that I stayed away from the crowd*. [P012-2]

The reduced social contact generally resulted in improved relationships with their immediate family members. Close relationships were established between patients and their loved ones, whereby patients felt they were being well cared for.

> *I think this has got me closer to my wife, as before you take certain things for granted and do not have time to appreciate the small gestures in life.* [P016-2]

Most patients hoped that upon completion of treatment with antineoplastic medicines, they would make up for this social isolation by planning activities such as a short holiday abroad. Patients realised that they would still need to follow certain restrictions. They requested opinions from healthcare professionals about these social activities to evaluate the possible risks involved.

> *To tell you the truth, I wished to go on holiday abroad with our friends. If something happened to me, what was I supposed to do then?! Before we used to go for 7 or 10 days but if the oncologist allowed me, I would go for a short break of around 3 days …* [P010-3]

Within 3 months following completion of treatment, patients were still slowly resuming their social activities as they were exploring their new limitations as cancer survivors. Every activity that patients were able to carry out successfully was considered as achievement and boosted their confidence.

> *I resumed my old routine such as going for short walks in my town, go to Valletta by bus … we have just arrived from a short visit to Lourdes. At first, I was afraid of the plane as I thought that sitting for a long-time would affect my tingling sensation on my feet, more so being in the air! However, from the positive experience we're looking forward to plan another short holiday.* [P001-4]

Other factors leading to social isolation

There were other factors exacerbating the social isolation. Adverse effects such as diarrhoea and fatigue reduced the patients' ability to socialise.

> *My life has changed a lot. I'm not going out as much … you will be afraid to go out in view of diarrhoea. I prefer to stay at home or otherwise to feel secure, I always plan beforehand where I can find a lavatory in the vicinity*. [P011-4]

The uncertainty about their well-being, particularly fatigue, prevented patients from committing themselves to participate in activities where their presence was crucial such as being a godparent.

> *Next Saturday I have the baptism of my daughter's son; however, I informed her to better select the in-laws to be godparent as I don't know how I would be feeling on that day. Moreover, I have just been informed that this new treatment may cause hair loss and sometimes I feel so weak that I don't feel like going out and at 7pm I would be already in bed.* [P010-3]

The role of pets

Pets were noted to be a great source of emotional comfort to patients and the decreased social contact led to increased affection towards pets. At initiation of treatment, patients who owned pets and particularly those living on their own found difficulty to follow precautionary measures whilst taking care of their own pets. Some patients even considered rehoming their pets with relatives. Other pet owners identified ways such as wearing gloves to clean the litter or re-arranged the house to segregate their pets to a restricted area.

> *After advice given by the Aurora nurses to avoid contact with animals, I decided to give my 2 birds to my niece*. [P005-1]

> *I had a problem with my pets but finally I managed to re-arrange my house so that my dogs and cats live in their own living area and not run around with me. If I don't find a pet sitter to clean their area, I clean it myself and wear gloves. I cannot abandon them now* [having cancer and receiving treatment] [P008-1]

Along the treatment journey, some patients found it difficult to leave their pets behind during their regular hospital admissions. Some patients described how pets served as a relief to share their emotions.

> *I have a cat at home, who I think helped me most emotionally. She became so bonded to me that when I feel weak or cry it comes circling around me, touching its fur against my skin. When I go back home after discharge she comes rushing towards the door and then sleeps on me!* [P014-3]

4.3.2.4.4. Sub-theme: Implications on financial status

Expenses linked to oncology care

At the start of treatment, patients were grateful that the national health service offered free access to oncology hospital services and treatment irrespective of the patient's income. As a result, patients did not envisage to encounter any financial burden.

> *I don't think I'll be affected badly in terms of finance. We all receive a free healthcare service. This is a gift that we don't pay anything!* [P002-1]

Along the treatment journey, patients experienced a higher financial impact than expected. Costs incurred were mainly related to purchasing of specific sanitary products and supportive medicines to prevent or control treatment-related effects. Other expenses were related to modifications in the house and payments for home help. Most patients' expenses remained stable over the treatment journey, though remaining high even following completion of treatment. Patients focused their expenses on their real needs and changed behaviours to cover these illness-related expenses.

> *I must buy specific products such as mouthwash and lip cream … currently I need to be financially supported by my brother. Lately … I requested my brother to provide me with my share of my father's inheritance.* [P005-2]

> *I'm no longer spending money without rationale. I'm thinking about cost cutting on small expenses such as cessation of cigarette smoking to transfer these savings to my new fund. The more I save, the better. This needs to be planned … We have a large house which I'm considering selling to live in a small apartment.* [P016-2]

Effect on patients' income

Prior to initiation of treatment, patients who were working had to take a decision on whether to continue or stop working. Despite being considered as an added burden, most of these patients decided to cease working due to their immunocompromised state. Moreover, some of the younger patients were concerned about how they would cope with reduced income whilst also sustaining their existing debts.

> *I still have an active loan on my house. The problem is that the doctor told me that I will spend at least 7 months away from my workplace … My income has been severely affected now that I am on long-term sick leave. I am depending on my siblings for financial assistance to pay the loan … In such circumstances, I am trying to make both ends meet so that my son and I remain living in our house.* [P011-1]

Some patients made the necessary arrangements to continue working during their treatment, whilst others were granted long-term sick leave while their job was protected.

> *My employer is supporting me in everything I require and is also very flexible. For example, I wish to work only 6.5 hours to see how I feel, and he agreed without any problem.* [P007-1]

> *Initially, I was reluctant to take long-term absence from work due to treatment [*chemotherapy*] as I had already been granted sick leave for surgery. But I had to stop due to the high risk of getting an infection.* [P006-2]

Patients appreciated that employers were very supportive and compassionate sometimes allowing a flexible working schedule and the opportunity of remote working. Some patients appreciated that work colleagues kept in touch.

> *But my company is so helpful that they paid me without having to go to work or repay! They went out of their way in such a situation; they were very flexible and allowed me to work from home. The network of support at work is important too. I have many good colleagues at work as for instance if somebody coughs, they tell me please go into the other room to reduce contact with the person who is coughing.* [P007-2]

Patients who were close to pension age were concerned about their pension entitlement since they stopped working during their last few years of their employment.

> *The fact that I'm on long-term sick, it's like stopping from work a bit earlier prior to my entitled pension age. This will affect me in the long term as the computation of the pension takes into consideration the income of my last few years of work*. [P004-3]

Pensioners felt secure that their pension would not be affected and consequently elderly patients seemed confident that they would not be affected much, unlike younger patients. Besides utilising the pension, they recognised that the time had come to resort to their own savings or to dispose of their assets to make good use of them. However, some patients were concerned whether their spouses would financially manage if they passed away.

> *I was not so much affected as I was cautious all my life to save pennies for our future in times of need. I know that I'm spending them well to buy particular products needed such as specific branded body cleansing products.* [P015-2]

Return to work

At the last treatment cycle, patients who ceased work were still anxious about their return to the same type of work due to possible physical effects such as fatigue during working hours. In fact, a patient was even considering shifting to part-time.

> *I was affected financially as I used to work and then stopped abruptly which made me more financially unstable … I'm not sure I'll be able to*

> *return to work. I'm concerned that if I feel tired at work, I would not be permitted to rest. At the same time, my employer is now asking for the date of my return. He accepted [returning at a later date], but the employer would be looking at the situation from their perspective.* [P004-3]

> *A colleague of mine who was receiving treatment for this illness used to come to work. But his work is behind a desk in an office, and he occasionally had to leave work to rest at home. This does not compare to my work as a cleaner where one requires physical strength.* [P011-3]

The return to work following completion of treatment was considered as a milestone in the patient's life to regain normality and was described as a moment of mixed emotions of anxiety and satisfaction for that individual patient.

> *I returned to work, thanks to God as from the beginning of this year … I felt anxious to return but soon got back into routine. I'm coping well at work… it fills me with satisfaction … I have been doing this work as carer for the last 30 years*. [P006-4]

Initiation of second line treatment with antineoplastic medicine was another reason given for not returning to work.

> *Obviously, my return to work is out of my plans as I'm receiving another new treatment … I'm spending my days in bed. [S011-3]*

4.3.2.4.5. Sub-theme: Seeking refuge in spirituality and religion

As from the start of treatment, almost all patients referred to religion and spirituality with their perception that cancer is a life-threatening illness leading them to increasingly seek spirituality and religion Common phrases that featured in the patients' interviews were '*with God's help*' [P010-1] or '*leave it [the fate of the illness] in God's hands'* [P001-1] [P002-1] [P015-1].

At initiation of treatment, faith was rekindled in some patients. They explained that one should put trust in both the medical and religious aspects to achieve healing. Patients considered God as a collaborator in this journey, whereby through their prayers, healthcare professionals would be enlightened with knowledge required for the provision of cancer care.

> *Ever since I received the diagnosis, I got closer to God. I was a person who rarely attended mass but now I wait eagerly for the priest to receive Holy Communion. I feel fulfilled with serenity and the hopefulness that I require*. [P008-3]

As treatment progressed, most patients' faith and spirituality intensified as they became more actively engaged in religious activities such as participating in religious rites and reading spiritual books. Moreover a few patients sought to perform good deeds to please God. The presence of the priest whilst being in hospital also supported patients' spiritual well-being.

> *As from the diagnosis, I engaged myself in this process in getting to know more about God. I'm feeling getting closer to him by receiving Holy Communion every day and reading the Bible.* [P010-2]
>
> *I feel better when praying for everyone in this world … Though I'm not working, I still wanted to assist disabled children by giving a small donation … In return I received rosary beads … felt so emotional that I cried a lot. It was like receiving a treasure.* [P006-3]

Very few patients raised their inner conflict between science and faith. They remarked how family members felt obliged to support the patient's journey to faith.

> *My brother-in-law made friends with a Nun who is praying on sick people. He is trying to convince me to talk to her … I believe in God but I feel that I trust more the scientific fate. [P016-2]*

The patients' trust in God was described to increase their hopefulness to open themselves to accept God's plan. They focused more on short-term achievable goals that brought comfort and meaning to themselves.

> *My body is showing signs of recovery … I say to myself it seems that Jesus is with me and is showing me signs that he is helping me … I don't know whether I am misleading myself.* [P013-2]

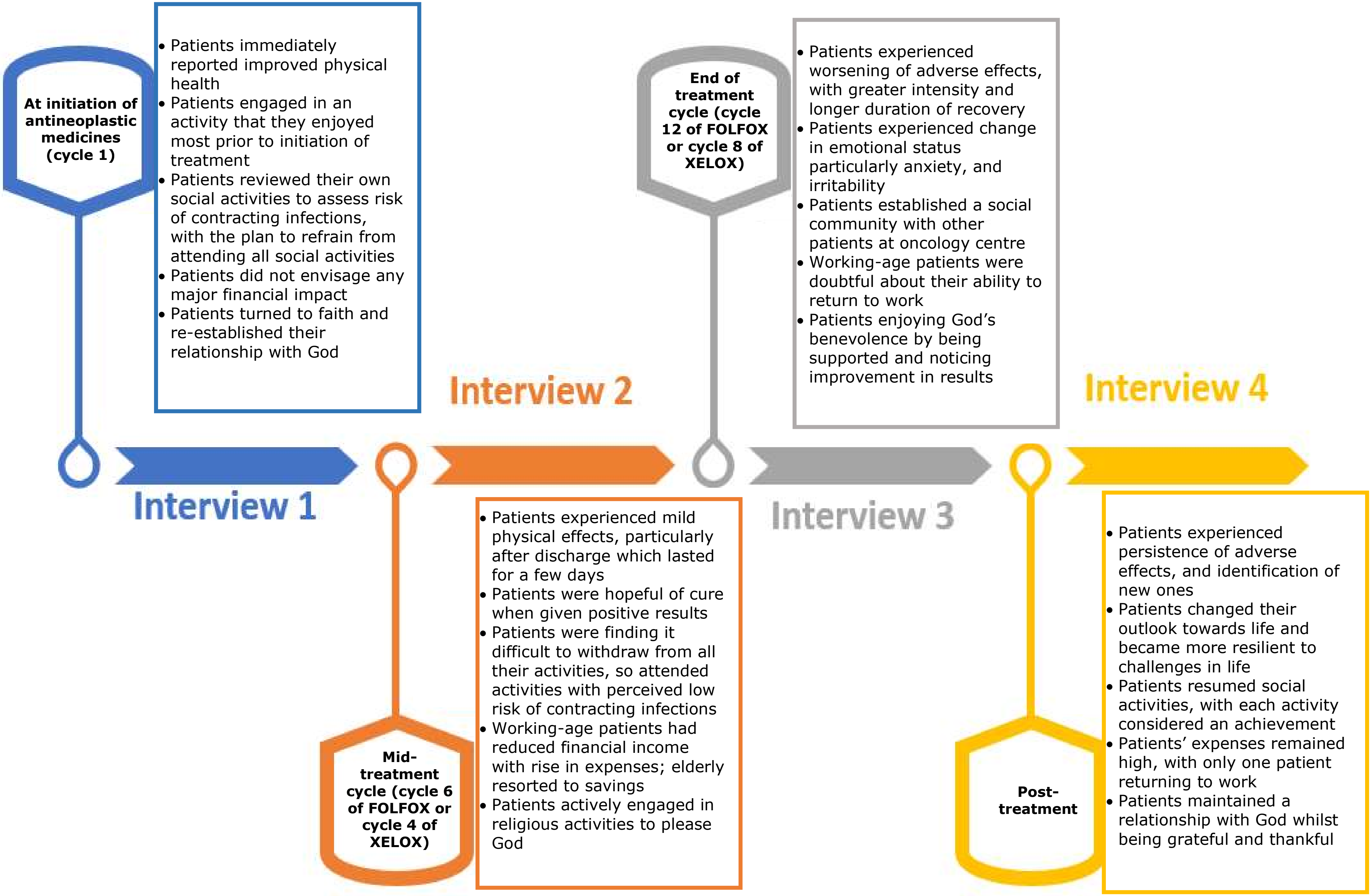
On completion of treatment, several patients described how they were enjoying God's benevolence by noticing improvement in results. Some patients attributed their ability to complete treatment only due to God's intervention.

> *God helped me to receive all the 12 cycles in one way or another… though it was highly traumatic …* [P014-3]
>
> *Ignorant is that person who does not believe in God … though it was hard [during the treatment journey], I'm amazed with how I used to obtain all my strength?! I think it's all from God …* [P006-4]

At three months after completion of treatment, patients still maintained their close relationship with God and patients seemed to be committed to continue this relationship throughout the rest of their life. A patient was thankful to God in giving her another chance to live as she was able to survive treatment with surgery and antineoplastics for metastasised cancer. Some kept their promise made at start of treatment to visit a place of worship such as Lourdes as a sign of gratitude following completion of treatment.

> *At first, I was afraid but thanks to God's mercy I'm cured. Physically I feel like the same person I was before … doing all the housework and everything. It's terrific that God cured me as it's unthinkable to be cured from 2 cancers when being unsure whether I could make it or not but I'm still alive today.* [P008-4]

Figure 4.6 highlights the longitudinal presentation of key points of Theme 4 at four specific time-points during the patients' treatment journey.



Interview 1

At initiation of antineoplastic medicines (cycle 1)

- Patients immediately reported improved physical health
- Patients engaged in an activity that they enjoyed most prior to initiation of treatment
- Patients reviewed their own social activities to assess risk of contracting infections, with the plan to refrain from attending all social activities
- Patients did not envisage any major financial impact
- Patients turned to faith and re-established their relationship with God

Interview 2

Mid-treatment cycle (cycle 6 of FOLFOX or cycle 4 of XELOX)

- Patients experienced mild physical effects, particularly after discharge which lasted for a few days
- Patients were hopeful of cure when given positive results
- Patients were finding it difficult to withdraw from all their activities, so attended activities with perceived low risk of contracting infections
- Working-age patients had reduced financial income with rise in expenses; elderly resorted to savings
- Patients actively engaged in religious activities to please God

Interview 3

End of treatment cycle (cycle 12 of FOLFOX or cycle 8 of XELOX)

- Patients experienced worsening of adverse effects, with greater intensity and longer duration of recovery
- Patients experienced change in emotional status particularly anxiety, and irritability
- Patients established a social community with other patients at oncology centre
- Working-age patients were doubtful about their ability to return to work
- Patients enjoying God's benevolence by being supported and noticing improvement in results

Interview 4

Post-treatment

- Patients experienced persistence of adverse effects, and identification of new ones
- Patients changed their outlook towards life and became more resilient to challenges in life
- Patients resumed social activities, with each activity considered an achievement
- Patients' expenses remained high, with only one patient returning to work
- Patients maintained a relationship with God whilst being grateful and thankful

Figure 4.6: The longitudinal presentation of key points identified in the theme Medicine and illness-related impact on patients

4.3.2.5. Theme 5: Personal support structure

4.3.2.5.1. Sub-theme: Establishing a support network

The need of a support network

Whilst patients reported minimal need of support at the first interview, the need for support increased along the treatment journey and peaked over the last few treatment cycles. Consequently, patients had to establish a support network and to shift their responsibilities. Their network was made of mainly family, close friends, neighbours, local community members, employers and work colleagues.

> *Being an elderly lady living on my own, I was considering … either to live in a care home or recruiting a full-time carer if my niece will not be available.* [P005-1]

> *I used to do almost everything independently at the beginning of treatment. But now I cannot hold a bottle of soft drink in my hands and sometimes even finding it difficult to get up from the chair. These instances make me cry as I cannot believe such deterioration in my strength. The assistance I received from my siblings and partner were indispensable to be able to make it all along.* [P011-3]

After completion of treatment, patients started regaining their independence and resumed most of their roles. Because of the persistent effects of peripheral neuropathy, the support was only needed for the tasks which were difficult to manage such as drying laundry.

> *Though I've always found help particularly from my husband whilst receiving treatment, I started doing almost everything myself again [three months after completion of treatment with antineoplastic medicines]. I'm challenging myself so that the numbness in my hands and feet don't take over the control of the rest of my body.* [P014-4]

All patients were thankful to those who assisted them throughout as their role was crucial for them to cope.

> *Support was necessary throughout, even when just giving me a word of advice. No one had to give me support but I still found individuals who provided me with their assistance. This made me learn to appreciate what others were doing for me.* [P008-3]

Role of family

All patients expected their own families, particularly spouses, offsprings and siblings, to be a key contributor to their support network. Exceptionally one patient did not resort to her family due to long-standing disputes.

> *When my husband is not at home, he phones me around four times a day now compared to none before … My daughter also helps by doing the shopping for me. [P009-2]*

> *I'm not relying on my family for help as they are negative individuals … we even had disagreements in the past. I trust my neighbour and some close friends who will help me if need be.* [P008-1]

A few patients remarked that the nurse-led information session served as an eye opener for their families to act as carers and prepare them in case of future unexpected events.

> *After the information session, my wife is being much more attentive in her cooking to ascertain that her meals are nutritious and well-cooked as recommended by the Aurora nurse … Also, she learnt that if I experience fever or any other symptom we have to report to the emergency department.* [P016-2]

Most patients continued to struggle to carry out their duties themselves but felt the need to keep on their fighting spirit and maintain their role within their own families. However, along the treatment journey, patients realised that the support network's assistance was crucial.

> *I feel that I need to do my part, by sustaining my fighting spirit and not stay depressed in bed.* [P001-2]

> *Although I'm young, I still require assistance. I feel very supported by my mother and my wife. This makes me feel better and even motivates me to look forward in my life … it is helping me psychologically.* [P007-2]

As the treatment progressed the actual supporting tasks required by the patients became more defined and these were assigned to specific family members.

> *I'm getting concerned about the side effects I'm experiencing, particularly the muscle pain and general feeling of weakness … As a result, there are a few tasks that I used to do myself that had to be shifted onto my husband.* [P014-2]

The family members had additional tasks such as transporting patients to hospital appointments and usually accompanying them during visits. Often family members asked questions and collated information during healthcare professional-patient conversations, particularly if the patient was not able to do so. Whilst the patients were in hospital, the significant others' role was reduced and mainly involved preparation of homemade meals and patient visits.

> *As my wife has a good memory, I ensure that she accompanies me to hospital appointments. I've instructed her to listen attentively to what is being said by the doctor, so that after the visit, I can ask her to re-explain everything and ensure that I've understood the doctor well. She even supports me by putting forward all my questions to the doctor … as*

> *I'll have 100 questions at home but when I come here, I forget everything. My wife is of great support*. [P010-3]

However, when the patients returned home, the significant others had to adopt a nursing role.

> *My wife knows exactly the schedule of treatment. I'm doing my best to keep to the 12 hours in between tablet administration … so both my wife and my mother are phoning me to remind me to take the medicines and then phone again sometime later to ensure that I have taken the tablets.* [P007-2]

Some patients expressed their concern of being a burden on their families. In some cases, patients refrained from notifying their significant others of symptoms experienced as they did not want to them to be concerned.

> *It is becoming difficult for my family to keep up with my needs and continue with their own life. I get worried seeing my husband tiring out with house cleaning and cooking etc. Hopefully the treatment is soon over, and I can resume the housework.* [P012-3]

> *I fell at home twice because I could not lift my leg to climb the stairs*. *My wife is still not aware about the falls I had, as I know that she will be too concerned.* [P015-3]

Moreover, patients were conscious that family members had to continue with their own daily schedule and challenges. Since the FOLFOX or XELOX treatment spread over a period of 6 months, patients were troubled about the frequency of hospital admissions and the impact that these visits had on their family members.

> *Because my niece has her own family too … hence making it more difficult for her to take care of me …* [P005-1]

Some patients complained that their significant others adopted a protective approach that further enforced social isolation, at times even going beyond the patients' wishes. There were instances where patients regarded their caregivers as interfering in their healthcare decisions such as insisting with patients to enquire further about their treatment with healthcare professionals. When patients were stripped off their roles within the family, some felt frustrated in having to follow orders particularly from their spouse.

> *My husband enforced everyone to follow a hygiene protocol prior to meeting me by washing their hands and using alcohol*. *Thankfully my siblings still visited me, though I think -he pushed them back as much as possible*. [P003-3]

> *In fact, they [the family] query a lot … there were things that I accepted without asking for further information as I didn't want to know … Then I told them that everything is happening to me and it's none of their business … as they continued to give their own advice without allowing me to make my own decisions.* [P014-3]

Role of close friends, neighbours and community

Some patients reported that close friends and neighbours kept regular contact with them, particularly when patients lived alone once they were aware of their diagnosis.

> *I received help just by telling them [neighbours] that I was diagnosed with cancer, without elaborating further about my illness … My neighbour, a married lady with 3 young kids, does the shopping for me, even going to a specific supermarket to buy my favourite sparkling water for me. I truly appreciate that.* [P008-3]

> *My siblings are all dead; I am the last survivor. Thankfully I have two friends who phone me occasionally. I really appreciate their help.* [P005-4]

Some patients claimed to feel appreciated when they realised that their friends were asking about their well-being.

> *I refused to attend a lot of the social activities, I used to attend before. Members of a society [of Malta Catholic Action], even those who are unaware of my illness, asked my husband about me. I'm really looking forward to starting again!* [P012-3]

A few patients spoke highly of the assistance received from other members of the community.

> *The chaplain looks out for me; he phones me and asks if I need anything. Even the grocer man at the corner of the street offers to carry the shopping home, as my daughter can't really help much in view of her current circumstances.* [P012-4]

Support from voluntary support groups

While receiving first-line treatment with FOFLOX or XELOX, none of the patients chose to join a support group.

> *I do not attend any support group as I do not feel the need … I have friends who offer support and encouragement.* [P012-1]

A few patients receiving second-line treatment for palliative intent accepted to be supported by hospice care providers who also provided home visits and social support.

> *Hospice also helped me. They often phoned me and even visited me twice at home. I can always count on them.* [P005-4]

4.3.2.5.2. Sub-theme: Self-regulation as a coping strategy

Developing a positive outlook on life

Being diagnosed with cancer made patients reflect and think about their own life in its entirety. The sudden change from living an active life to being unwell altered the individual's outlook on life.

> *I'm trying to adopt some measures mentioned in the session to be able to cope such as frequent resting … I'm also trying to think positively by placing trust in treatment to be effective.* [P013-1]

Along the treatment journey, the occurrence of unpredicted symptoms and other obstacles became a daily occurrence allowing them to develop the necessary coping skills. Patients tried to focus on positivity and adjustments in lifestyle to maintain wellbeing.

> *The chemo not only affected my daily routine, but I had to adapt my life according to the circumstances … I noticed that now I'm no longer grumbling on housework as I used to do before* [prior to diagnosis]*.* [P008-3]

Patients reflected on their achievements during their lifetime. They reorganised their priorities in life, with their focus being on taking care of their own self and appreciating the simple things in life. As treatment progressed, patients started looking at death as another inevitable milestone in life and learnt to live with uncertainty due to risk of death and cancer recurrence. This changed patients' preference to not planning too far into the future.

> *We'll see what happens … one can't worry about these things. Life must go on*. *Nowadays, when someone gives me a small gift, even if it is very simple, I really appreciate it and I feel very enthusiastic to make use of it.* [P006-3]

> *Upon being referred to SAMOC [oncology centre], I said to myself I'm already 72 years and have my luggage prepared in case God wants me near Him. That's why I don't feel afraid to die!* [P012-3]

Adopting coping and self-care strategies

After receiving the diagnosis of cancer, most of the patients went through a process of acceptance and denial. However, some patients still denied the reality of their illness despite being briefed about their diagnosis, hence attributing their symptoms to factors other than the illness or treatment itself.

> *I still can't believe this. The weight loss I'm experiencing might be due to the stress I'm bearing after my brother's death. To add to this,*

> *recently I suffered from a bad cold which made me feel weaker.* [P005-1]

> *I tried to explain to my son that I can suffer from this [cancer] like anybody else. I'm not special! The least I can do is to follow the treatment regimen, as required.* [P011-1]

Also a few patients avoided to speak about cancer with relatives or friends.

> *When my friends come over to visit me at home, I instruct them to talk about other subjects … to try to forget the current situation.* [P014-1]

At the start of treatment, patients planned to make lifestyle changes to counter their perceived impact of treatment, mainly the assumption of feeling weak and sick after administration. They planned to be more physically active, follow a balanced diet, consume vitamins, reduce cigarette smoking and alcohol consumption to boost their immune system and promote relaxation.

> *I'm taking regular vitamin C and ginger to boost my immunity. I'm trying this cannabis oil as well, which I bought from the pharmacy … in this way I ensure that it is not a counterfeit product. I take 2 drops a day sublingually and makes me feel calmer.* [P016-1]

> *I was advised to go walking when feeling lethargic. Despite my scepticism, I started going for a walk after the first treatment cycle. The first time I was exhausted after 5 minutes but the second time I walked for 15 minutes … now I'm doing brisk walking for 30 minutes. I'm feeling much better both physically and mentally.* [P009-2]

Most patients developed self-care strategies and described how they were more motivated to follow precautions when they understood the rationale behind them or when they experienced symptom improvement following the actions taken.

> *I noticed that through nibbling on healthy natural foods such as prunes, I'm controlling my nausea and constipation quite well. I wear gloves to be able to touch the soil and remove the weeds as it is my passion to take care of my plants. I know that the gloves decrease my contact and reduce the risk of contracting any infection.* [P013-2]

Along the treatment journey, patients had to forsake some hobbies, such as attending social activities, diving, gardening and taking care of pets. As part of self-care, patients engaged in activities that involved nature and outdoors, such as walks by the seaside, buying indoor plants and meeting with relatives in a garden. Patients also tried to engage in activities that improved their moods and maintained a positive outlook by reading children's fiction books, listening to music, and cracking jokes.

> *I really enjoyed myself this Summer especially when my husband and I meet other couples in a public garden. … I also relax when I read books, particularly children's books. I feel that my mind focuses on an imaginary fantasy world, which allows me to forget our adult's problems and enhances my positivity.* [P014-2]

> *I wake up early at 5am, turn on music on low volume with dim lights whilst quietly sipping coffee and smoking a cigarette on the terrace. That is really relaxing … it feels like I'm in heaven. It allows me to forget all my problems including that I'm receiving chemo.* [P006-2]

At the same time, patients were looking forward to the end of their treatment journey since their long-term plans had been on hold. Most elderly patients were looking forward to resume supporting their children and grandchildren.

> *I want to continue living to support my children and their grandchildren and enjoy my life with them*. [P010-3]

> *This [Illness and treatment] withheld all our plans. After finishing the treatment, we shall proceed with buying the flat … I may also seek the option of a private health insurance so that if it happens again, I will be covered.* [P007-2]

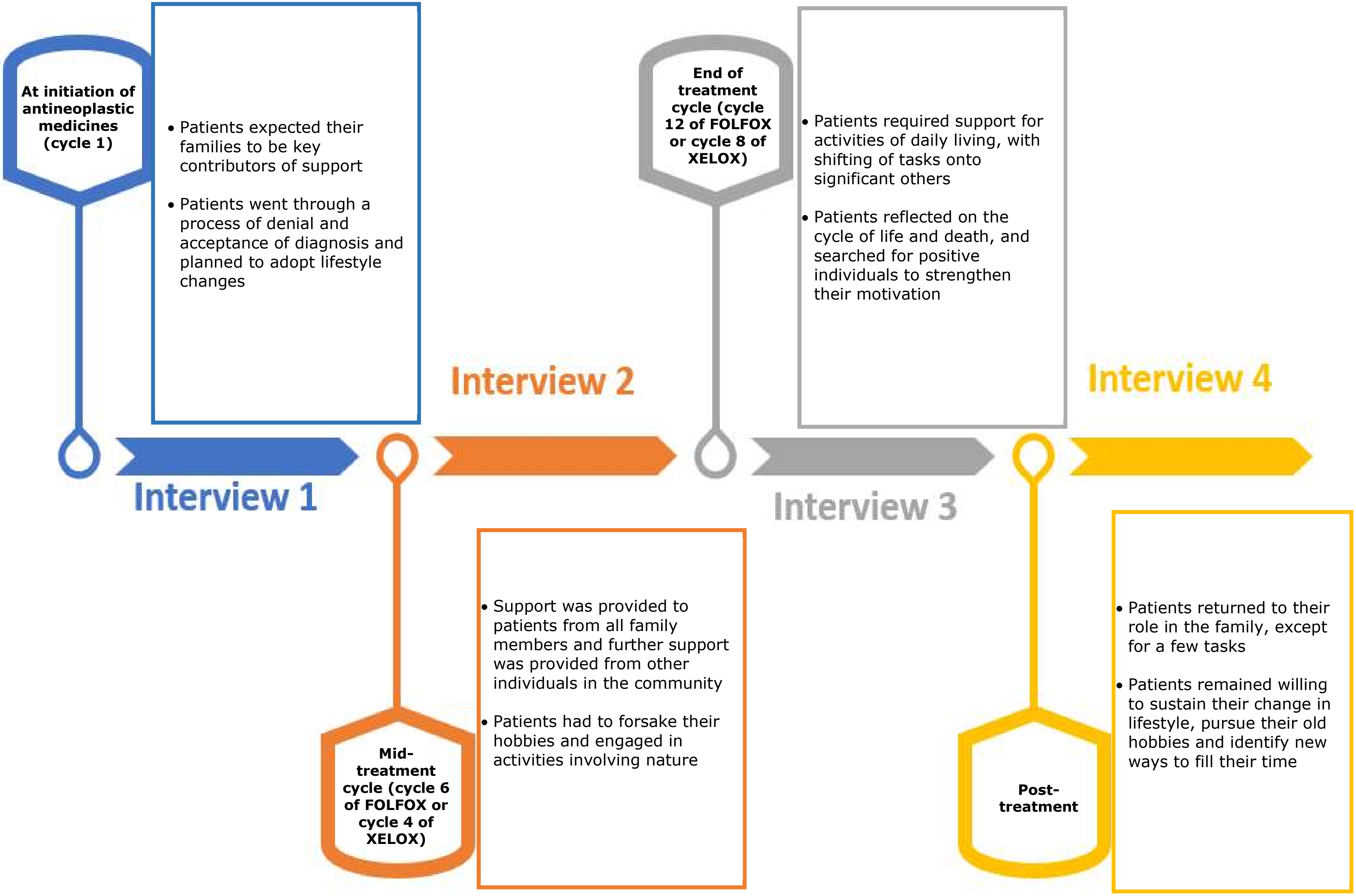
Patients who completed their treatment with antineoplastic medicines felt relieved that their treatment was over. Patients were willing to sustain their change in lifestyle including their healthy eating habits and exercise as well as decrease in their smoking patterns for life. At this point, patients aimed to pursue their old hobbies whilst a few identified new ways to occupy their time.

> *Unlike before, my life is no longer taken for granted … I used to assume that since I'm not feeling anything, I'm healthy. Now I really appreciate the real meaning of life … I took out my sewing machine and re-started practicing my hobby again. I'm also planning to attend the lace-making course or join a community group*. [P008-4]

Some patients on second-line treatment at this stage tried to avoid negative thoughts about cancer and treatment. They became more introverted and refused to speak to others about their situation. These patients preferred to just follow healthcare professionals' advice.

> *I don't feel like thinking, talking and nothing, I'm not interested any more … I'm going to live step by step and whatever has to happen happens.* [P011-4]

Figure 4.7 highlights the longitudinal presentation of key points of Theme 5 at four specific time-points during the patients' treatment journey.



- Patients expected their families to be key contributors of support
- Patients went through a process of denial and acceptance of diagnosis and planned to adopt lifestyle changes

- Support was provided to patients from all family members and further support was provided from other individuals in the community
- Patients had to forsake their hobbies and engaged in activities involving nature

- Patients required support for activities of daily living, with shifting of tasks onto significant others
- Patients reflected on the cycle of life and death, and searched for positive individuals to strengthen their motivation

- Patients returned to their role in the family, except for a few tasks
- Patients remained willing to sustain their change in lifestyle, pursue their old hobbies and identify new ways to fill their time

Figure 4.7: The longitudinal presentation of key points identified in the theme Personal support structure

4.4. Discussion

4.4.1. Summary of key findings

This study identified five themes which encompassed the patients' experience with antineoplastic medicines throughout the treatment:
(1) perceptions and knowledge of the illness and treatment,
(2) the healthcare system in relation to the illness and treatment,
(3) patient's involvement in treatment decision-making and the experience of medicine-taking practice, (4) medicines and illness-related impact on patients, and (5) personal support structure.

The findings of this study showed that patients perceived treatment with antineoplastic medicines as challenging and faced the prospect of the treatment journey in fear. However, this did not deter their high expectations and belief of achieving cure irrespective of treatment intent. Towards the end, patients were coming to terms with the fact that cure was not always possible showed awareness of their own misconceptions. Deficit in the patients' knowledge was evident at initiation of treatment, particularly about alarming symptoms suggestive of colorectal cancer. Patients' knowledge was noted to improve as treatment progressed and they became aware of the different antineoplastic medicines and their specific adverse effects. Whilst at initiation of treatment, the patients' knowledge and perception were influenced by the experience of family members and friends irrespective of cancer type or treatment, as treatment progressed their main influence were other patients receiving similar treatment on the oncology ward.

Almost all patients accepted treatment with antineoplastic medicines based solely on their oncologist's recommendations. Along the treatment journey, they made sure to adhere to the planned treatment schedule to secure the full benefits from antineoplastic medicines. They also evaluated the risk-benefit aspect of treatment to assess its effectiveness. In terms of antineoplastic medicines, the provision of information prior to initiation of treatment was crucial to patients. However, feedback provided about the group information session indicated that the information provided was non-specific resulting in patients feeling overwhelmed. Patients' trust in healthcare professionals was tainted with provision of conflicting information and lack of empathy. Despite this, all patients praised the individualised attention and accessibility of the nurse navigators who assisted them throughout the treatment journey, particularly when patients were recovering at home in between cycles. At initiation of treatment, patients were gaining familiarity with the healthcare system and did not put forward any recommendations. Along the treatment journey, patients became critical of healthcare services and requested more awareness of the available cancer services. Improvements in service provision such as increased awareness of psychological services and the development of new services were recommended with most patients suggesting the establishment of peer education and support service as well as a symptom control unit within the oncology centre.

During the treatment journey, patients experienced substantial physical, psychological, social and financial effects. Their helplessness was reflected in seeking refuge in spirituality and religion to achieve cure. Notwithstanding the patients’ anxiety and fear to initiate treatment, most patients became optimistic in completing treatment following their successful receipt of their first few treatment cycles. The severity of adverse effects worsened as treatment progressed, with peripheral neuropathy being a persistent symptom even after completion of treatment limiting their activities of daily living. The medicine and illness-related impact called for the patients’ need to develop their own personal support structure as from initiation of treatment. Patients expected their families to be the core of their support network. Furthermore, their adoption of coping strategies such as lifestyle changes and engagement in uplifting activities reduced the impact of illness and treatment on their daily life.

4.4.2. Interpretation of findings

Colorectal cancer remains a serious public health problem. Despite being the second commonest cancer in Europe (European Commission 2022), its diagnosis still proves to be challenging due to its non-specific presentation. Delayed presentation and diagnosis of cancer stem from poor knowledge about cancer and recognition of symptoms combined with negative beliefs and pessimistic attitudes (Jassem et al. 2014). In relation to the **first objective** of research which explores the patients’ beliefs and knowledge with antineoplastic medicines, results from our study showed that the patients' limited knowledge about the management of colorectal cancer gave rise to various misconceptions which were later clarified through their own experience along the treatment journey.

The patients' negative perceptions of cancer and the use of antineoplastic medicines were clearly exhibited by their initial reactions of fear, shock and devastation upon disclosure of diagnosis and proposed treatment with FOLFOX or XELOX. This response is like that of other individuals across several countries worldwide as cancer is considered to be the most feared illness in modern society (Hong et al. 2010). Additionally, colorectal cancer ranked second place in a survey classifying illness that induced fear amongst more than 2000 individuals in the UK (Cancer Research UK 2011).

Despite the common occurrence of fear associated with colorectal cancer, patients in our study demonstrated poor knowledge on alarming symptoms suggestive of colorectal cancer including altered bowel habits. This is similar to the findings of the systematic review by McCutchan et al. (2015) who evaluated individuals' knowledge, beliefs and barriers on cancer symptom presentation. Based on 60 studies, McCutchan et al. (2015) reported good level of knowledge about specific cancer symptoms with lumps and bleeding being the commonest recalled and recognised symptoms. However, knowledge was generally poor with regards to identification of non-specific cancer symptoms such as unexplained weight loss and fatigue; often misattributing such symptoms to other benign causes (McCutchan et al. 2015). As a result, some patients in our study had similar experiences of misdiagnosis. Therefore, it is imperative for healthcare professionals to attain a clear description of patients' symptoms during consultation.

Whilst some patients in our study failed to recognise the importance of screening, others claimed that early diagnosis and short time to antineoplastic treatment initiation were important determinants for achieving cure. This contrasts to the findings by the Health Information National Trends Survey (HINTS) where the general public in America exhibited good knowledge about the importance of colorectal cancer screening (89.9%, n=1778) (Rutten et al. 2009). Despite this, the respondents’ knowledge about survival was found to be low; with over 20% (n=460) of respondents underestimating the survival rates from colon cancer (Rutten et al. 2009). In contrast to our study, patients’ negative perceptions about cancer seemed to be outweighed by their perceptions of the curative potential of antineoplastic medicines. Likewise, a qualitative study exploring the attitudes to cancer revealed that individuals who were never personally diagnosed with cancer appeared to be ‘in two minds’, with an initial response to cancer being related to fear, trauma or death and a coexistent rational understanding that cancer can be manageable or even cured due to improvement in the available treatment (Robb et al. 2014). The inconsistency between the patients’ knowledge and the scientific evidence is of great concern as this may potentially affect patients’ health choices.

Misconceptions about antineoplastic medicines were also commonly shared amongst patients in our study and were particularly related to the perceived occurrence of treatment-induced severe alopecia and debilitating fatigue. Irrespective of gender, patients showed their concern about alopecia and were equally surprised of being spared from this effect by their treatment (FOLFOX or XELOX). This probably stemmed from the idea that the term ‘chemotherapy’ encapsulates a single antineoplastic medicine that treats all cancer types; something patients in our study realised was untrue along the treatment journey. In contrast to our study, several studies identified nausea and vomiting as the most dreaded expected adverse effects prior to initiation (Lorusso et al. 2017) and during treatment with antineoplastic medicines (Dubey et al. 2005, Sun et al. 2005). The progress made with regards to the use of antiemetics which contributed to reduced severity of vomiting might be reflected in the patients’ lack of concern to vomiting in our study. Interestingly, nausea and vomiting were also recognised in these studies as the most important adverse effect that influenced patients’ treatment decision (Dubey et al. 2005, Sun et al. 2005, Lorusso et al. 2017). These findings emphasise the healthcare professionals’ role in identifying and addressing the patients’ concerns about expected adverse effects of treatment, particularly since patients in several studies appeared to be willing to make trade-offs between certain adverse effects and different treatment regimens (route and schedule) (Dubey et al. 2005, Sun et al. 2005, Beusterien et al. 2014). Indeed, patients should be well-informed about the potential adverse effects as misconceptions may lead to emotional distress which in turn impede recovery and overall health outcomes.

At initiation of treatment, patients' influences towards treatment stemmed from past experiences of family members or close friends who had cancer, irrespective of cancer type or treatment. As treatment progressed, patients became more influenced by mass media, particularly television and radio programmes. Like our study, Balmer (2005) who explored the patients' perspectives on the use of media-produced information, revealed that patients became more sensitive to information provided by media when becoming ill. As information provided by the media may occasionally be incomplete or distorted, this may lead to false optimism amongst patients regarding efficacy of cancer treatments (Balmer 2005). The indisputable power of the media should be used towards improvement in transfer of scientific knowledge from researchers to the public, particularly to individuals with lower levels of education (Passalacqua et al. 2004). Keeping in mind the influence of media on patients with cancer, this imparts responsibility on journalists to be better trained to disseminate news on scientific matter. As individuals' negative beliefs and poor knowledge may adversely influence patients' decision on treatment, the development of education campaigns is necessary to improve cancer awareness. Such campaigns should not only aim to improve individuals' knowledge about symptoms for cancer but also address misconceptions about treatment options and cancer survival (McCutchan et al. 2015).

Receiving a cancer diagnosis brings about an instant transformation from an individual to a patient who is required to navigate across a broad and complex healthcare system, which is often very challenging (Walsh et al. 2010, Kokorelias et al. 2021). With respect to the **second objective**, the themes 'Healthcare system in relation to the illness and treatment' as well as 'Patients' involvement in decision-making and their experiences of medicine-taking practice' provided understanding of the patients' approach to the antineoplastic medicine-taking practice along the treatment journey. Some patients were concerned about the delay in initiating treatment. This is a common multifactorial problem in healthcare systems worldwide, due to patient factors (need of further investigations due to effects of treatment) or system factors (waiting for a procedure date or a specialist review). A recent study showed that a four-week delay for initiation of adjuvant treatment with antineoplastic medicines resulted in a 13% increased risk of mortality in patients with colorectal cancer (Hanna et al. 2020). As a result, national quality indicators in cancer care were put in place, though these may vary between countries. For instance, the target gap period between the decision to the actual provision of definitive treatment should be within 31 days in UK national health service (National Health System 2015, Hanna et al. 2020) and 84 days in Malta (Ministry for Health 2016, Ministry of Finance 2022). Hence efforts should focus on reducing delays in initiating cancer treatment related to system factors to achieve improved survival outcomes. These may include policies, expanding the specialist workforce capacity and training as well as making better use of information technology.

The WHO also acknowledges the importance of patient participation in healthcare services (Nelson et al. 2020). Based on the ethical principle of autonomy, modern clinical practice places emphasis on the individual’s right of self-determination and freedom to make their own choices about treatment (Marron et al 2020). Following on, Malta published its National Cancer Plan in 2017 advocating in favour of patients’ participation in cancer care by adopting shared decision-making (Ministry for Health 2017). However, lack of patients’ involvement in treatment decision-making was still evident in this study. Street and colleagues (2005 p. 960) described that “patient participation in medical encounters depends on a complex interplay of personal, physician and contextual factors” and culture played a major role in our study preventing the implementation of shared decision-making. Whereas all fifteen Maltese patients did not challenge the proposed treatment, the young non-Maltese patient described active involvement in treatment decision despite being under the care of the same consultant. This included the provision of treatment options followed by a period to re-think the decision, with the patient ultimately deciding to accept a combination of oral and parenteral antineoplastic treatment. In contrast, the other patients’ passive agreement to the oncologist’s treatment decision was anticipated as they voluntarily relinquished their autonomy to the oncologist perceived as having the knowledge, means and authority to bring about improvement in their health. This finding is supported by a recent quantitative study on assessment of patients' preferences in their involvement in decision-making process where 60% (n=151) of Maltese adult patients preferred a passive role in decision-making about cancer treatment (Azzopardi et al. 2017).

Life expectancy was identified by a recent systematic review to be a key attribute in accepting treatment with antineoplastic medicines for the management of colorectal cancer (Kowal et al. 2022). Studies published in the 1990s showed that patients were willing to accept toxic treatment even for only a 1% chance of cure (Slevin et al. 1990, McQuellon et al. 1995). However, recent studies in Canada and Australia showed that a small survival benefit of one month was still important for patients with colorectal cancer (Brundage et al. 2001, Blinman et al. 2010). Despite this, patients in UK preferred to trade-off life expectancy for treatments that caused less adverse effects such as pain, fatigue, alopecia, nausea and vomiting (Albassam, Noyce and Ashcroft 2011). Another great concern is the disparity on treatment choice between the patients' and healthcare professionals' perspective, whereby patients were noted to accept treatment with a lower chance of benefit (cure and symptom relief) in comparison to healthcare professionals (Slevin et al. 1990, Balmer, Thomas and Osborne 2001, Harrington and Smith 2008). Therefore, this highlighted the importance of patients' engagement in making informed decisions about their cancer care based on realistic expectations of treatment outcome and personal beliefs prior to initiation of treatment (Leighl et al. 2011, Zafar et al. 2013, Jiang et al. 2016, Ogawa et al. 2018).

Antineoplastic medicines are generally part of a complex treatment strategy for the management of colorectal cancer, with its use having various intents ranging from curative to prolongation of life and palliation (Mack et al. 2015, Guo et al. 2016). In our study, patients showed a lack of knowledge about their treatment intent despite consenting to treatment and attending a one-to-one meeting with their oncologist as well as a nurse-led group information session. Besides, patients with incurable colorectal cancer in our study inaccurately believed that the use of antineoplastic medicines may achieve cure. Patients' expectations and goals of care became more realistic along the treatment journey; shifting from high hopes of cure soon after diagnosis to controlling spread of cancer and prolonged survival towards completion of treatment. Therefore~~,~~ this raises doubts about the patients' ability to make an informed decision about treatment with antineoplastic medicines for incurable cancer. In view of this, patients may accept a futile long-course treatment without achieving the expected benefits at the expense of quality of life, increasing healthcare costs and impeding an adequate planning of their end-of-life (Ghandourh 2016). Similarly, a nationwide prospective observational cohort study by Weeks et al. (2012) in USA showed that most patients with metastatic lung (69%, n=710) and colorectal cancer (81%, n=483) who were receiving antineoplastic medicines for 4 months inaccurately believed that their palliative treatment had a curative potential. Additionally, a multicentre quantitative cohort study by Mack et al. (2015) in USA recognised that only a third (33%, n=240) of patients who were diagnosed with metastatic lung or colorectal cancer in the previous 4-6 months were aware that the use of antineoplastic medicines was 'not at all' likely to cure their cancer. Patients who were well informed of their advanced cancer diagnosis still received treatment with antineoplastic medicines at their end of life care. Despite this, patients who accepted the incurable nature of their cancer were more likely to utilise hospice care; this being considered as a marker of high-quality end-of-life care (Mack et al. 2015). Therefore, patients' understanding of treatment intent of antineoplastic medicines is a critical aspect of informed consent as this may lead to a broader impact on care.

Antineoplastic medicines can be administered efficaciously both orally as well as parenterally. Studies in the literature review by Eek et al. (2016) which evaluated patients' preferences on cancer treatment administration found that oral treatment was preferred in view of its ease of administration, perceived increased efficacy and possibly better past experiences. A randomised cross-over study by Twelves et al. (2006) who assessed patients' preference for oral capecitabine and parenteral 5-FU/LV regimen on 97 patients with advanced colorectal cancer, showed that the majority of patients (64%, n=62) retained their preference of oral treatment. Despite the fact that oral medicines are often perceived to offer a better quality of life (Given, Spoelstra and Grant 2011, Eek et al. 2016, Jacobs et al. 2019), most Maltese patients claimed that even if a choice was given to them, they would still opt for parenteral formulations of antineoplastic medicines considering equal efficacy for both formulations. Patients preferred to being under the observation of trained healthcare professionals during its administration as the main reason for this. Additionally, the Maltese patients' preference needs to be considered in the light of the short travelling distance from home to hospital.

There is a widespread recognition that effective healthcare professional-patient communication is a key factor to ensure comprehensive cancer care by promoting patients' satisfaction and reducing uncertainty (Northouse et al. 2007, Parker, Aaron and Baile 2009, Song et al. 2012, Kwame and Petrucka 2021). The findings of our study emphasised the patients' need to maintain empathic conversations with healthcare professionals during the treatment journey. Several studies highlighted that respectful encounter between patients and healthcare professionals promoted encouragement and strength in patients (Mussener et al. 2008, Jagosh et al. 2011, Wessel et al. 2013). Patients' experiences of disrespectful encounters with healthcare professionals resulted in negative consequences on patients' health and trust in the healthcare system (Wessel et al. 2013, Mansson et al. 2019). In our study, patients especially those without co-morbidities, felt unprepared to enter this unfamiliar world in the hospital setting. This gave rise to expectations of patients being greeted with empathic and compassionate healthcare professionals that further promote an atmosphere of openness and trust and showed appreciation when they were made to feel welcome. Recent studies showed that such an environment would encourage patients to clarify priorities, reset goals and focus their hopes on achievable possibilities from treatment (Cowley et al. 2000, Bittencourt Romeiro et al. 2016, Husebo, Karlsen and Husebo 2020). Healthcare professionals should also be able to handle patients' emotional reactions to information provided with empathy.

All patients in our study showed interest in being informed about their illness and treatment with emphasis on prognosis and incidence of adverse effects, information which patients claimed was lacking. Rather than a 'one-size-fits-all' approach as utilised in the nurse-led group information session, patients in our study requested tailored information specific to cancer type and treatment to accommodate their individual needs along the treatment journey. These findings reiterate the findings of the qualitative study by Kirk, Kirk and Kristjanson (2004) in Australia and Canada amongst patients receiving palliative care and their relatives. Here it was emphasised that information provision to patients must be individualised at all stages of the illness. Additionally, Marcus (2014) reported that verbal education should be part of a multimodal patient education session that involves a multidisciplinary approach and takes in consideration the patient's learning style, literacy, and culture. In turn, healthcare professionals require the skill, time, and training to engage in verbal education. In view of lack of studies identifying the appropriate timing of information provision, Fee-Schroeder et al. (2013) assumed that ideally patients' education on treatment should occur prior to initiation of their treatment cycles. However, patients in our study preferred to be provided with information throughout the duration of the treatment.

With respect to the **third objective**, the themes 'Medicines and illness-related impact on patients' and 'Personal support structure' provided understanding of the patients' approach to the burden experienced by patients with colorectal cancer during treatment with antineoplastic medicines. Quality of life is made up of four dimensions namely physical, psychological, social, and spiritual well-being. This is a daily concern for patients during cancer treatment (WHO quality of life assessment group 1996, Lin and Bauer-Wu 2003). As patients with cancer commonly consider their quality of life to be much worse than that of the general population, improvement in quality of life should be aimed for patients with both curative and palliative intents (Rohde et al. 2017). Along the treatment journey, patients in our study adopted various coping strategies to mitigate the effects of treatment and illness to optimise their quality of life. As the current treatments prolong the five-year survival rates, aspects related to quality of life have become increasingly important. Poor quality of life may adversely affect the patient's willingness to continue and complete the treatment successfully (Carelle et al. 2002).

Along the treatment journey, patients in our study experienced various physical adverse effects, particularly fatigue and peripheral neuropathy. Towards the last few treatment cycles, these effects were described by patients to increase in their intensity and persisted for a longer duration. As with our findings, Xian et al. (2021) reported worsening of fatigue from moderate to moderate-severe over six months (average score 39.48 to 46.42 at baseline and six months respectively from a total score of 75). Whilst patients recovered from fatigue in-between cycles, the persistent occurrence of peripheral neuropathy affected most patients in our study and interfered with the patients' daily life. Studies (Attal et al. 2009, Gebremedhn, Shortland and Mahns 2018) identified >90% of patients receiving oxaliplatin complaining of cold-triggered symptoms (paraesthesia, dysesthesia or pain), increasing in duration and severity with repeated administration. In 70% of cases, prolonged exposure to oxaliplatin induced severe chronic peripheral neuropathy, whereby patients required dose reduction or discontinuation of oxaliplatin (Wilson et al. 2002, Attal et al. 2009, Miaskowski et al. 2017), further adversely affecting cancer control and progression-free survival (Selvy et al. 2020). Due to its high prevalence, patients in our study rarely reported this adverse effect whilst receiving treatment and were more concerned when peripheral neuropathy persisted following completion of treatment. Likewise, Ali, Mohamed and Yousef (2020) revealed that only a fifth of patients (20.9%, n=23) from 121 patients treated with XELOX or FOLFOX informed doctors about neurotoxicity. This highlights the patients' need to receive better awareness about treatment-related adverse effects such as neurotoxicity and fatigue, so as to allow early identification and regular assessments amongst patients at risk of developing such adverse effects.

Treatment with antineoplastic medicines was identified as the treatment modality that caused the most significant psychological distress (Herscbach et al. 2008, Ceilleachair et al. 2012, Maguire et al. 2018). The only study that examined the first 100 days of 120 patients after receiving a cancer diagnosis revealed that patients suffered from intermittent periods of anxiety and depression (Weisman and Worden 1976). Patients with colorectal cancer had the highest level of acceptance of illness and this improved the negative emotions associated with the illness and treatment

(Czerw, Religioni and Banas 2020). In our study, most patients seemed to be more anxious at initiation and completion of treatment. Even though patients felt the need for psychological support, it was only made available to patients upon their request. Following completion of treatment, some patients emerged from the treatment journey as more resilient and with a more positive outlook towards life. McCaughan et al. (2012) advised healthcare professionals to provide more emotional support to patients who experience persistent anxiety and male patients who have a higher tendency to be reluctant to discuss their psychological distress with healthcare professionals.

The immediate cessation of work by almost all patients in our study following cancer diagnosis promoted adverse repercussions on the patients' psychosocial well-being and long-term financial pressures. Sanchez, Richardson and Mason (2004) identified treatment with antineoplastic medicines to cause the greatest impact by delaying their return to work. Patients in our study remarked that the persistence of adverse effects such as fatigue, long duration of treatment and the nature of their work impeded them from returning to work. Return to work represents a positive move towards recovery and return to normality (Sanchez, Richardson and Mason 2004). According to Den Bakker et al. (2020), more than one third of patients with colorectal cancer (37.2%, n=118) in the Netherlands returned to work within 1 year after initiation of sick leave. Considering this, the healthcare system should partner with community organisations to provide financial counselling and assist patients in taking a proactive role in managing their finances during treatment and beyond. This is important due to increased prevalence of colorectal cancer and older retirement age in developed countries.

According to the latest scientific survey entitled State of the Nation 2022 amongst 1064 individuals in Malta, around two thirds (58.1%) of patients claimed that religion plays an important role in their lives; these were particularly women (70.6%), elderly (66+ years – 76.5%) and with low levels of education (87.4%) (Newsroom TVM, 2022). As patients in our study shared similar demographics, it was expected that patients would find comfort in religion and spirituality. Most patients in our study, even those with lack of faith, rekindled their faith in God as from diagnosis and sustained this beyond completion of treatment. As a result, they became actively engaged in religious activities. Our findings agree with the outcome of the meta-analysis by Jim et al. (2015) where religion and spirituality amongst patients with cancer was found to be associated with better patient-reported physical outcomes through behavioural and emotional self-regulation. Like previous studies (Park et al. 2009, Aldwin et al. 2014), patients in our study adopted a healthy lifestyle, participated in religious activities and their faith instilled hope, comfort and love. This stresses the importance of spiritual care as an essential component of overall patient care to address the patients' spiritual concerns.

As from the start of treatment, patients in our study established a personal support network, mainly family members. Its importance was further stressed along the treatment journey when patients required assistance for activities of daily living. Besides the strong family support, an interesting finding in our study was that some patients formed their own peer support group with patients whom they met at the ward whilst receiving their parenteral treatment at the oncology centre. They acknowledged that peer support compensated for social isolation and improved their awareness about adverse effects by observation and self-evaluation of the severity of their own adverse effects. These were similar to the findings highlighted in the sparse literature investigating peer support services among patients with colorectal cancer (Ieropoli et al. 2011, Kanters et al. 2018). Whilst healthcare professionals should acknowledge patients' interest and enthusiasm in developing an illness-specific peer support programme, they should assist its establishment and be at the forefront to refer patients to such programmes.

4.4.3. Strengths and limitations

Numerous strengths were identified in this study. First of all, this qualitative study is reported in accordance with the Standards for Reporting Qualitative Research guidelines (O'Brien et al 2014). As the study followed an Interpretative phenomenological analysis, its theoretical underpinnings of phenomenology, ideography, and hermeneutics were adopted. This allowed a detailed insight into each patient’s experience and how patients were making sense of their experience with the diagnosis of cancer and treatment with antineoplastic medicines (Smith and Osborn 2015). A strength of this study is the longitudinal design which offered valuable insight into how patients’ beliefs, practice and burden changed over time. The adoption of a qualitative methodology using a series of semi-structured one-to-one interviews is also of merit in allowing a rich exploration of the patients’ beliefs, practice and burden at each time-point along the treatment journey.

As Malta has only one national oncology centre, this was considered an ideal location for recruitment of newly diagnosed patients with colorectal cancer initiating antineoplastic medicines. By employing a purposive sampling, this further ensured identification and selection of patients with different patient’s characteristics (age, gender, lifestyle) to be recruited in the study.

A sample size of 16 patients may be considered as a large sample for an IPA study, but this was necessary to cater for the possible high attrition in being a longitudinal study involving patients with cancer. With only 4 patients discontinuing their participation in the study over a 9-month period, this resulted in oversampling and an overwhelming amount of data. Though data saturation is not essentially required for data collection and analysis in an IPA study (Brocki and Wearden 2006), data saturation was still attained in this study with no new data being generated from the patients’ interviews.

Various strategies were undertaken to enhance the trustworthiness of the research. These include:

a) The research team included experienced qualitative researchers with different cultural backgrounds (German, Scottish, Maltese) and this prevented the team from being 'blind' to cultural ideas and practices in the data that is maybe taken for granted (credibility)
b) Detailed documentation of the method followed was provided (dependability)
c) The development of an interview guide was based on the adapted conceptual model generated from a comprehensive systematic review (Chapter 3) and this data generation tool was piloted prior to its use (credibility)
d) Transcription accuracy check and independent data analysis were carried out by another researcher (dependability)
e) Verbatim quotations from interviews were used to support all themes (confirmability)

Whilst the study was carried out in line with research quality markers for robust qualitative IPA studies, the findings were limited by the outlined biases and should be interpreted with caution. The main limitation of this study is that the data was generated in Malta, where a tax-financed healthcare system is followed. Hence the findings may lack transferability to other countries following a different healthcare model. By providing a detailed description of the research setting, the readers may consider the transferability of the findings to their own setting.

Also, this qualitative study focused on patients with colorectal cancer receiving specific treatment with antineoplastic medicines. Therefore the findings may be applicable only to patients receiving FOLFOX or XELOX as first-line treatment of antineoplastic medicines for 12 or 8 cycles respectively and should be interpreted with caution with regards to - transferability to other patient groups and settings.

Bias related to recruitment might have been present as only those patients interested in the study and who accepted to receive antineoplastic medicines shared their perceptions and experiences. Also, patients who accepted to participate in the study may have been more motivated and held more positive attitudes towards cancer and its treatment, leading to a bias in the findings. For interviews 3 and 4, the sample consisted of only patients receiving FOLFOX, therefore findings may be biased towards the use of parenteral antineoplastic medicines.

In an intensely emotional experience such as disclosure of diagnosis of cancer, it cannot be assumed that every participant's experience of this phenomenon was captured in its entirety and there may have been limitations of the spoken word. Social desirability bias might also have been present with patients answering questions which are favourable to the research student. This bias was minimised by the fact that the research student did not have any previous contact with the participants of the study, though she worked at the oncology centre where the study was conducted.

The research student also acknowledges the lack of patients and public involvement in the study design due to resources and time constraints. Despite this, patients were requested to show their interest in obtaining access to any publications of the study and dissemination of the study findings.

4.5. Conclusion

The findings of this research offered insights into the patients' lived experience throughout the treatment journey with antineoplastic medicines and beyond. This longitudinal study demonstrated that the experience of patients with colorectal cancer was complex as from initiation of treatment with antineoplastic medicines. It has been shown to be affected by the individual and contextual factors. The study highlighted the lack of patient's knowledge on treatment, the impact experienced on their life and the need to establish a personal support structure to mitigate this impact. Hence patients undergoing antineoplastic treatment need more than fulfilment of medicine administration from hospital. This calls for the need to develop tailored services to address the patients’ concern and empower patients to be active participants in their care as from the early stage of treatment.

4.6. Implications for next phase

The findings elicited from the patients’ interviews highlighted that patients with colorectal cancer find themselves in a complex life situation as from the early stage of the treatment journey. As the patients’ experience resulted in changes in their knowledge and beliefs affecting their needs along the treatment journey, the patients’ personal support network became indispensable. Further knowledge about the patient’s experience with antineoplastic medicines was sought from the perspective of individuals considered as highly involved in the patients’ care. These were referred to as significant others in the context of this research (Chapter 5).

Chapter 5

Patients' experience with antineoplastic medicines: a longitudinal study from the perspective of significant others

(Phase III)

5. Introduction to the chapter

This chapter provides a description of the longitudinal qualitative study with significant others of patients with colorectal cancer exploring their perspectives on the patients' lived experience with antineoplastic medicines. The study identified the contribution that significant others make to the patient's oncology care. By eliciting the perspective of the significant others, the research provides a more comprehensive understanding of the patients' beliefs, practice and burden of antineoplastic medicines. The research aim and objectives of the study as well as the method employed for data collection are presented in this chapter. An interpretation and discussion of the empirical findings of the study are also reported.

5.1. Research aim and objectives

The aim of this phase of the research was to explore longitudinally the significant others' perspective on the patients' experiences with antineoplastic medicines for the duration of the treatment journey.

The specific objectives of this longitudinal study in the context of treatment with antineoplastic medicines for colorectal cancer were to:

- Explore the perspective of significant others on the patients' knowledge and beliefs
- Explore the perspective of significant others on the patients' approach to medicine taking practice
- Explore the burden experienced by patients from the perspective of the significant others

5.2 Method

5.2.1. Study design

A longitudinal qualitative study was conducted using in-depth interviews with significant others at the start and after completion of treatment with antineoplastic medicines (24 week interval). This research approach was chosen to complement the longitudinal study of patients (Phase II) described in Chapter 4. Justifications for following this method are provided in Chapter 2.

5.2.2. Setting

This study took place at Sir Anthony Mamo Oncology Centre, as described in Chapter 4.

5.2.3. Inclusion and exclusion criteria

Individuals initiating treatment with either FOLFOX for 12 cycles or XELOX for 8 cycles who participated in Phase II of the study (as described in Chapter 4) were asked to nominate at least one person and up to a maximum of 3 persons who in their opinion were highly involved in their care. By asking the patient to nominate the significant other, the research student ensured that a person who is closest to the patient was recruited. Participation of the significant others was voluntary and his/her involvement continued as long as the patient continued participating in the Phase II study (Chapter 4).

Significant others were eligible if they were 18 years old or over, understood the objective of the study and consented to participate. All nominated significant others by their respective patients were willing to participate.

5.2.4. Recruitment of participants

The significant others participating in this study were identified by the patients participating in Phase II study. Their only common characteristic was that they were involved in caring for a patient diagnosed with colorectal cancer who received treatment with FOLFOX or XELOX for 6 months.

A detailed participant information leaflet (Appendix 5.1) was given to each patient recruited in Phase II to be handed to their significant other(s) and enquire whether they object in disclosing their personal details to the research student. The identified significant others were then personally approached or contacted via phone by the research student to inform them about the study and enquire whether they would be interested in participating in this study. A convenient date and time were set to conduct the interview.

5.2.5. Development of the data generation tool

Semi-structured face-to-face interviews were used. An adapted interview guide (Table 5.1) for the significant others was developed based on the interview guide for the patients described in Chapter 4. The use of open-ended questions allowed the participants to elaborate on the patients' and their own experience during each interview.

The semi-structured interview guide was piloted with four significant others. Since no major changes to the interview guide were necessary following the pilot study, the data was incorporated into the final dataset. The same interview guide was used at both time points, with minor amendments made to the structure of the questions to reflect the time of interview (blue text in Table 5.1)

Table 5.1: Interview guide for the significant others

PLEM major themes from original model (Mohammed, Moles and Chen 2016)	**PLEM themes from the adapted model*** (Brincat et al. 2020)	**Interview questions**
Characteristics of significant other		Can you describe what merits you to be nominated as a significant other by the patient?
Medicine - related beliefs	Family members, healthcare professionals, media and culture influence	What does the term 'chemotherapy' mean to the patient? Can you describe the thoughts and feelings experienced by the patient when informed that he/she will be starting treatment with chemotherapy? What do you think has shaped his/her thoughts and feelings around chemotherapy?
	General attitude towards medicine	What do you think the benefits of chemotherapy will be?
		What are the patient's main concerns about starting chemotherapy?
Medicine taking practice	Accepting medicine	Has the patient been explained how he/she shall be receiving the chemotherapy? How would you describe the patient's experience of taking chemotherapy? Can you tell me how the patient followed the treatment schedule for oral and/or intravenous chemotherapy?
		Does the patient have a network of support (family members, friends, support groups)? How do they help him/her?
	Modifying or altering medicine regimen or dose	Has the patient ever experienced any dosing adjustment in the treatment by the doctor?
Medicine-related burden	Medicine characteristics	Are there any aspects of chemotherapy such as the pharmaceutical form (intravenous or oral formulation), colour of size of the tablet, infusion time that might affect the patient?
	Medicine routine	Do you envisage any problems for the patient to follow the treatment schedule as prescribed?
	Medicine adverse events	Do you know whether the patient reported side effects to the doctor or other healthcare professionals?
	Medicine social burden	Do you feel that chemotherapy will have an impact on the patient's daily life?
	Healthcare associated medicine burden	What are the patient's experiences with the healthcare system?

*Questions in blue text were included in the interview guide and used for the second interview

5.2.6. Data generation

All interviews with the significant others were undertaken by the research student in a private room at Sir Anthony Mamo Oncology Centre during the visiting hours. These were conducted with the significant others on their own to facilitate the latter to talk openly about their experiences. As the patients were receiving their parenteral treatment at the oncology centre, the nurse-in charge was informed that the interview was being carried out so that the significant other could be reached if need be. This provided reassurance to the significant others. Also, the ward environment offered the significant others a relaxed environment away from their caring responsibilities.

If the significant others were willing to proceed with the first interview, they were asked to read and sign the consent form (Appendix 5.2) and fill in their demographic details. Prior to the second interview, the aim and objectives of the study were reiterated and the research student answered any queries related to the information sheet or the study. A verbal re-affirmation of the consent was also obtained. They were reminded that their participation was voluntary with all information disclosed treated as confidential. Participants were advised that if the information given was suggestive of risk of harm to self or if they became visibly distressed, then the interview would be terminated and the necessary support would be provided as described in Chapter 2.

In-depth interviews with the significant others were held between October 2018 and March 2020 in either Maltese or English according to the individual’s preference. This allowed the participants to reflect on the patients’ experience along the treatment journey. The first interview took place on the second day of the patient’s cycle 1 with FOLFOX or XELOX. If the significant others were interested to continue their participation, an appointment for the second interview was made by contacting them by phone a week prior to the patient’s last treatment cycle (cycle 12 of FOLFOX or cycle 8 of XELOX). The second interview was then conducted after 24 weeks from initiation of antineoplastic treatment.

Anonymity was ensured throughout the whole study as described in Chapter 2. Interviews were digitally audio-recorded and subsequently transcribed verbatim by the same research student onto a password protected online document. A 10% sample of transcripts was randomly selected using randomizer.org and cross-checked by a native Maltese speaker independent to the study to ensure accuracy.

5.2.7. Data analysis

Transcript-based analysis in the original language was undertaken as it was considered a rigorous form of analysis. All anonymised transcripts were analysed thematically using framework analysis according to the steps outlined by Ritchie and Spencer (1994), as described in Chapter 2. This includes five stages of framework analysis, namely familiarisation, identifying a framework, indexing, charting followed by mapping and interpretation.

The analysis of each interview was conducted by the research student and two other members of the research team. All were pharmacists fluent in Maltese, with experience in hospital pharmacy and qualitative research. The software Nvivo® 20 was used to assist in the analysis of qualitative data.

Analysis of transcripts was undertaken through a deductive approach. The research team agreed to use the themes and sub-themes developed for Phase II of the study (Chapter 4) as a priori codes for the analysis of this study to ensure the focus on the patients' experience of treatment from the significant others' perspective. Any data that did not fit the a priori coding system was assigned a new code. The identified framework was piloted on one interview to refine the a priori categories, if needed. This step was done by the research student and two members of the research team (PVB/AT). A reflexive approach was adopted.

Quotations from the transcripts were selected to support and contextualise the presented findings. As the data was mainly in the Maltese language, quotations were translated into English and reverse translated by a native bilingual member of the research team to retain the original meaning.

5.2.8. Research governance

Ethical and governance approvals were granted, as outlined in Chapter 4, as part of a single large longitudinal study involving patients and their respective significant others.

5.3. Results

5.3.1. Participant demographics

The sample size in this study consisted of 16 participants. Whilst all recruited participants signed the informed consent prior the first interview, only 12 of them remained eligible for the second interview (Table 5.2) due to attrition from the patients' sample.

Table 5.2: Eligible significant others for the study

Interview number	**1** **(Week 1)**	**2** **(Week 24)**
Total number of participants	16	12

The first and second interviews were completed by 16 and 11 significant others respectively (Table 5.3). Two significant others had their interviews cancelled due to COVID-19 pandemic. One of these significant others had her interview first postponed due to health reasons and then cancelled in view of the outbreak of the Covid-19 pandemic.

Table 5.3: Overview of the interviews conducted with significant others

Participants	Interviews	
	1	2
S001	√	√
S002	√	√
S003	√	√
S004	√	√
S005	√	√
S006	√	√
S007	√	Patient discontinued antineoplastic treatment so significant other was not interviewed
S008	√	√
S009	√	Patient discontinued antineoplastic treatment so significant other discontinued
S010	√	√
S011	√	√
S012	√	√
S013	√	Patient voluntarily withdrew from the Phase I study so significant other was not interviewed
S014	√	√
S015	√	COVID-19 suspension for interview with significant other
S016	√	COVID-19 suspension for interview with significant other
Total	**16**	**11**

√ Interview completed

Demographic information about the significant others is detailed in Table 5.4. They were predominantly females (n=12), spouses (n=6) with their age varying between 31 and 72 years (mean 50.1 ± 14). Interviews conducted lasted on average of 40 minutes.

Table 5.4: Demographic characteristics of significant others

Participant	Gender	Age (years)	Prior treatment (patient)	Antineoplastic treatment (patient)	Intent of treatment (patient)	Relationship to patient	Nationality	Educational level	Employment	Marital status	Lives (with)
S001	Female	68	Surgery	FOLFOX	Curative	Sibling	Maltese	Secondary	Pensioner	Married	Patient
S002	Female	38	-	FOLFOX	Palliative	Sibling	Maltese	Secondary	Full-time	Single	Patient
S003	Male	69	Surgery	FOLFOX	Curative	Spouse	Maltese	Primary	Postgraduate	Married	Patient
S004	Female	31	Surgery	FOLFOX	Curative	Offspring	Maltese	Secondary	Full-time	Single	in a separate household from patient
S005	Female	51	-	FOLFOX	Palliative	Niece	Maltese	Secondary	Housewife	Married	in a separate household from patient
S006	Female	39	-	FOLFOX	Curative	Offspring	Maltese	Secondary	Full-time	Divorced	Patient
S007	Female	36	Surgery	XELOX	Palliative	Spouse	Polish	Postgraduate	Full-time	Married	Patient
S008	Female	36	-	FOLFOX	Curative	Healthcare professional	Maltese	Postgraduate	Full-time	Married	in a separate household from patient
S009	Male	65	Surgery	FOLFOX	Curative	Spouse	Maltese	Secondary	Pensioner	Married	Patient
S010	Female	63	Surgery	FOLFOX	Palliative	Spouse	Maltese	Secondary	Housewife	Married	Patient
S011	Female	28	-	FOLFOX	Palliative	Sibling	Maltese	Secondary	Housewife	Married	in a separate household from patient
S012	Male	72	Surgery + stoma	FOLFOX	Curative	Spouse	Maltese	Primary	Pensioner	Married	Patient
S013	Male	39	-	FOLFOX	Palliative	Offspring	Maltese	Secondary	Full-time	Single	in a separate household from patient
S014	Female	33	Surgery + stoma	FOLFOX	Curative	Offspring	Maltese	Postgraduate	Full-time	Single	in a separate household from patient
S015	Female	46	-	FOLFOX	Curative	Offspring	Maltese	Secondary	Part-time	Married	in a separate household from patient
S016	Female	64	Surgery	FOLFOX	Palliative	Spouse	Maltese	Secondary	Pensioner	Married	Patient

5.3.2. Themes and sub-themes

The findings generated from interviews with significant others are presented in accordance with themes and sub-themes outlined in Table 5.5.

Table 5.5: Themes and sub-themes identified from the interviews with significant others

Themes	Sub-themes
Perceptions and knowledge of the illness and treatment	Perceptions about illness and treatment
	Knowledge about illness and treatment
	Influences on attitudes and knowledge about illness treatment
The healthcare system in relation to the illness and treatment	Experiences of patients of cancer services as part of the healthcare system
	Healthcare professionals' communication with patients and others
	Recommendations for services
Patient's involvement in treatment decision-making and their experience of medicine-taking	Influences on acceptance of treatment
	Experiences of administration of antineoplastic medicines and other medicines
Medicine and illness-related impact on patients and others	Impact of physical effects on patients and others
	Impact of psychological effects on patients and others
	Social consequences for patients and others
	Implications on financial status
	Seeking refuge in spirituality and religion
Personal support structure	Establishing a support network
	Self-regulation as a coping strategy

5.3.2.1 Theme 1: Perceptions and knowledge of the illness and treatment

5.3.2.1.1 Sub-theme: Perceptions about illness and treatment

Perception of illness

At the beginning of treatment, most significant others lacked experience of colorectal cancer and use of antineoplastic treatment. Their comments were purely based on their perceptions of the patients' illness and its treatment. In contrast, interviews held with the significant others at completion of treatment reflected views after living through the patients' actual experience of receiving six months of treatment with antineoplastic medicines.

From the start of treatment, cancer was considered by some significant others as a common illness of unknown aetiology, for example, one interviewee asserted that '*it is not just us, every family has a member suffering from this* [cancer]' [S010-1]. This high incidence of cancer was attributed to pollution, use of pesticides and genetic factors.

> *The progress* [in science] *also brought other risks such as the use of pesticides. I am aware of the effects of pollution and when I buy vegetables* [from a greengrocer]*, I request those available inside the shop rather than those left in the van outside the shop as these will be all covered in pollutants … hopefully will reduce the cancer risk.* [S011-1]
>
> *For instance, we don't know the cause of death of my grandma as she lost her appetite and died suddenly … similar symptoms to my mother … Then I begin to wonder that if both my grandma and my mother had* [cancer]*, there is a high chance that I will have it as well … When I went to the doctor, I was told that I had a 100% increased risk of suffering from colorectal cancer.* [S014-1]

Given the common perception that cancer is a fatal illness, some significant others mentioned that patients were afraid to seek medical assistance once they displayed symptoms suggestive of cancer (such as rectal bleeding).

> [In the case of any other illnesses] *if one feels any symptom, they will seek medical help. But in the case of cancer, fear takes over with the consequence that one doesn't seek help despite signs such as rectal bleeding. There are many individuals I know, who don't want to carry out any tests due to fear of a diagnosis. They insist on doing nothing but unfortunately then it will be too late.* [S005-1]

In line with this perception, one significant other encouraged the patient to draw up a will following the disclosure of a diagnosis of cancer to settle any pending issues prior to the patient physical deterioration and eventual death.

> *As her sister* (soon after diagnosis)*, I encouraged her to write up a will.* [S011-1]

Perception of treatment of colorectal cancer

Whilst patients and significant others perceived cancer as a life-threatening illness, the recommendation for the patients to start treatment were perceived as an opportunity to achieve a cure by the majority of significant others. This provided hope without the significant others questioning the effectiveness of treatment.

> *As soon as he was told that he had cancer, we were all shocked … and he burst into tears. He is being given chemo to control and cure it* [cancer] *… so that gives us hope.* [S002-2]

On hearing that the surgical intervention was successful, patients and significant others perceived this to mean that the cancer had been completely removed and they assumed that there would be no need for further treatment. Thus, they were surprised when they were informed that the patient had to start treatment with antineoplastic medicines following surgery. At the beginning of treatment most significant others were still optimistic that the treatment with FOLFOX or XELOX would be effective in achieving a cure.

> *I was under the impression that it* [cancer] *had been removed completely* [with surgery] *so as soon as I learned that she was getting chemo I thought that this was because surgery had not been effective and there is no hope. I had thought that once it was removed it was out.* [S014-1]
>
> *We weren't aware of chemotherapy at the start, but the surgeon gave us this news* [need for chemotherapy] *on our second visit; it was around a month after surgery. The surgeon informed us that the surgery was successful, but any traces* [of cancer] *need to be eradicated with the chemotherapy. I suddenly exclaimed 'What?!' …* [S001-1]

Over the course of the treatment journey, the significant others' perceptions of the effectiveness of treatment changed, with some becoming critical while others remained optimistic of achieving a cure. Only some significant others understood that treatment may result in an improved life expectancy as opposed to a cure. This emphasised their lack of awareness of the concept of palliative treatment. As treatment progressed, more significant others recognised that treatment with antineoplastic medicines was not going to achieve a complete cure.

> *I know that this improves survival and helps it* [cancer] *not to grow by suppressing its growth. However, it seems that she's* [the patient] *hoping more for a cure.* [S005-2]

The significant others who remained optimistic about the curative intent of treatment right up to its completion preceded to shift their concern to the possible recurrence of cancer.

> *I'm expecting him to be better soon as I believe that chemo was effective. Hopefully it will take quite some time if it is to recur.* [S003-2]

Perception of the treatment journey

At the start of treatment there was a strong perception amongst significant others that the cancer journey would be unpredictable. The effectiveness of antineoplastic treatment and occurrence of adverse effects were understood to depend mainly on specific patient-related factors; further worsening the patients' anxiety. After completion of treatment, some significant others asserted that the patients' actual experience of treatment was not as terrible as expected at the start of treatment.

> *I think that it involves a lengthy process that one cannot predict …* [S004-1]

> *The word chemo sounds much scarier than it is in reality. Let me put it this way … it is a change in lifestyle, it is a hectic thing but at the end of the day, I mean it is treating the good and the bad. It is a treatment using medicines, the same like any other medicine.* [S014-2]

A few significant others were anticipated that antineoplastic treatment would result in a disruption of normality to both the patient and them. In contrast, completion of treatment was considered to be the patient's opportunity to return to their pre-diagnosis routine. Significant others were concerned about the burden the patients' treatment posed on themselves and hoped that the completion of treatment would results in the patient resuming their previous lifestyle.

> *Last time I was deeply concerned that he would be experiencing extreme fatigue that makes him unable to come out of bed. However he experienced this only occasionally. Thus, making me highly confident that he will return to his previous normal soon after finishing it* [antineoplastic medicines]. [S001-2]

5.3.2.2. Sub-theme: Knowledge about illness and treatment

Knowledge about antineoplastic medicines and their effects

At the start of treatment some significant others reflected on the patients' and their own lack of knowledge about cancer and its treatment and criticised the insufficient information given to the patients by healthcare professionals. The information given during the nurse-led group information session at the start of treatment was believed to be rather vague as it focused on general aspects of treatment with antineoplastic medicines. The information provided was not specific to the patients' cancer or treatment. This resulted in confusion and information overload. Worse still important information on possible adverse effects were not applicable to all patients, resulting in more confusion and a feeling of anxiety.

> *When we attended the Aurora session, I think we got more confused particularly my poor wife who is a bit sensitive. I'm not complaining that they were not explaining adequately, but they were speaking in general … if there are 100 patients with cancer to receive chemo, we're speaking about 100 different situations.* [S012-2]
>
> *For the information session not everyone had the same type of cancer … the nurse informed us that not everyone in the group was going to receive the same medicine and experience the same side effects.* [S005-1]

The information deemed as most important to the significant others was related to the patients' weakened immune system which could result in an increased susceptibility to infections. Significant others felt responsible to ensure the implementation of day-to-day preventive measures in the hope to minimise the patients' risks.

> *I am very worried that he* [the patient] *would eventually suffer from a weak immune system … increasing his risk of developing infections.* [S016-1]
>
> *I'm afraid that she* [the patient] *might be weak where she won't cope. The chemo is good but it affects the immune system.* [S014-1]

A further aspect of poor knowledge was the safe handling of contaminated body waste such as cleaning of patient's vomit using double-gloving and performing a separate laundry of patients' clothes for the first few days post-treatment. This lack of knowledge persisted throughout the treatment journey except for a small number of significant others.

> *There's nothing you can do except to clean the vomit … I'll try to use gloves to clean it, though I can't bear them* [gloves] *on. I haven't been informed about any safety precautions to be taken.* [S005-1]

> *Thankfully she did not vomit as I don't know how to clean it properly, except to the use of cloth and water.* [S006-2]

Knowledge about supportive medicines

Information given was limited to antineoplastic medicines without any consideration given to supportive medicines. In fact, the lack of significant others' knowledge about the safe storage and disposal of supportive medicines at home was evident. This was exemplified by one significant other explaining that any expired medicine was being disposed of in a sharps bin to avoid them being thrown away with the general waste.

> *I have a yellow bin for collecting the insulin syringes and put all my expired medicines there. When it is full, I take it to Wasteserv and get another one … Otherwise, if I dispose them* [medicines] *with general waste they will end up in the water table. In my opinion, this is the best way of disposal for medicines.* [S001-2]

Knowledge about cancer research

On completion of treatment, some significant others acknowledged the patients' and their own lack of awareness about research being conducted in the field of cancer and the availability of emerging treatments. Some significant others complained that despite news of the discovery of breakthrough treatment in the media, no further information was provided such as the anticipated day of release to the market. This was frustrating for the significant others and patients with advanced cancers who were desperate for additional effective treatment options.

> *I'm relieved that you asked this question about research at last … There was a healthcare professional visiting from abroad who was doing research on new cancer medicine and I took a screenshot and showed it to Dr X. I enquired whether something like this could be beneficial for him* [the patient]. *She* [the oncologist] *replied that if it was something beneficial, the government provides it for him. It* [new cancer medicine] *was shared on the news and then disappeared; possibly because the research on it was not successful …* [S010-1]

5.3.2.1.3 Sub-theme: Influences of attitudes and knowledge about illness and treatment

The influence of family members' and other acquaintances' experience with cancer

A strong influence on the patients' and significant others' attitude and knowledge about cancer and its treatment was based on past experiences of family members and acquaintances. Negative attitudes stemmed from accounts of others who died shortly after treatment, resulting in both patients and significant others considering antineoplastic treatment as ineffective, worsening their fear. In contrast, a significant other whose sister had a recent positive experience with the use antineoplastic medicines for breast cancer retained high hopes for a comparably positive treatment outcome for her mother.

> *Two of my mother's friends received chemo for breast cancer and it wasn't effective … and in fact they eventually died. Hence, we have this bad connotation upon hearing the word chemo.* [S015-1]

> *We received my mother's* [cancer] *diagnosis soon after my younger sister finished chemotherapy for breast cancer. Thankfully she [her sister] was recently informed by her oncologist that she has achieved cure and is coping quite well. Both of us* [the patient and significant other] *are highly optimistic that she* [patient] *will have a similar experience …* [S006-1]

The influence of significant others

The significant others believed that they themselves represented a major influence on the patients. In some cases, it was the significant others' insistence that motivated the patient to be screened or seek medical advice leading to the eventual diagnosis of cancer. As a result, a few significant others felt guilty and unsure whether they had acted in the patient's best interest as their persistence for the patient to be screened or seek medical advice had resulted in this devastating diagnosis.

> *I always encourage him by saying 'Come on, we'll see at a later stage. Sometimes I question whether this is all my fault as he did not want to perform the screening test. He had already received it [invite to perform the colorectal screening test] another time and did not accept to do the test.* [S001-1]

Some significant others highlighted the patients' reliance on the significant others' knowledge throughout their treatment. Patients apparently refrained from searching information online themselves due to the fear of a negative psychological impact. The knowledge acquired by the significant others or other family members allowed them to ask healthcare professionals more specific questions when attending hospital appointments. Due to the inconsistencies in the retrieved literature however, some significant others used the hospital appointments as opportunity to confirm this information with the healthcare professionals.

> *Though she [the patient] read the booklets given to her, she did not search on the internet. I didn't search anything as I know that I'll end up overthinking her situation. But my husband and son did search online.* [S011-1]

> *I used to research prior to attending appointments, to be prepared - a variety of research including medical papers, followed by critical assessment. I read as much as possible prior* [to initiation of treatment]. [S003-2]

The influence of healthcare professionals

The healthcare team also emerged as a key influence on the patient, who mainly relied on information provided by them. From the early stages of treatment onwards, the patients' attendance at the oncologists' consultation followed by a voluntary attendance at the nurse-led information session resulted in improvement of knowledge about illness and treatment.

> *The Aurora session helped a lot. Explanations were given … the information session of Aurora was informative. We took notes, of what we should do and what we should avoid. The emphasis was on food such as what food to consume … there was a lot of information!* [S003-2]

The influence of the patients' own personality

Some significant others noted that throughout the treatment journey, the patient's personality affected their degree of willingness to obtain further information about the illness and its treatment. Whilst some patients were embarrassed and afraid, others appeared confident and showed a keen interest to know more about their illness.

> *She did not enquire a lot but still asked very few questions to her doctor; as she's a timid person, she is one who doesn't talk much.* [S005-2]

The influence of other patients' experiences

Most patients and their significant others were influenced by the experiences of other cancer patients. This was particularly true in the early stages of treatment. Patients were noted to engage in conversations with other fellow patients to share their experiences with antineoplastic treatment. However, some significant others advised patients to be cautious not to allow other patients' experiences to act as an indicator of their own fate. There was an understanding amongst significant others, that treatment is tailored to the individual and that treatment outcome is unpredictable. As treatment progressed, patients were noted to have gained their own personal experience from their earlier treatment cycles.

> *He [the patient] spoke about his situation and asked others who went through this experience. However, I'm always emphasising that he is not to pay attention to other's accounts even if they have exactly the same cancer!* [S016-1]

The influence of media

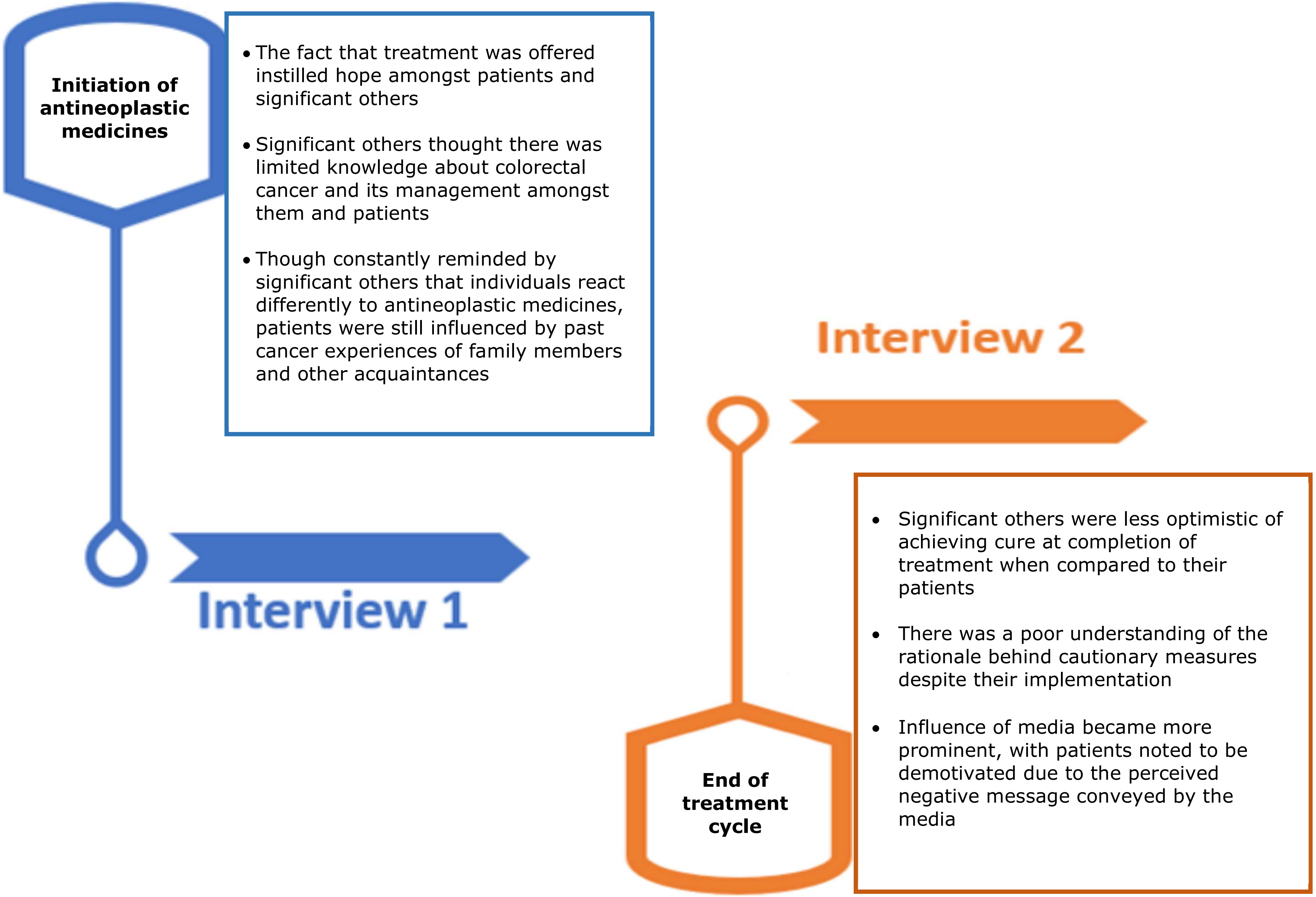
The media was also noted to have a significant influence on patients and their significant others attitude and knowledge. A few significant others criticised a specific television programme for conveying unhelpful messages that induced fear and negatively influenced the general public's view on the use of antineoplastic medicines. It was recommended that media needs to moderate such programmes to minimise misinterpretations which may affect a patients' compliance with treatment. Some significant others stated that the media often disheartened them to the extent that they either changed the station or switched television off all together.

> *Sometimes the media causes much more harm than good … even the issue of hair loss often the media depicts a patient with cancer including on adverts etc as a bald person. However now I am aware that this depends on the type of chemo and therefore is creating unnecessary fear.* [S010-1]
>
> *Even if we hear anything about the subject* [cancer or antineoplastic medicines] *on the radio or tv, we switch it off … he doesn't want to hear about anything else. I do the same, switch it off as well. We prefer if they don't mention anything … although they do that with a good intention … as the public need to know. But I think that the more they emphasise, the more fear they create. There should be dedicated time slot to be aired not all the time!* [S001-2]

At both interviews, significant others highlighted the need for more public awareness and knowledge about colorectal cancer and its treatment. They suggested that media campaigns should show success stories of patients with cancer. These may assist in easing fear, breaking the taboo and promote early cancer detection by self-referral or uptake of the screening programmes.

> *The more healthcare professionals speak about cancer and treatment both to patients and public, the better. By making individuals in our society aware of the patient's needs, you can adapt your behaviour and know how you can help such a patient.* [S004-1]
>
> *It's good to do a short programme of around 20 minutes to raise awareness.* [S006-2]

Figure 5.1 highlights the longitudinal presentation of key points of Theme 1.



- The fact that treatment was offered instilled hope amongst patients and significant others
- Significant others thought there was limited knowledge about colorectal cancer and its management amongst them and patients
- Though constantly reminded by significant others that individuals react differently to antineoplastic medicines, patients were still influenced by past cancer experiences of family members and other acquaintances

- Significant others were less optimistic of achieving cure at completion of treatment when compared to their patients
- There was a poor understanding of the rationale behind cautionary measures despite their implementation
- Influence of media became more prominent, with patients noted to be demotivated due to the perceived negative message conveyed by the media

Figure 5.1: The longitudinal presentation of key points identified in the theme Perceptions and knowledge of the illness and treatment

5.3.2.2: Theme 2: The healthcare system in relation to the illness and treatment

5.3.2.2.1 Sub-theme: Experiences of patients of cancer services as part of the healthcare system

The effect of hospital environment on the patients' experience

Many significant others remarked that the hospital environment was considered an important aspect for cancer care as patients spent various days admitted in hospital for each cycle. Receiving treatment in a welcoming and sociable environment was noted to reduce the patients' anxiety during their hospital stay. Furthermore, the integration of an oncology centre as adjunct to the acute hospital was perceived to be a way to reduce the cancer-related public stigma. The fact that patients were treated in a comfortable environment which is not overcrowded made patients feel that they were treated with dignity and respect.

> *The environment here is totally different from Boffa* [old oncology centre] *… it was a small hospital, overcrowded … Every time I went there, I get that unpleasant feeling of a lump in my throat. Having the oncology centre situated next to/connected to Mater Dei Hospital* [acute hospital] *reduces the possibility of being labelled as a cancer patient … My sister feels very welcome each time she comes here* [oncology centre]. [S011-1]

At the beginning of treatment, significant others noted that patients preferred a single room due to privacy concerns. However, as treatment progressed, patients' preference shifted to shared rooms. Some significant others remarked that patients started to see their days in hospital as an opportunity to meet with other patients, share their experiences and establish new friendships. Only the significant other of the non-Maltese patient complained that mixed gender wards were a potential for embarrassment.

> *When she's admitted for treatment here, she doesn't feel depressed. She's happy and looks forward to coming here. Sometimes when I phone her, she tells me that she is talking to the patient next to her. She made friends here as well … it was a positive experience.* [S006-2]
>
> *When my husband was in this ward the first time, there were people of different genders and age. It was quite confusing and surprising for me as I have never seen something like this, you know! The male patients were staying in same room as female patients. I think women may feel more uncomfortable with this situation.* [S007-1]

The effect of hotel and ancillary services in hospital

Significant others observed that patients generally considered the meals provided to be of poor quality. As a result significant others felt pressure to prepare nutritious and tasty food for the patients during their hospital stay.

> *The food is terrible! If they were to improve the meals provided, they would indirectly be supporting us [significant others] as they reduce our burden. I have to run home after he's admitted to go shopping and prepare a fresh meal for him … I was expecting that what they preached during the information session would be applied in practice as we're taking care of the same patient!* [S010-1]

Other ancillary services were more popular. The fact that '*we* [patient and significant other] *were provided with hospital transport as we did not have anyone to take us to hospital'* [S001-1] was welcomed by all. However the transport service was unable to adequately cater for all hospital appointments requiring the significant others to organise transport privately; a situation that was made worse by the lack of available parking spaces on site.

> *She had a hospital appointment at 8am but was still waiting for transport at 8.30am. She panicked. So I called my friend to bring us to hospital … Otherwise they offer a great service.* [S012-2]

Quality and timeliness of cancer services within the healthcare system

Most significant others praised the coordinated and efficient healthcare services offered to patients following the initial cancer diagnosis. They also commended on the short waiting times for diagnostic investigations and to attend referral appointments.

> *Upon receiving the diagnosis, all the necessary tests were carried out and all appointments were within a short time span … in fact within 3 weeks all tests were done!* [S005-1]

> *From our experience, the general hospital makes you wait many hours; as there are many patients all attending at the same time ... Here it is much better … because you know that you are coming on the hour and so really you do not have to wait a lot.* [S007-1]

The positive healthcare experiences were balance by some negative ones which in some cases resulted in patients' personal setbacks. The main problems related to misdiagnosis and missed follow-up appointments for patients with a positive colorectal screening test. These resulted in delayed diagnosis, subsequent difficulty to accept the final diagnosis and potentially serious consequences to patient's health.

> *The day I took her to emergency, I was rather annoyed as the doctors reiterated that my mother was suffering from nothing serious… so for me this is a huge red alert! If it wasn't for my insistence together with my friend who is a nurse, my mother might be dead today … then they ordered a CT scan for her which showed the cancer … This must be a misdiagnosis!* [S014-1]
>
> *'It was difficult for my wife to regain trust in the healthcare system after she experienced that incident [patient did not receive the screening test result]. Though she sent the sample by post to the screening centre, she never received an official result. She took initiative to follow it up … ending up with a devastating shock upon obtaining the positive result of noticing some traces. She could have ended up in a worse situation!'* [S009-1]

In addition, the significant other of the non-Maltese patient complained about the administrative burden associated with repeated requests to submit the same documentation at every hospital visit, in order to get re-imbursed for local treatment.

> *It's quite bureaucratic … because they know you're coming here … like 10 times in 1 month and you have to show them this same paper every time!* [S007-1]

Looking back, some significant others reflected on the discrepancies between the information provided during the nurse-led information session at the start of treatment and the actual practices adopted by the oncology centre. They described situations where patients were prescribed supportive medicines which seemed to contradict the advice given during the initial information session. Another example was the lack of specific infection control policies such as sharing of waiting rooms with other potentially sick individuals at the emergency department.

> *… For instance, the hand washing procedure - if I was advised how to do hand washing correctly, I expect them to lead by example … not done in a rushed manner.* [S012-2]
>
> *I expect that whatever has been recommended [at the information session at the oncology centre] would be followed here [oncology centre] … They [nurses] advised against the use of chemicals but then why did they prescribe Difflam® mouthwash filled with alcohol and benzene to treat her severe mouth ulcers? ... One of my major concerns was infection. Case in point, we went to Gozo hospital for an outpatient appointment and it was overcrowded. I advised my wife to stay outside. Then I informed the nurse that my wife shall be waiting outside as she is receiving chemo.* [S003-2]

The patients’ experience of holistic care

All significant others were grateful that healthcare services were provided free of charge, which spared patients and their families from financial worry; allowing them to focus on the patients’ health.

> *I always emphasise how lucky we are to live in such a country with free healthcare service. Nonetheless nothing is perfect in life … there’s always room for improvement or something that we don’t like.* [S010-2]

The patients’ overall experience of the cancer services was considered by all significant others to be a positive one. Most significant others recognised the outstanding dedication of healthcare professionals towards their patients from the start. They were grateful for the healthcare professionals’ care and assistance. This further led to an establishment of a partnership between the patient and the healthcare professionals along the treatment journey. The oncologists and nurse navigators were mentioned by the significant others as being highly involved in the patients’ care from the point of diagnosis onwards.

> *Healthcare professionals in this hospital always tried to help my mum whatever she requested … even when they noticed that she was anxious prior to blood withdrawal, they tried to calm her down by talking to her and supported her accordingly. Support is available within the healthcare system … that cannot be denied.* [S014-1]

Some healthcare professionals even catered for the individual patient’s sociocultural needs; for example, a patient was discharged from hospital prior to the Christmas period.

> *They [healthcare professionals] really took care of my husband … even after the operation as he had his operation just before Christmas! They really did everything to send him home over Christmas.* [S007-1]

Along the treatment journey, some significant others recognised that there were hospital policies which were strictly adhered to, such as requests by significant others to stay with the patient at night-time. These requests were turned down as this was only allowed for patients at end of life.

> *He heard others saying that they* [the significant others] *accompany their father or mother during the night whilst in hospital … But I’m not allowed to stay here at night too …* [S001-2]

5.3.2.2.2. Sub-theme: Healthcare professionals' communication with patients and others

The importance of honesty when disclosing information

Communication of healthcare professionals with patients and others was recognised to be a critical aspect of the patients' experience throughout their entire treatment journey. The initial major emphasis was put on the disclosure of the diagnosis to the patient, with issues relating to the completeness and detail of information given.

> *The way how to deliver the news is crucial … Words have the power to make a patient feel better or bring him down … The truth should still be disclosed to the patient, though it may be difficult to accept.* [S012-1]

The issue of being truthful about the cancer diagnosis clearly raised different opinions amongst significant others. Some were being overprotective towards their patients and considered the complete factual disclosure of the cancer diagnosis to be insensitive. Others believed that the amount of information disclosed to the patient should ideally depend on the patient's preferences. Some argued that patients were still naïve at that point, lacking the experience and knowledge to ask further probing questions. Patients were noted to be in shock at the time of diagnosis which significantly impacted their ability to fully comprehend the information provided. This resulted in some significant others considering it to be their role to ask questions to help address the gaps in the patients' knowledge.

> *Healthcare professional should not expect the patient to ask for further information as the patient is inexperienced and maybe scared to ask for certain details. They [Healthcare professionals] should be the one who provide them with the necessary details.* [S014-1]
>
> *At that moment in front of the oncologist, she became emotional and I think it was very difficult for her [the patient] to understand what was happening. Though she was hearing what the doctor was saying, she still did not understand anything. As a result of the shock, the mind does not process things, and then it was only later that she was making sense of what had been said. I think it's a good idea that the patient will be provided with a pre-prepared document stating the exact diagnosis and a treatment plan to be taken home and think about it.* [S004-2]

The one nurse navigator who was participating in the study as a significant other confirmed that the practice adopted by the local oncologists was to directly answer patients' questions but not to elaborate further.

> *If the patient enquires further, then we [nurse navigators] proceed to disclose the whole truth. We provide all the information they request …*

> *First enquire what the patient knows and look out for words the patient is using … so we're exploring the patient state of mind.* [S008-1]

The effect of language and non-verbal cues

Significant others generally agreed that the communication process was challenging and required patience, empathy and refined communication skills. They remarked that the choice of words used by the healthcare professionals were noted to carry different connotations to the patients. Though simple terms were used by healthcare professionals such as the word 'treatment' instead of 'chemotherapy' or 'blemish' instead of 'cancer', some significant others claimed that these still resulted in the misinterpretation of the illness and treatment. To mitigate this, the nurse navigator who acts as a significant other for one patient described how she carried out an assessment of the patient's knowledge and subsequently used the same words utilised by the patient in the conversation.

> *The oncologist was mentioning the word treatment all the time and was speaking very softly. I noticed that my father was not understanding ... Whilst we were waiting for the doctor to get the consent form, I informed my father that she was recommending chemo. He told me "what?!" … It was good that I explained to him during that short break as she came back with the nurse navigator and asked him to sign the paper … It would have confused him when the doctor didn't mention anything and then nurse was mentioning chemo ...* [S015-1]

Communication was made more complex when patients and significant others encountered foreign healthcare professionals who could not speak Maltese. Some significant others described how patients found it difficult to explain their concerns in clear English. The provision of translators as well as official letters provided in dual languages were requested.

> *As soon as I enter the doctor's office and notice that he's a foreigner, I was anxious that we're not going to understand each other well … He does not understand English like me. So, if there's a doctor who is not Maltese, I think it's only fair to have a Maltese nurse with him* [the patient] *to explain to him clearly what is being said … this is something we're looking forward to have!* [S001-1]

Non-verbal communication was also identified as important to ensure effective communication between healthcare professionals and patients or their significant others. Most significant others commented on the impact of healthcare professionals' personality and attitude on the patient's emotions. Those healthcare professionals who showed compassion and empathy towards the patients were fondly remembered. Simple gestures such as greeting and smiling at the patient were suggested to support communication. This enabled the development of a compassionate relationship which promoted a comfortable environment for both patients and significant others to speak without fear.

> *You feel welcome by her* [oncologist's] *gestures… Her smile and even her attitude. She told us that if we need anything we can always phone her. Looking at her smiling, made us feel comfortable to speak to her.* [S011-1]
>
> *I noted an absence of greeting particularly in the other hospital. Nobody greets you with a good morning in the* [acute] *hospital; a greeting makes you feel welcome … There's a huge need to meet people with a smile.* [S012-1]

Patients' experience of different means of information provision

Different modes of communication were used by healthcare professionals during the treatment journey. These included face-to-face communication with oncologist supplemented by written material and the nurse-led group information session.

Prior to the start of treatment, the consultation with the oncologist involved a face-to-face session with the patient, often in the presence of the significant other and the nurse navigator. Most significant others praised the approach adopted by the oncologist to support their consultation with the use of a treatment-specific information sheet and a bilingual (Maltese and English) booklet on colorectal cancer. Some oncologists also provided a website link to the MacMillan patient information pack from the UK setting. Most significant others expected that patients would at least be provided with a provisional plan of the entire treatment journey. They criticised the fact that the surgeon and then later the oncologist focused their explanation solely on the current treatment strategy with no further information being given about alternative or subsequent treatment options.

> *I don't think it was good that they did not mention anything to us that he will be needing this treatment* [significant other referring to chemotherapy]. *We were then informed after one month at the out-patients appointment.* [S007-1]

Very few significant others actually read or observed the patients reading the written documents provided, with some complaining about the use of technical terms in the booklet impeding comprehension. One significant other requested an easy-to-follow information booklet which provided clear and simple messages with the use of pictograms. They also requested information on red flag symptoms that warrant emergency care and a list of mild symptoms that could be self-managed at home.

> *She was given a specific booklet about treatment which she just gave a quick look at… it was too technical, like university language.* [S005-1]

> *I preferred to be given a user-friendly list without any detailed explanations e.g. shellfish with a big NO, tomatoes with the skin on is also another NO. These simple things would have great impact. I have the booklet from Aurora which lists all the side effects that may happen with ticks next to each … in fact upon noticing all those ticks I closed the book immediately without reading it as I was getting anxious …* [S016-1]

The nurse-led information session at the start of treatment was an opportunity for the patient to identify a significant other and bring them on board for support. The session provided the patient and the significant other with the knowledge on how to cope with the experience of the illness and treatment.

> *We had the session organised by Aurora, where my mother was invited to take other members of the family.* [S014-1]

Significant others also commented on the lack of consistency and reliability of the information provided by the healthcare professionals. This lack of information furthered a sense of anxiety, anger and uneasiness amongst patients and significant others. Being faced with conflicting information from different healthcare professionals confused patients and significant others and undermined their trust in the healthcare professionals.

> *The information that we gathered from the information session confused us more as one was saying one thing and another saying another thing. Then you wonder who is right …* [S004-1]

5.3.2.2.3. Sub-theme: Recommendations for services

Need for improved awareness about available cancer services

At the time of the first interview, significant others were still getting acquainted with the cancer services provided. Most significant others commented on the lack of information provided about such services; with patients left to discover these services on their own. As a result, patients were not encouraged to use the available services if needed depending solely on the referral by the oncologist or the nurse navigator.

> *There should be much more awareness on services being provided here as sometimes a service is not utilised because the patient isn't aware of its availability.* [S010-1]

A significant other commented that she learnt about the patient's eligibility for the 'blue badge' scheme for reserved parking only towards the end of treatment.

> *I've got to know that the blue sticker was made available to those receiving chemo to park closer to hospital … it could have been provided for the duration of the treatment.* [S001-2]

A need for improvement in the current oncology services

Recommendations were made by few significant others to improve the nurse-led group information session. These included that the sessions consist of smaller groups of patients and the need for the provision of tailored information specific to cancer type and treatment. Moreover, they requested that there would be more than one information session along the treatment journey; with at least one at the start of treatment which focuses on the procedures to be followed during treatment administration whilst subsequent sessions should emphasise how to cope with the occurrence of adverse effects. Some significant others also recommended the use of online material such as webinars and recorded videos specific to the local context. These may be easily accessible to patients and significant others and can be revisited and viewed at convenient times.

> *It could be better to be run in small groups, as I think that there's a difference between the different needs this gives you more space to express yourself … everyone has different needs, even in the way the information is delivered.* [S012-2]

> *The information session was beneficial, but … it could best be done after the first cycle or mid-way through so that you would already have an idea of what the treatment consists of. If done prior to the second cycle, they could explain the side effects better than prior to the first cycle where the patient had never received such treatment before.* [S001-2]

Recommendation of new services within the healthcare system

Most significant others were very forthcoming with suggestions for improvement of the current cancer care services. During the first interview, most recommendations focused on how to deal with the diagnosis and coping with the upcoming antineoplastic treatment cycles. The need for the support of a psychologist for patients at the point of receiving the cancer diagnosis was seen as imperative. It was also recommended that this service should be extended to the significant others, as the latter may ease their own anxiety, improve their psychological wellbeing and be in a better position to support the patients.

> *I thought about the psychological effect when my husband was being informed that he is sick …You should speak with someone who will assess your feelings and how you're dealing with the news. But psychological help was not provided.* [S007-1]

Improvement to the accessibility to the patient's healthcare team was a major need by most significant others. They suggested regular dedicated contact time with the medical team throughout the duration of treatment, to allow patients and significant others to ask about any difficulties encountered. Another recommendation was for the significant other to be informed about the assigned nurse taking care of the patient during the hospital admission. This was expected to improve their relationship with healthcare professionals and ensure personalised continuity of care by simplifying transfer of information between the patient or significant other and the healthcare team. These recommendations were reiterated in the second interview showing that this gap remained an issue. In fact the significant others explained that along the journey, they had to visit the oncologists at their private clinics and incur out-of-pocket expenses to consult with the oncologist when they needed help.

> *I would like to know his assigned nurse at least for that particular day, as due to their shifts there might be different nurses along the treatment cycles. That way I can liaise with the assigned nurse … The patient will also build up confidence to ask certain questions … you know that your nurse will listen to you and don't have to repeat the same concern to different nurses.* [S001-1]

> *There should be dedicated time, particularly in the afternoon, where the consultant is available to discuss certain problems … without having to interrupt the medical team during the ward round for a quick conversation.* [S011-1]

Some significant others recommended the establishment of patients' support groups as part of cancer care that could be either peer led or facilitated by healthcare professionals. Sharing of experiences with other patients was considered beneficial to enable patients to support each other, develop coping skills and support them by not feeling alone in such a situation. The availability of an online forum or 24-hour support line were also suggested.

> *If they introduce a buddy system, I think it will help patients a lot. If my husband* [the patient] *meets other patients who have already experienced the same treatment journey, he may be more encouraged to start treatment.* [S016-1]

> *In Malta it is not the custom to establish support groups. They don't understand the benefits reaped from these sessions. I used to attend such groups as part of domestic violence abuse group. It would induce a trigger to speak about your own problems even if you're an introvert. I don't like to express myself with my own family but feel more comfortable with individuals I don't know.* [S006-2]

At initiation of treatment a few significant others were concerned about the type and intensity of physical exercise considered as safe for patients receiving treatment with antineoplastic medicines. Hence, they recommended the provision of an individualised physical activity program to encourage patients to keep physically active.

> *Though my husband is interested in taking up physical exercise, I don't encourage him much with exception of walking as a basic exercise … We're not aware what type of exercise he can engage in, so having a physiotherapist providing him with a physical exercise programme would make a difference … just a list of appropriate exercises is enough.* [S016-1]

At completion of treatment, significant others focused more on services that could be provided in the patients' home. The introduction of an oncology and palliative outreach team was suggested to ensure adequate patient follow-up.

They also recommended the provision of ambulatory care where patients may be provided with parenteral antineoplastic medicines by using a portable pump and flushing of port-a-cath in the comfort of the patients' homes. This would allow significant others and patients to continue with their routine whilst at the same time getting the perceived added benefits of parenteral antineoplastic treatment. However, the significant others emphasised the crucial need of relevant training and the need for a stronger support structure.

> *New services that should be introduced include provision of ambulatory chemotherapy and the setting up of an oncology outreach team … Another service includes the introduction of a palliative outreach team in the community setting. It's good to treat patients in their home setting when it's permitted.* [S008-2]

> *If a choice was provided, I'm sure that the use of pouch [ambulatory pump] would have interested him; if this is available locally … as opposed to being confined to the hospital, it would allow him to continue with his normal life. But I think that training will be essential as you're dealing with chemo outside the hospital setting!* [S010-2]

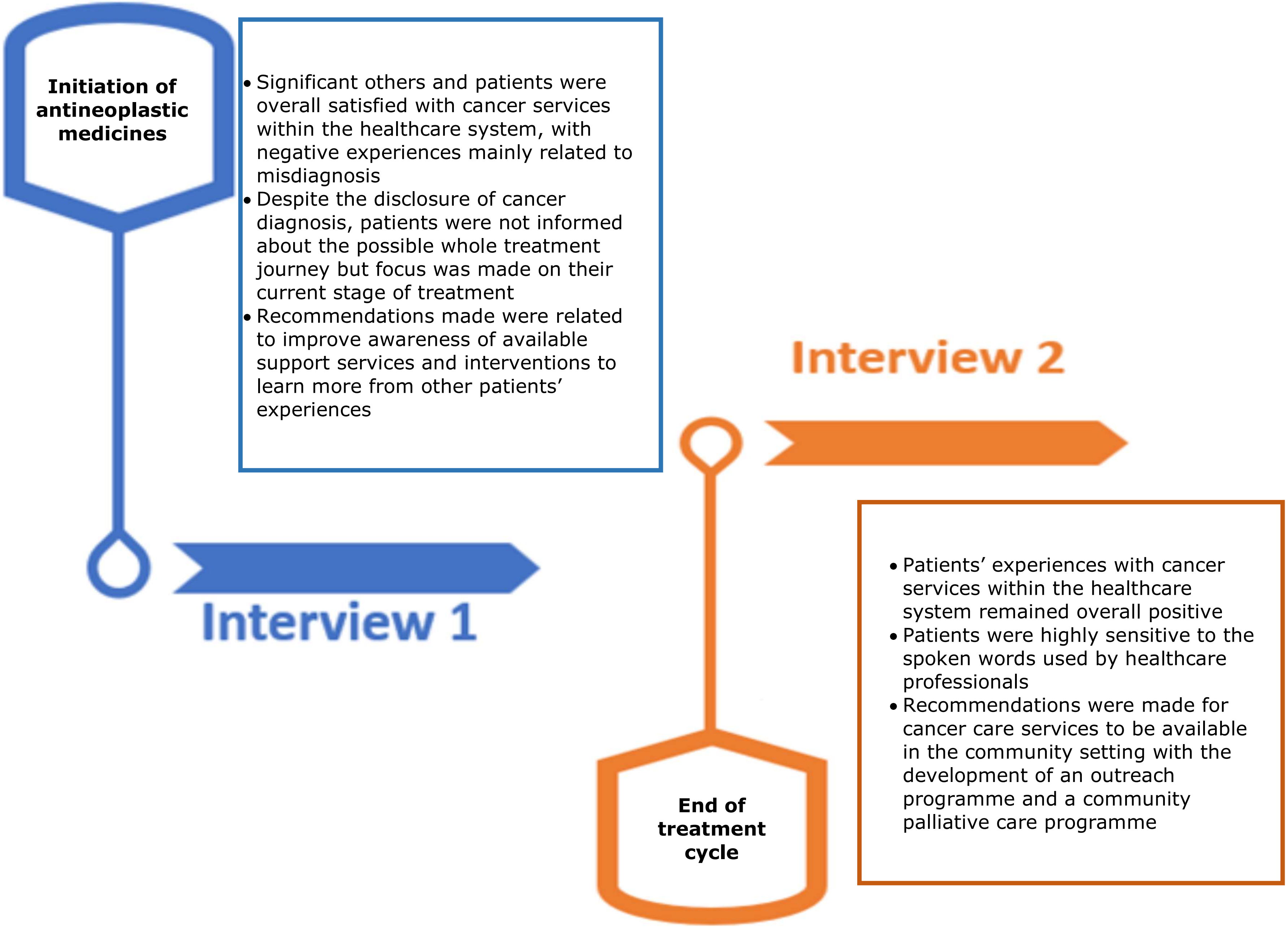
Another major recommendation was the setting up of a symptom control unit at the oncology hospital to review patients experiencing complications from treatment with antineoplastic medicines. The significant others showed great dissatisfaction with the current service that patients received at the emergency department upon their visits.

> *Patients suffer from effects related to chemo … so why do they have to be admitted at Mater Dei [acute hospital] and go through the whole process of admission and many unnecessary tests? At some point, a symptom control unit should be set up dedicated for oncology patients … I think that it is even cost-effective as an oncology trained doctors treat such symptoms much more effectively than other doctors … When going to emergency, we're occupying beds that can be utilised for other patients and also not safeguarding the immunosuppressed patients [S008-2]*

Some significant others also mentioned the importance of having a survivorship care plan following completion of treatment including the availability of social activities for survivors to allow them to be re-integrated in society. They acknowledged that services may be limited due to increased workload without improvement in staff complement.

> *It could be beneficial that social activities are organised for patients to meet other patients following completion of treatment to share their experiences of how they adapted to their new routine.* [S012-2]

Figure 5.2 highlights the longitudinal presentation of key points of Theme 2.



- Significant others and patients were overall satisfied with cancer services within the healthcare system, with negative experiences mainly related to misdiagnosis
- Despite the disclosure of cancer diagnosis, patients were not informed about the possible whole treatment journey but focus was made on their current stage of treatment
- Recommendations made were related to improve awareness of available support services and interventions to learn more from other patients' experiences

- Patients' experiences with cancer services within the healthcare system remained overall positive
- Patients were highly sensitive to the spoken words used by healthcare professionals
- Recommendations were made for cancer care services to be available in the community setting with the development of an outreach programme and a community palliative care programme

Figure 5.2: The longitudinal presentation of key points identified in the theme The healthcare system in relation to the illness and treatment

5.3.2.3. Theme 3: Patient’s involvement in treatment decision-making and their experience of medicine-taking

5.3.2.3.1. Sub-theme: Influences on acceptance of treatment

Influence of the oncologists’ recommendations

From the significant others’ descriptions, a stereotypical hierarchy of roles emerged with the oncologists taking the lead in the decision–making process and patients passively accepting the treatment. Most significant others felt reassured that the oncologist’s treatment recommendation was based on the diagnosis and patient’s best interest. Whilst clarifying that the responsibility for final consent rested with the patients, significant others felt that it was important for them to accompany patients to the oncologists’ meeting to support the patients’ decision.

> *The consultant [oncologist] decided the way forward and she just agreed. She [the patient] took her decision on what the consultant told her … as that was the option of achieving cure.* [S006-1]

> *I’m not going to interfere in his decision if he decided against taking the treatment. He is old enough to make his own decision. However, I still encourage him to do whatever is required.* [S016-1]

At initiation of treatment, most significant others described that patients had limited or no involvement in the decision-making process. This was evidenced by the significant others’ use of words such as ‘*blindly follows’* [S002-1] and ‘*accept whatever they offer’* [S016-1]. According to most significant others, patients completely trusted ‘*what was being said’* [S001-1] by the oncologists as they considered them to be experts in this field.

> *He blindly follows the advice being given by the consultant and accepts whatever medicine is recommended to him.* [S002-1]

> *As from the start, he* [the patient] *took the decision that since he was suffering from this* [cancer]*, he would do whatever is needed and accept whatever they* [the healthcare professionals] *offer.* [S016-1]

The significant other of a non-Maltese patient described that the patient was given a choice of treatment options and then allowed a few days to reflect, ask and ultimately make a decision. This patient decided in favour of oral antineoplastic medicines in combination with a short parenteral infusion as this treatment regimen offered him the flexibility of home care. He was the youngest and only patient who got this treatment regimen in this study.

> *Personally, I was not involved in the decision … but the doctor [oncologist] spoke to us, gave him two options where it was explained in simple terms what the difference between the two is. The doctor also gave us one week to go home, re-think and then come back to him with a decision on the plan after re-discussing any queries. He was really helpful and nice! My husband does not want to stay in hospital. He hates hospitals, so he opted for the day case treatment and then he'll take tablets at home.* [S007-1]

At completion of treatment, some significant others reflected on the decision-making process. Some significant others hinted that the patients' decision was taken because of the way the information was phrased by the oncologist. They remarked that patients consented to treatment without being given all the information about their illness and treatment including the prognosis. After realising that there were different available treatment options, significant others expressed the need for patients to be actively involved and have a shared responsibility together with their oncologist to decide what's best for them. A few significant others expected patients to prefer the oral option as this spared the patient from being confined to hospital.

> *She [the patient] took her decision on the way the message was conveyed by the consultant - as that was the option of achieving cure.* [S006-2]

> *When the oncologist Dr X spoke to him, she explained to him that that was the only way to kill the bad cells. So he just followed her advice.* [S010-2]

> *I think if there was a choice, yes – all options should be put forward and the patient left to decide.* [S004-2]

> *Looking back, he might have considered different forms of treatment such as tablets … Also I would have preferred him to stay at home.* [S001-2]

> *I think she would have chosen to take treatment at home as she doesn't like to get out of her home to stay here. For instance, she has to come here for bloods. She would like to come here for short visits but not for 3 days at a stretch. She would have considered receiving treatment at home ...* [S006-2]

Influence of independent advice of specialists

A few significant others described how the advice of specialists from abroad was sought through familial connections. This allowed an independent opinion to be obtained regarding the patient's illness and treatment. Furthermore, they also confirmed that the local practice followed international guidelines.

> *I have been listening carefully to the surgeon and both oncologists – the one here [at the oncology centre] and my relative in Switzerland and everything seems to be making sense. Fortunately, we have an oncologist in our family who practices abroad and we enquired about FOLFOX. He gave us an explanation over a Skype call. Then when the surgeon explained to us, he said that he was considering that treatment too.* [S003-1]

Influence of patients' awareness on survivors

Some significant others mentioned that patients put their hope into treatment and felt that they stood a better chance to achieve cure in comparison to those patients who refused treatment. Throughout the treatment journey, significant others remarked that patients' awareness of close relatives who survived cancer re-enforced their hopes and motivated their decision in favour of acceptance of antineoplastic medicines.

> *Mainly the patient accepted treatment with the aim to get cure. The concept would be that I receive chemo to be cured.* [S008-1]

> *Again, thanks God we* [the patient and significant other] *have a living proof as my boyfriend's mum had cancer 12 years ago and received chemo as well … her experience fills us with hope* [S014-1]

> *I emphasise this with her that my father lived for further 12 years following diagnosis … though he lived his life with a stoma, he died at 91 years of age … She got to know that a lot of her neighbours have suffered from it and started sharing their own experiences. One of them told her that she took this treatment 2 years ago whereas another one was currently receiving it. We met another one of her neighbours here … Seeing these living testimonies fulfil her with hope.* [S005-2]

Influence of treatment with antineoplastic medicines

At initiation of treatment, some significant others were quite vocal that patients should be given treatment with antineoplastic medicines in a hospital environment as the patients would be under the constant surveillance of trained healthcare professionals.

> *I understand that the patient might have preferred to stay at home but I think that this would cause more disruption in our life as I'll end up calling her all the time to check on her which would disrupt my concentration at work. However by having treatment in hospital my mind is at rest.* [S009-1]

Most significant others considered that the severity and reversibility of adverse effects, particularly those related to aesthetics might have influenced its acceptance by patients. Alopecia was the adverse effect of major concern to patients. Significant others noted that the patients were relieved and willing to accept treatment upon learning that the antineoplastic medicines administered, did not carry a risk of hair loss.

> *I was not involved in the decision. She made the decision on her own exactly after speaking to the doctor. She was worried a lot about hair loss but the professor assured that this would not happen; this fulfilled her with courage.* [S013-1]

5.3.2.3.2 Sub-theme: Experiences of administration of antineoplastic medicines and other medicines

The expectant adherence with antineoplastic medicines

At initiation of treatment, most significant others had the perception that taking antineoplastic medicines was similar to taking chronic medicines. They did not anticipate difficulties in patients' adherence to treatment, if patients were already accustomed to taking medicines for other chronic conditions.

> *Whilst at home, she remembers to take the chronic treatment on her own. So, for now I don't think she'll require any assistance to remind her about her new treatment. Then we'll re-evaluate as time goes by.* [S014-1]

> *My mum reminds him to take the medicine most of the time, those diabetes and blood pressure tablets … he leaves everything in her hands. She carefully prepares his treatment and then gives them to him exactly on time. Both of us will surely support him to follow this new treatment schedule.* [S015-1]

Along the treatment journey, significant others recognised the priority given by patients to the illness and treatment over all the other things in life. While significant others highlighted the efforts made by patients to adhere to the treatment schedule as accurately as possible, a flexible treatment schedule allowed patients not to miss unique life event celebrations. Postponement of antineoplastic medicines was noted by significant others to cause considerable distress to patients, with concerns relating to adverse impact on the effectiveness of treatment. A significant other suggested that doctors should notify patients before the scheduled appointment by phone in case of possible treatment postponement.

> *When he was informed that treatment had to be postponed, he was very upset. So am I! Then I tried to explain to him, that it was necessary to do so as otherwise treatment would cause more harm than benefit.* [S001-2]

The experience of changes along the treatment journey

At initiation of treatment, most significant others admitted that like patients they were not aware of the name and dosage of antineoplastic medicines being administered. This made it difficult for them to identify changes in the dose. Along the treatment journey, a significant other who was following the patient's treatment closely described how he happened to notice a change in dosage by chance; therefore, highlighting that healthcare professionals were not communicating any changes in the treatment proactively. Most significant others mentioned that the patients' knowledge about the process of administration of antineoplastic medicines was limited to the treatment schedule. In fact, patients were noted to record the total infusion time to ensure that their usual treatment regimen was administered. Patients also lacked information on their oral supportive medicines taken in hospital, with patients being advised by significant others to ask nurses about their tablets prior to ingestion due to a potential risk of medicine errors.

> *I don't ever recall of being informed that her dose was reduced … I don't know … she never mentioned that the dose was changed. She always spends two days* [in hospital] *and is discharged on the third day.* [S005-2]
>
> *Upon checking the label on the outer bag, I noticed that the last 2 bags of 5-FU were increased by 150ml. I enquired with the nurse about this increase and informed me that the dose was adjusted according to patient's weight … We weren't informed about it … so when I noticed that increase, I was shocked and worried. It would have been the doctors' duty to inform us that the dose shall be increased.* [S003-2]

The use of port-a-cath for administration of antineoplastic medicines

Some significant others highlighted that negative treatment experiences were mainly related to the occurrence and management of treatment adverse effects. All patients except one with a history of venous thrombosis, accepted the oncologist's recommendation to have a port-a-cath inserted to reduce the risks of treatment complications. As expected by significant others, the port-a-cath use provided patients physical and psychological benefit by sparing them from needle pricks and provided them with a sense of freedom from infusion lines. Despite the fact that the main concern of significant others was related to catheter related infection, in practice the most frequent complication experienced by patients was catheter related thrombosis.

> *At the beginning she was anxious about the port-a-cath and remained against it till the end. She suffered repercussions, as every time she was due for treatment she was afraid that they would not be able to detect a suitable vein.* [S014-2]
>
> *During every hospital visit, the doctors always assured us that everything was going well. Then she had a problem with port-a-cath use, where she suffered from thrombosis and had to undergo port-a-cath removal. That was another hurdle!* [S012-2]

The monitoring of treatment and its outcome

Initially, at the time of the first interview all patients were chemotherapy-naïve making it difficult for most significant others to predict the outcome of such treatment. However, some significant others expressed their fear of complications related to the administration of parenteral antineoplastic treatment. Along the treatment journey, most significant others gained familiarity with the sequence of events each cycle of antineoplastic medicines followed. Significant others described that though the medicine taking practice was physically and psychologically demanding, it was less difficult than anticipated. They described a cyclical patients' experience, whereby a patient was '*rejuvenated'* [S011-2] during administration of antineoplastic medicines followed by feeling '*shattered'* [S011-2] with the adverse effects of antineoplastic medicines for the first few days following treatment.

> *I was concerned about the treatment … We'll have to see how the body will react to this treatment … it all depends on whether his body accepts it or not. I don't know what is going to happen; he has just started this treatment, today being the second day of the first* [treatment] *cycle.* [S002-1]
>
> *The patient experienced a rollercoaster of events. Initially there wasn't any problems and the patient felt quite normal, but then problems cropped up along the journey due to low blood parameters and so on. Initially it's difficult for them* [the patients] *to comprehend what they're going to experience. As not everyone is the same, I can't predict beforehand.* [S008-2]

The experience of managing adverse effects following administration of antineoplastic medicines

Most patients and significant others experienced a major challenge in managing adverse effects experienced at home in between cycles. These worsened with treatment progression. Deciding on the severity of the adverse effects experienced and deciding on when to go to the emergency department was a particular challenge. This resulted in frequent visits to the emergency department where they had to wait for hours in the same waiting room with other patients. Despite the patients being given a chemotherapy alert card which was meant to give them priority, this was of little use in practice. Consequently, patients tried to minimise their presentation at the emergency department and phoned the nurse navigator instead for advice or reported their adverse effects to healthcare professionals during the patient's hospital review prior to treatment administration.

> *They explained to us that if we notice that she has fever or anything abnormal, such as diarrhoea, we should take her immediately to hospital. They also gave us a card so that her case is prioritised.* [S013-1]

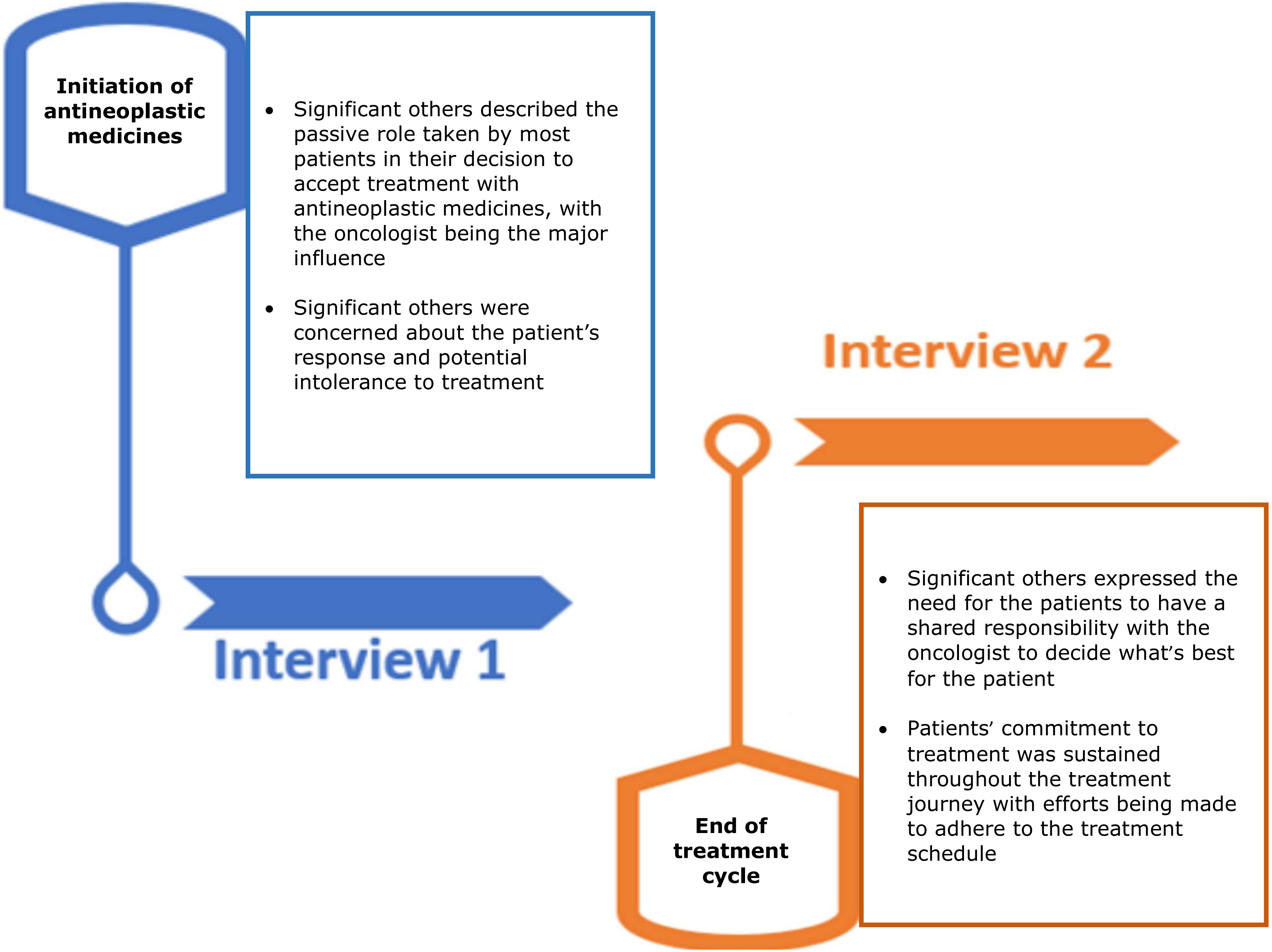
> *I entered the emergency department and informed the first nurse I met that my husband was receiving chemo… she replied that there are ¾ of the persons in the waiting room receiving chemo. My husband insisted that he has this card and that he was strongly advised not to be close to sick persons. … Then the nurse realised that the intention was not to skip the queue and placed him in a room at the end of the corridor.* [S010-2]

The experience of taking complementary supplements with antineoplastic medicines

At the start of treatment, some significant others revealed that patients were made aware about the possible interactions between antineoplastic medicines and complementary herbal supplements. Despite this, some patients were noted to still make use of herbal teas with the intention of improving the effect of antineoplastic medicines on cancer. Significant others remarked that this may be due to lack of reinforcement of knowledge along the treatment journey, the impact of media or perceived need to maximise treatment efficacy.

> *He might have come across some posts on Facebook that ginger is 10000 times more effective than chemo. So, we bought ginger. I prepare a mug of ginger tea for him to drink prior to going to sleep.* [S010-2]

Figure 5.3 highlights the longitudinal presentation of key points of Theme 3.



- Significant others described the passive role taken by most patients in their decision to accept treatment with antineoplastic medicines, with the oncologist being the major influence
- Significant others were concerned about the patient's response and potential intolerance to treatment

- Significant others expressed the need for the patients to have a shared responsibility with the oncologist to decide what's best for the patient
- Patients' commitment to treatment was sustained throughout the treatment journey with efforts being made to adhere to the treatment schedule

Figure 5.3: The longitudinal presentation of key points identified in the theme Patient's involvement in treatment decision-making and their experience of medicine-taking

5.3.2.4. Theme 4: Medicine and illness-related impact on patients and others

5.3.2.4.1. Sub-theme: Impact of Physical effects on patients and others

At initiation of treatment the major concerns of most significant others were related to adverse effects that may affect the patients' physical strength. This was mainly due to adverse effects such as fatigue being perceived as impacting the patients' independence and subsequently impacting the rest of the family including significant others. Alopecia was commonly perceived by several significant others to be of most concern to patients despite being reassured by their oncologists that treatment with FOLFOX or XELOX did not cause hair loss. In practice most patients did not get alopecia at completion of treatment, though a few patients still experienced hair thinning.

> [I'm concerned about] *the side effects* [that] *might cause a change in lifestyle and she is no longer independent. If she is tired to such an extent that she is bedbound, this will have repercussions on all the family, if we ever get to that stage.* [S004-1]
>
> *She* [the patient] *was highly concerned of losing her hair when hearing about the treatment. Actually, she only experienced hair thinning.* [S005-2]

As treatment progressed, all significant others noted that patients experienced mild physical adverse effects, with fatigue and peripheral neuropathy being the most prevalent. Some significant others viewed the effects of peripheral neuropathy as a new experience with uncertainties over its presentation, impact and a lack of confidence on how best to offer the necessary support to patients. All physical effects worsened along the treatment journey and became more pronounced towards completion of treatment. Other effects included mouth ulcers, altered taste and appetite, changes in bowel habits and skin rash. Vomiting was only experienced rarely with the significant others claiming that the patients' symptoms were well controlled with the use of supportive medicines.

> *This* [Fatigue] *did affect her as she reduced the number of errands and had to rest in between … she walks slowly and gets tired easily consequently requiring frequent rests.* [S004-2]
>
> *Side Effects were kept under control whilst being here. Anti-inflammatory and antiemetic agents were administered through the vein, so the patient didn't suffer a lot of side effects except for one episode* [of vomiting]. [S003-2]

Furthermore, a few significant others taking care of young patients of child-bearing potential raised their concerns about effects of antineoplastic treatment on the reproductive system. Fertility was briefly discussed by the oncologist with the patient and the significant other, but it appeared that the subject was still considered a taboo.

> *The doctor discussed this thing about family with us … and touched on fertility issues but we are not very open minded and ready to engage in this type of discussion … The doctor also referred us to another department for sperm banking.* [S007-1]

The significant other of the patient who refused port-a-cath insertion referred to chemical phlebitis as being the worst effect.

> *The effect on the veins was the worst, especially during bloodletting. She also suffers from cold hands, tingling sensation without even touching cold surfaces … and also has occasional mouth ulcers. Physically she feels tired.* [S014-2]

Most significant others did not expect that the physical effects such as peripheral neuropathy would persist for months following completion of treatment.

> *The tingling sensation caused by this treatment* [FOLFOX] *creates fear in thinking that he continues to experience this effect or gets worse. Otherwise this will restrict him in carrying out some daily tasks.* [S010-2]

> *She's still suffering from a few side effects, but these are effects that will persist. We [nurse navigators] advised her that she can dye her hair and continue with her life. However effects such as peripheral neuropathy will persists for some time, literally persistent … These are not switch on and switch off; therefore takes time to resolve.* [S008-2]

5.3.2.4.2. Sub-theme: Impact of Psychological effects on patients and others

Despite being familiar with the patient's character, most significant others found it difficult to predict any psychological effects that the patient may experience along the treatment journey. According to several significant others, the cancer diagnosis totally transformed the life of patients and their immediate family.

> *It's a mix of despair, fear, anxiety and crying … from that moment [disclosure of diagnosis] onwards happiness and laughter are no longer permissible for her and her immediate family. It's like living an unknown situation; a sudden change from a hectic lifestyle, busy like a bee to quietly here in bed. It's a great shock, like the world has fallen on us. What are we going to do now? How are we going to help her? What are the wishes of my sister, as a patient? Crying?! I couldn't stop crying, as I was hearing her sobbing.* [S011-1]

> *She was distraught ... She was miserable after she read what can happen to her … I'm more concerned about how she'll cope with further news, information and occurrence of side effects during the whole treatment process. I'm worried about any possible panic attacks whilst being alone at home.* [S009-1]

At the start of treatment, significant others described the patients' mental health as distressed, anxious and fearful of the unknown. Some significant others explained that patients suffered from mood swings or got upset quite easily, particularly in the early stage of treatment. According to some significant others, the first treatment cycle was characterised by patients being highly anxious upon arrival to hospital and shifted to the patients' feeling calm and serene during the actual parenteral administration of antineoplastic medicines.

> *Yesterday morning his emotions were uncontrollable … he was lost in thoughts, anxious and uncertain about what was going to happen. He has a personality type that is expressive; he is unlikely to keep everything to himself.* [S010-1]

Their initial shock and intense emotions at the start of treatment changed to reassurance following acceptance of the illness, understanding the treatment outcome and increased familiarity with the process of treatment administration. As treatment progressed, most significant others noted an improvement in the patients' psychological wellbeing, experiencing less fear when compared to initiation. On the other hand, towards completion of treatment, patients were noted to become irritable probably secondary to uncertainty of the future and as expected by most significant others constant worry persisted throughout the treatment journey.

> *She was afraid … though they were providing reassurance, she was still engulfed in fear until she accepted the situation. Then she calmed down.* [S005-2]

> *She already has a difficult personality but now at the end of treatment she is extremely irritable. Though you know that this might be the consequence of her illness, at that moment she is very difficult to tolerate her.* [S006-2]

Up until completion of treatment, some patients continued to be highly sensitive to comments made by the general public on cancer and its effects. The fact that patients' conversations with others revolved around the same subject with repetition of the same word of advice distressed both the patients and the significant others. A few significant others found it challenging to deal with patients who kept their thoughts to themselves making the significant others feel helpless.

> *Every time I speak to anyone I meet, I always hear the same phrase 'Oh how sorry, I don't know what to say'. I can't bear to hear this anymore ... 'I don't know what to say.' I noticed that the patient gets agitated at the greeting 'how are you?' as the situation is obvious with the individual being in hospital … it's like you are aware of my situation. It's imperative to think before you speak out even a simple word!* [S014-1]

5.3.2.4.3. Sub-theme: Social consequences on patients and others

Significant others remarked about the reluctance shown by most patients to disclose their diagnosis to all family members and friends at initiation of treatment. As most considered the diagnosis of cancer as confidential information, they concluded that it is up to the patient to decide whether and at what point to share the news. They reported that some patients chose to share the news with whoever they met whilst others shared it only with those who commented about their change in appearance. A significant other expressed the patient's concern to disclose the diagnosis of cancer to his frail elderly mother, with the risk of worsening the latter's health problems.

> *Thankfully he [the patient] isn't keeping everything to himself and isn't concerned about telling others. The fact that he got thinner, he often receives complements about obtaining a better body shape. Surprisingly he doesn't seem to be annoyed and usually clearly states the truth about his diagnosis!* [S016-1]

> *We had a dilemma as to whether to inform our mother as she's elderly and had a stroke. We were all worried that this* [news] *would add to her problems but then we decided - actually, he decided to go and tell her - and that's what he did.* [S002-1]

Significant others commented that as from the point of diagnosis, the patients were noted to retreat into themselves possibly due to the stigma related to the illness. They noticed that patients with a stoma distanced themselves from other people due to embarrassment.

> *She was more affected by the stoma* [than antineoplastic treatment*] as she was embarrassed about this initially … until she accepted the situation. Then she started wearing trousers and ignored whatever was being said.* [S014-2]

The distress caused by this social isolation got progressively worse over the treatment journey. Significant others remarked that the patients' adherence to the treatment schedule and the need for regular hospital stays increased their isolation. The implementation of cautionary measures to avoid contact with others to minimise risk of opportunistic infections also resulted in patients missing out on social events. Other self-imposed measures such as not being able to use public transport to safeguard the patient's health, further compounded that feeling of patients' isolation.

> *The treatment affected the weekends, to be exact every other weekend. Today we were invited to a wedding which we did not attend. We also spent both Easter and New Year's Day here [hospital] too. The expectation is to spend these festivities with the family. We did not. Obviously, it affected us socially.* [S003-2]

During the treatment journey, other aspects that were noted by significant others to worsen the patients' social isolation included experiencing adverse effects, fear of experiencing unpredictable symptoms when being alone outside their own home and worsening of symptoms by harsh weather conditions, particularly the hot weather.

> *During her treatment journey, she never went to Valletta* [the capital city] *on her own … she's anxious to catch the bus in case she suffers a dizzy spell. She just walks up to the square of her hometown, though it's still not easy as it's uphill. If something happens in her hometown, someone will know her; all her neighbours know her and can help.* [S005-2]

In view of the patients' vulnerable state, some significant others became overprotective of the patient and tried to reduce the patients' interaction with others where possible. On the other hand, the significant others felt helpless about the patients' social isolation which continued to worsen until completion of treatment.

> [We implemented] *a number of precautions particularly related to hygiene ... which I think impeded other relatives to visit her too. Whoever comes home, needs to follow a protocol of using alcohol rub. If any relative feels sick, I informed them to just phone and don't visit her.* [S003-2]

On completion of treatment, the social consequences experienced were worse than expected at the start. As a result, most patients were noted by significant others to put their life on hold by decreasing their social engagement to a bare minimum. Their world became constrained mainly to their home and the oncology centre, resulting in them meeting the same group of individuals throughout the entire treatment journey.

> *The fact that she cannot go to work and abroad upset her most … as she enjoys holidays abroad. She could not even attend her brother’s funeral in England … also that of her nephew locally.* [S006-2]

Some significant others presumed that elderly patients would be less likely to suffer from drastic social consequences because they considered them to already lack friends or be house bound. Therefore, the regular hospital admissions for treatment were considered as an opportunity to meet new acquaintances. As the treatment progressed, patients of all ages built friendships with other patients on the ward through spending time together and sharing of experiences. Significant others were concerned that following completion of treatment the friendship built during the inpatient stay would be lost.

> *I think she’ll continue to live her life normally; I’m not predicting any major changes in her routine. She already doesn’t have any friends and prefers to stay indoors. Hopefully she will be sharing her room with friendly patients and engage in conversations with them whilst being in hospital.* [S013-1]

> *Another thing I’m concerned about is the fact that upon completion of treatment she will lose the friends she made at the hospital. Her life is going to change, for sure.* [S014-2]

5.3.2.4.4. Sub-theme: Implications on financial status

At initiation of treatment, most significant others did not expect patients to have any major financial constraints since patients’ treatment with antineoplastic medicines for cancer is funded through the public health service. However, along the treatment journey, significant others complained about additional expenditure. Besides the patient’s needs to consume freshly packed products and other essential hygiene products, patients had to buy supportive medicines out of pocket to control adverse effects. As these medicines were either reserved for potential emergency situations or used for short duration, this resulted in unnecessary expenses and wastage.

> *Thanks to having a free healthcare system, I’m not anticipating any major financial impact. If one had to receive this service privately this treatment is costly.* [S016-1]

> *Apart from social, psychological and emotional effects, there were financial effects. We had to buy specific food and hygiene products together with medicines, sometimes being bought as a prevention … they were not used and wasted.* [S003-2]

Some significant others anticipated that elderly patients' potential financial problems would stem from their modest pension which had to cover the cost of living combined with now increased expenses.

> *My parents must live on dad's pension of 750 euros per month. It is already really difficult to make ends meet. Though there are things that are provided by the hospital such as the treatment itself, there are other things that blow up the expenses. A lot of expenses were related to private doctors' visit in order to obtain diagnosis as one refers you to another … Specific products must be bought during the treatment such as alcohol-free mouthwash … all of these have a higher cost price.* [S014-1]

In the case of young patients who were still in the working age group, most patients ceased to attend work. A significant other was grateful to the employer that supported her young husband to continue attending work by offering a safe workplace with flexible working conditions.

> *Regarding his work, he discussed the situation with his boss and they were very cooperative. He may go to work late [flexible hours] and arranged his desk to be separate from other colleagues … It could be that the treatment is going to affect us financially as it could interfere with the work but the company where my husband works is being very helpful.* [S007-1]

Reflecting at the end of treatment, the financial burden experienced by patients who ceased their full-time work was worse than anticipated at the outset. In fact, these patients relied mostly on financial assistance provided by the social services and to a lesser extent financial support from the significant others. For example, a significant other was critical of the quick decision taken by the patient of immediately resigning from work prior to initiation of treatment leading to the patient's complete reliance on social services and possible financial hardship even in the future.

> *She* [the patient] *had to stop work, which led to financial problems. They gave her a hard time to resign from work and benefit from social services. My other sister rushed her to take a decision … They didn't give me time to explain … Financially she is now dependent on social services.* [S011-2]

Most significant others emphasised the need for prioritising expenses. For example, a spouse devised a financial plan from the start of treatment to maintain their financial situation without compromising his wife's health.

> *Obviously* [a mild financial impact is expected]*. For instance, she needs a special toothpaste … We must make ends meet on one pension, so to boost this income I try to do some renovation works in our neighbourhood.* [S012-1]

A significant other claimed injustice against patients receiving antineoplastic medicines as they did not qualify for additional financial support, when compared to patients with other chronic illness such as diabetes. This significant other expected financial support from the government given that patients with cancer were advised against attending work due to health-related risks associated with the intake of antineoplastic medicines.

> *I heard that elderly persons may receive financial assistance from social services for illness such as hypertension, diabetes etc. So why are persons receiving chemo not entitled for such benefit? To make the situation worse, this treatment makes them [cancer patients] so vulnerable that they have to stop attending work to avoid encountering other persons.* [S004-2]

5.3.2.4.5. Sub-theme: Seeking refuge in spirituality and religion

Most significant others noticed that as from the initiation of treatment, patients turned to faith to give them a sense of control over their feelings of helplessness. Significant others accepted that religion could play a role in achieving a cure for patients, but this was only second to receipt of treatment. They considered the synergistic effect of the use of medicines together with their religious beliefs to provide hope for many patients as the latter felt guided by a source greater than themselves.

> *To her* [my mother] *chemotherapy is hope and glory from God.* [S014-1]

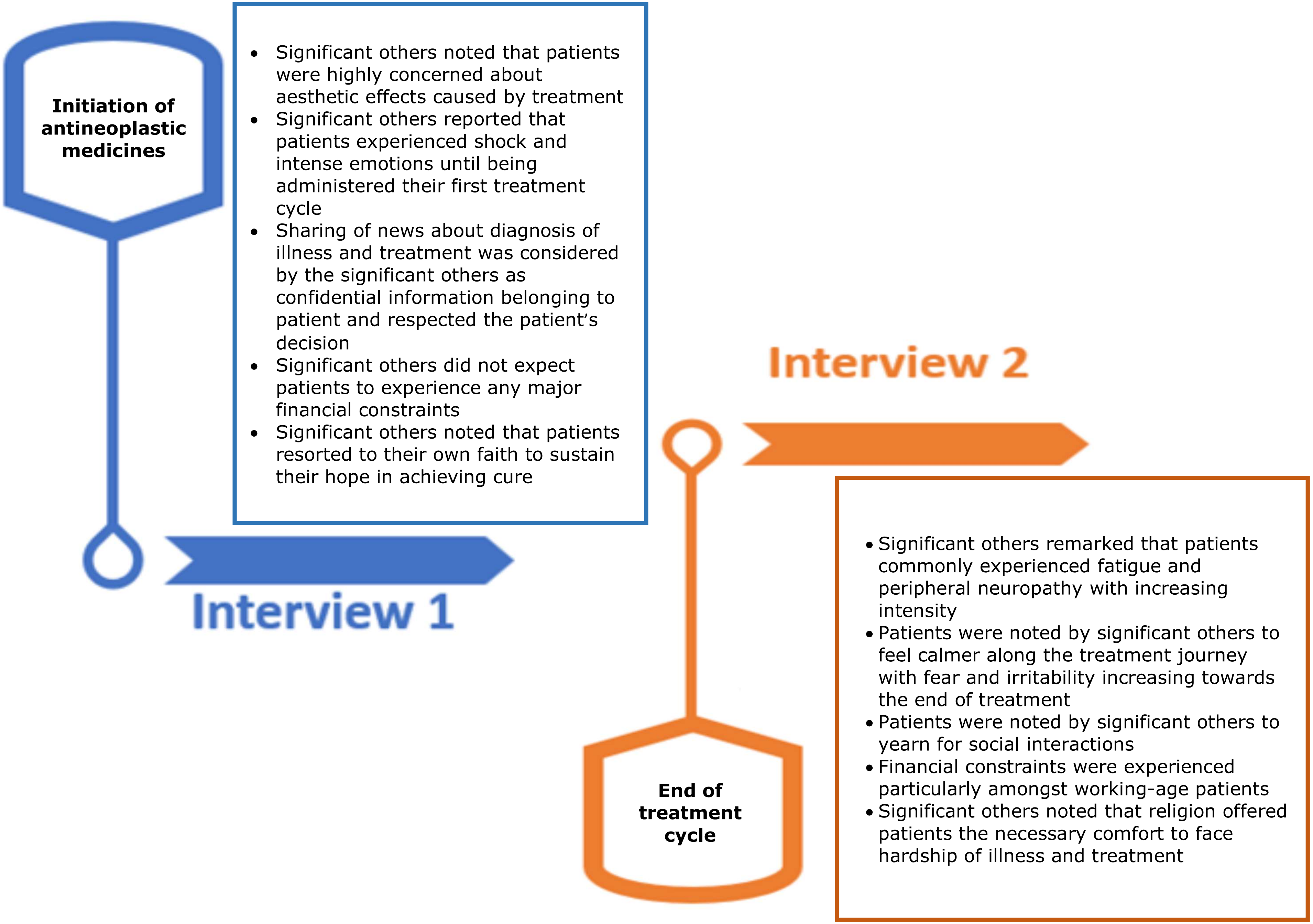
Significant others noted that patients resorted to prayers and attended church. Prayers were used as a coping strategy by patients along the treatment journey to maintain hope. The physical presence of the patients in church with other individuals improved the patients' social well-being. Although a patient was noted by his significant other to initially abandon his religious practice altogether, most patients were noted to attend religious services in person in spite of everything.

> *She* [the patient] *is very resilient and underwent tests full of hope. She has a strong belief in Jesus and prays a lot, which fills her with optimism. Other than science, she has to leave everything in God's hands. If one loses hope, then there is nothing to look forward to! Hope is half the cure!* [S005-1]

Upon completion of treatment, religion was noted by significant others to provide patients with the necessary comfort to face the hardship of illness and treatment, as identified through their frequent remarks of leaving their future in God's mercy.

> *Doing God's will … and let everything that has to happen, happen ...* [S005-2]
>
> *It was a shock to us that she [the patient] was diagnosed with cancer. She received the treatment as recommended but she was also accompanied by God all along the way.* [S012-2]

Figure 5.4 highlights the longitudinal presentation of key points of Theme 4.



- Significant others noted that patients were highly concerned about aesthetic effects caused by treatment
- Significant others reported that patients experienced shock and intense emotions until being administered their first treatment cycle
- Sharing of news about diagnosis of illness and treatment was considered by the significant others as confidential information belonging to patient and respected the patient's decision
- Significant others did not expect patients to experience any major financial constraints
- Significant others noted that patients resorted to their own faith to sustain their hope in achieving cure

- Significant others remarked that patients commonly experienced fatigue and peripheral neuropathy with increasing intensity
- Patients were noted by significant others to feel calmer along the treatment journey with fear and irritability increasing towards the end of treatment
- Patients were noted by significant others to yearn for social interactions
- Financial constraints were experienced particularly amongst working-age patients
- Significant others noted that religion offered patients the necessary comfort to face hardship of illness and treatment

Figure 5.4: The longitudinal presentation of key points identified in the theme Medicine and illness-related impact on patients and others

5.3.2.5. Theme 5: Personal support structure

5.3.2.5.1. Sub-theme: Establishing a support network

Building the patients' support network

The significant others considered themselves to be part of the patients' personal support network and focused their responses on their role in the patients' care. Most significant others were the patient's next of kin and given their relationship to the patient perceived that it was their duty to assume this caregiving role to their parents, spouses or siblings.

> [He nominated me as his significant other because] *I'm his wife and he knows that I take care of him. I have been taking care of him since we got married ... and that is how it should be.* [S016-1]

Besides immediate family members, most significant others named close friends or neighbours as part of the patients' personal support network.

> *It's me together with my other siblings who help our father with whatever is required … I think he's well supported by the family … He even has some close friends who call him regularly.* [S015-1]

The impact of a lack of support network in circumstances of family disagreements became more evident along the treatment journey. A patient nominated the nurse navigator as a significant other because she fell out with her family resulting in obvious lack of support.

> *She experienced diarrhoea, a severe episode of diarrhoea … so she had to wash the trousers and hang it in her room in the ward … as no one was visiting her here and she did not have a lot of clothes with her.* [S008-2]

Significant others suggested that a patient had every right to freely identify any individual to be included in his personal support network, irrespective of kinship. They also remarked that these nominated persons should respect the patients' decisions irrespective of their own opinion. Almost all significant others intended to prioritise the patient's needs over their own personal plans, with the aim of easing the patient's burden.

> *I was surprised to be chosen as a significant other. Though I feel capable to support her, I'm afraid that we don't agree much and often argue.* [S006-1]

> *Though I'm against his decision to continue working, I agreed to continue to help him at the shop and make the necessary sacrifices … He's very optimistic as a person, so I shall try to sustain his high spirit whilst trying to be more optimistic myself.* [S016-1]

> *I have to find time to visit my mother here … this becomes part of my routine for the remaining weeks, not allowing me to plan for the future.* [S004-1]

Whilst it seemed that most patients wanted a single support provider, significant others felt the need to share the burden with the patient's support network along the treatment journey; even though this was occasionally against some patients' wishes. Also, these patients were noted to refuse further assistance from voluntary organisations as they felt well supported.

> *He has only me to support him. He doesn't want to involve others not even our own children … no one … this is making me tired! He's reserved and doesn't even want to tell his siblings. I accompany him to an appointment for the port-a-cath as he gets lost in these corridors. He feels safe when I'm with him.* [S010-2]

> *I prepared the necessary meals for her [the patient], whilst my daughter took care of her child whilst she's in hospital. Either me or my sister accompanied her to all hospital appointments. On the other hand, her partner did the necessary errands for her.* [S011-2]

> *Staff from the Hospice [voluntary organisation] occasionally phone her to check whether she needs anything. She refuses their assistance as she feels that she does not need it.* [S005-2]

As treatment progressed, a few significant others considered caring for the patient as an opportunity to strengthen their relationship and show gratitude in return for assistance provided to them by the patient in the past. However, to some significant others' dismay, some siblings were disinterested in the patient's progress and in providing support along the treatment journey.

> *I think that our relationship got stronger as we're keeping in much more regular contact, particularly by phone … it has a positive effect!* [S004-2]

> *She was there for us when we were children as our mother died young … doing our laundry and assisting with homework. Hence it's now my turn to help her… I love her as if she was my mother.* [S005-2]

> *Being the only female sibling amongst 5 male siblings, I must take care of my unmarried brother. I phoned them all to inform them about our brother's diagnosis to be prepared in case of need of further support. Do you believe that none of our siblings except one brother and a sister-in-law helped him during this period?! The others didn't even bother to phone. When we mention our brothers, I notice that he gets emotional with watery eyes. He would like to be supported by them too.* [S001-2]

The role of significant others

At the early stage of treatment, most patients continued to live independently. Thus initially, most significant others perceived their duties to consist mainly of tasks such as running errands, accompanying patients to hospital appointments, providing transport and preparing fresh meals in accordance to healthcare professionals' advice. However most significant others were uncertain about how their role would change in the future as they were unable to predict how the treatment and illness would affect the patient and themselves.

> *As this is still the first cycle of treatment, I don't feel prepared for what to expect; until now she's doing everything independently.* [S006-1]

Though the significant others' provision of care to the patient was sporadic at initiation of treatment, the need for their support became more demanding as treatment progressed. Each treatment cycle brought additional challenges not only to the patient but also to the significant other especially due to worsening adverse effects. The role of the patients' support network evolved to include seeking information and managing adverse effects by asking for medical assistance or administering supportive medicines.

> *I had to perform the chores that were previously being done by the patient such as shopping, household chores. As a significant other you need to notice her limitations and these tasks should be taken over by another person or persons assisting the patient. In this case it was only me.* [S003-2]

By accompanying patients during consultation visits throughout the treatment journey, some significant others felt the need to act as the patient's advocate. As the significant others knew the patient very well, they could ask questions to fill in gaps in patients' understanding and ask for clarifications. A significant other described that a patient's companion to hospital should be knowledgeable on the subject, be able to ask relevant questions, make good use of the limited time available to meet with the healthcare professional and have good memory to remember all the information being provided. This highlighted the importance of having significant others accompanying the patient to hospital visits.

> *I was always with her when she had the information explained to her, but I forgot all the details provided soon after. Though I understood everything at that time, it's difficult for me to remember everything and I get really anxious. So, I encouraged my wife to be accompanied by my*

> *sister, if not all three are allowed into the doctor's office. In contrast to me, my sister is knowledgeable as she's interested in these things and knows what questions to ask.* [S009-1]

Experienced significant others who were either cancer survivors themselves or cared for other patients with cancer in the past felt more adequate to provide support to the patient.

> *I have already been through this illness so I know what it means* [to be a patient] *… I shall be helping her as best I can … I know the fear as I have experienced this. I'm not saying my siblings don't care for her but I can empathise with what is she going through ... I help her whenever I can* [S011-1]

The majority of the significant others described how they gained experience whilst caring for the patient throughout the treatment journey. A few significant others claimed that they learnt what to expect and how to deal with situations by observing other patients in the ward whilst visiting the patient.

> *I accompanied her in every circumstance, in every meeting and enquired when I felt I needed to. I was inquisitive but I'm satisfied with the outcome.* [S003-2]

Though all significant others maintained their commitment over time, most significant others felt out of their depth to take care of the patient, particularly with personal tasks. As from the beginning of treatment, they recognised their helplessness in assisting patients in the management of specific adverse effects such as vomiting and dizziness. In view of the patient's vulnerable state and being under specialist care, others remarked that they were cautious to make any recommendations to treat the patient's mild symptoms.

> *Till a few days ago, I used to be his carer but now I'm afraid … I used to tell him take this or that and you'll feel better … now I even refuse to advise regarding application of a cream … What I know is that if he has fever, I have to take him to A&E. However, I don't know whether this applies if he has a mild cold. Is he allowed to apply nasal spray? How many times does he have to feel sick for me to take him to hospital? I don't know* [S016-1]

Some were surprised at their own skill to '*somehow*' [S005-2] cope. It was their unpreparedness for the caregiving task that made their situation difficult. In fact, some significant others often felt ignored by the healthcare system to be active participants in the patient's care throughout the treatment journey.

> *In our case we always coped somehow. Although he's weak, he is not laid back … We coped until now, but I don't know what is going to happen next* [S010-2]

> *The healthcare system should not forget the carer … it was difficult to meet her healthcare team during the ward rounds to discuss these issues. When I was lucky to meet them, they were evidently in a hurry.* [S011-2]

Their supportive role throughout the treatment ensured that patients could focus entirely on the illness and treatment. Some significant others even offered emotional support and a sense of security as they felt able to encourage the patients to overcome their obstacles. A few significant others claimed that fulfilling their role was more challenging when the patient was not living in the same household. This is because the significant others would not be able to constantly monitor the patient's wellbeing and relied solely on patient's requests. Communication was identified as an essential factor for an effective support network. In fact, some significant others mentioned how the use of digital technology played a major role in the provision of support including the use of phone calls and posts on social media.

> *Supporting my wife* [patient] *all along the journey, I tried to understand what she was experiencing … I tried to find solutions for her to mitigate the effects of treatment … I encouraged her to speak about her emotions when she seemed to be feeling badly.* [S003-2]

> *She still lives on her own. Though I offered to stay at home with her to help her, she refused. She insisted that if she needs help, she'll let me know.* [S005-2]

> *When our children phoned her [the patient], she was over the moon. The use of technology makes the difference and helps in maintaining communication.* [S012-2]

Some significant others felt that their support throughout the treatment journey was essential for patients to cope and maintain an independent lifestyle.

> *To be honest, I think that if it wasn't for me supporting her throughout her treatment, she would not have been able to cope due to tingling effects in her fingers.* [S012-2]

As anticipated by the significant others at initiation of treatment, the tasks previously performed by the patients had to be taken over by them as the treatment progressed. This allowed patients to rest and regain their physical strength.

> *I would like to reverse back because before he used to run errands for me such as doing the shopping. But during the treatment I had to do the shopping myself. He comes along with me but stays outside.* [S001-2]

5.3.2.5.2. Sub-theme: Self-regulation as a coping strategy

Adoption of cognitive re-appraisal

Upon realising the diagnosis, changes in the patients' behaviour made the significant others doubt the patients' ability to cope with the situation. The significant others described how patients frequently employed denial as a psychological defence mechanism. This was evident from the way in which patients repeated the same question about the diagnosis and their avoidance to discuss their illness and treatment outside of the hospital.

> *He's asking me repeatedly to explain the diagnosis and treatment involved; this could be a strategy to accept or deny the situation. Through hearing repetition of diagnosis, this will sink in leading to acceptance of the situation*. [S010-1]

> *We never talk about cancer and his treatment outside of here* [the hospital]. *As soon as I start the conversation, he seems to be annoyed so I stop talking about it. When we come to hospital, I just mention something, and that's fine. But once at home he does not tolerate any mention of it* [the cancer]. [S001-1]

Some significant others recognised the efforts of patients to keep strong not worry their families and those around them, keeping in mind the pressure put on all. Most patients were noted to live day by day and maintain a positive outlook in an effort to limit the patients' concerns. The patients' determination and their fighting spirit was noted by significant others to be crucial to enable them to settle into their new routine and not let the adverse effects take control of their own lives.

> *Though he* [the patient] *had a lot of fear, he didn't cry … he knew about my recent health problems and didn't want to see me worrying.* [S001-1]

> *She still does most of the chores herself as she insists on carrying out the things herself despite being tired.* [S004-2]

Adoption of a healthy lifestyle

According to significant others, the diagnosis of cancer and the potential for adverse effects made the patients reorganise their priorities. Though all significant others were willing to assist their patients, some still expected the patients to play their part by doing their best and demonstrating an effort to cope with the situation. All of this depended on the patients' ability to accept the diagnosis and move forward.

> *Her* [the patient's] *inner strength is needed to withstand the side effects, though we'll help her as needed … she needs to be tenacious to make that extra effort to move forward and combat life.* [S013-1]

Coping strategies were employed by patients as from the start. Health was noted by some significant others to become a priority even for the young patients who previously took this for granted. The significant others commented on the patients' efforts to follow a healthy lifestyle by stopping smoking or performing physical activity.

> *Our life has slightly changed now but we have to prioritise other things. Though we were chasing our dreams to get a better job, better money to be able to buy things and then when we thought that we can rest and start thinking about having a family … all this came about. Hopefully he regains his health, and we are able to go back to our normal life and routine.* [S007-1]

> *It seems to be the opposite as he now intends to increase his physical activity.* [S002-1]

Some significant others emphasised the importance of boosting the patient's physical strength by resorting to herbal medicines including the use of vitamins and cannabidiol oil. Further coping strategies were practised by most significant others to deal with adverse effects, such as adherence to strict hygiene protocols, using gloves when needed to prevent peripheral neuropathy and repeating numbers in reverse to maintain good memory.

> *As soon as we were informed of the diagnosis, I immediately went to the pain clinic and discussed the diagnosis with the healthcare professionals there. We got CBD oil … we'll do everything that is necessary … I also bought vitamin pills for him … Vitamin C and ginger.* [S016-1]

> *Immediately upon arriving home after visiting my mother in hospital, I wash myself and change my clothes … as I might be carrying microbes on me.* [S010-2]

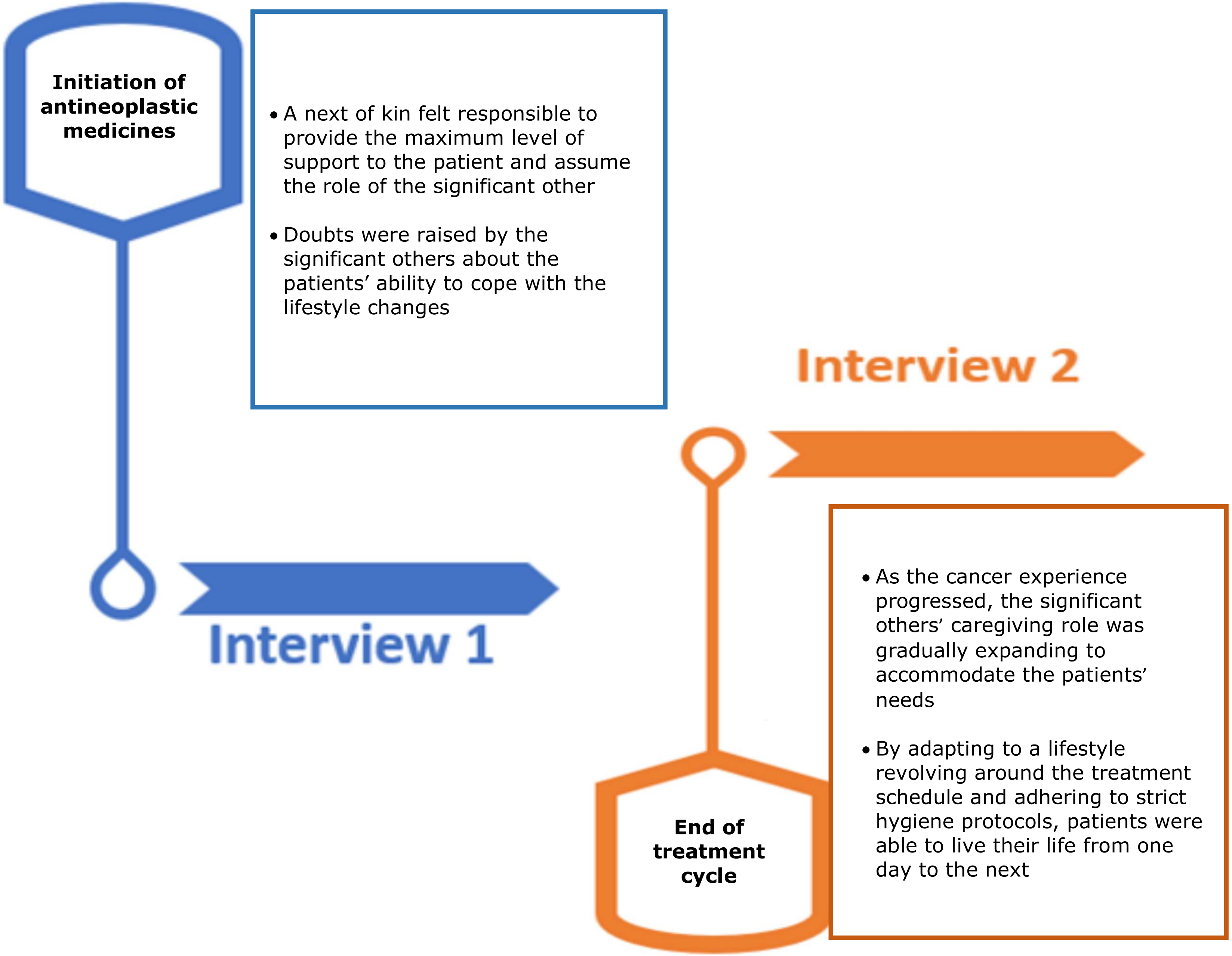
> *I advised her to say the numbers in reverse when she's alone – 1234 then 4321 … to keep herself alert and aid her memory.* [S011-2]

As the treatment progressed, both patients and significant others were trying to adapt to changes in their lives, mainly revolving around each treatment cycle. This became their new routine, hoping that the patient's last treatment cycle would bring about the return to their pre-diagnosis routine.

> *I'm worried nonetheless … but I'm trying to be proactive, to prepare myself psychologically for what we're expecting as side effects … in the meantime I'm offering the necessary care and support to the patient … I'm already proactively taking over particular roles and responsibilities in the family management; roles that were previously assumed solely by my wife.* [S003-1]

> *Her wishes are to return to her previous routine, where she does all the chores herself, though she has some limitations and side effects from chemo. But we'll see as we go through it step by step*. [S008-2]

Figure 5.5 highlights the longitudinal presentation of key points of Theme 5.



- A next of kin felt responsible to provide the maximum level of support to the patient and assume the role of the significant other
- Doubts were raised by the significant others about the patients' ability to cope with the lifestyle changes

- As the cancer experience progressed, the significant others' caregiving role was gradually expanding to accommodate the patients' needs
- By adapting to a lifestyle revolving around the treatment schedule and adhering to strict hygiene protocols, patients were able to live their life from one day to the next

Figure 5.5: The longitudinal presentation of key points identified in the theme Personal support structure

5.4. Discussion

5.4.1. Summary of key findings

Several key findings were identified from the semi-structured interviews with significant others in relation to the knowledge and beliefs, medicine-taking practice and burden of patients receiving antineoplastic medicines. Some significant others acknowledged cancer as a common illness and perceived it as life-threatening. Despite this, the oncologist's recommendation of treatment with antineoplastic medicines instilled both patients and significant others with hope and it was considered the means to achieve cure. As treatment progressed, significant others became less optimistic in achieving cure as compared to patients. Though significant others constantly reminded patients that each individual may react differently to antineoplastic medicines, patients were still influenced by past experiences of cancer of family members and cancer survivors. As treatment progressed, the media was noted to dishearten patients instead of contributing to an improvement to their knowledge.

Significant others remarked that patients immediately consented to the treatment recommended by oncologists, without asking any further questions. At completion of treatment, most significant others criticised this passive role adopted by patients in accepting treatment with antineoplastic medicines and expressed the need for patients to be involved in a shared decision-making with the oncologists. Patients' commitment to treatment was sustained throughout the treatment journey with efforts made by patients to adhere to the treatment schedule. Patients were noted by significant others to be overall satisfied with the cancer services given throughout the treatment journey. Recommendations for improvement concerned mainly the development of cancer care services in the community setting.

Significant others remarked that patients frequently experienced fatigue and peripheral neuropathy, with increasing intensity along the treatment journey. This affected patients in performing activities of daily living. According to significant others, patients experienced shock and intense emotions particularly prior to being administered their first treatment cycle. Although patients were noted by significant others to be calm along the treatment journey, fear and irritability increased towards the end of the trajectory. As treatment progressed, the social and financial impacts on patients were greater than expected. Significant others noted that as from initiation of treatment patients resorted to faith in God, with religion and spirituality increasing its importance in the patients' life.

The fact of the diagnosis of cancer and the initiation of treatment were considered by the significant others as confidential information belonging to the patient, with significant others respecting the patient's decision not to share this information. Being a significant other was described as an implied natural obligation to provide support for their loved ones. As treatment progressed, the significant others' caregiving role gradually expanded to accommodate the patients' expanding needs. Despite most significant others' initial doubts, almost all patients were able to cope with the changes in their lifestyle and maintain an independent lifestyle throughout the treatment journey.

5.4.2. Interpretation of findings

Given the crucial role played by the significant others in patients' care throughout the treatment journey with antineoplastic medicines, it was imperative for the research student to explore the patients' beliefs, practice and burden from the perspective of significant others. Whilst most existing studies focused on the significant others' challenges and needs in caring for patients with cancer (Soothill et al. 2001, Kim and Given 2008, Sercekus et al. 2014, Sklenarova et al. 2015), there were only a few studies that captured the significant others' perceptions about the patients' experiences (Comaru and Monteiro 2008, Barni et al. 2016, Norton et al. 2019) and none of these focused on colorectal cancer.

Linnarsson and his team defined the term significant others as "all persons close and significant to the patient, regardless of biological or legal relationship" (Linnarsson, Rubini and Perseius 2010 p.3102). Throughout this research, the term 'significant others' was predominantly used for two main reasons. Firstly, the individuals nominated in this study had a specific role in the relationship with the patient prior to becoming caregivers and therefore their initial role was considered as the most significant. Secondly, at initiation of treatment patients were highly independent without recognising the degree of assistance they might eventually require along the treatment journey. In the literature, there are various terms used interchangeably that refer to significant others, namely carers, caregivers, family or next of kin (Romito et al 2013). As a result, the interpretation of the findings of this study was made in the light of the available literature that encompasses these various terms.

Similar to other studies involving caregivers of patients with cancer (Stenberg, Ruland and Miaskowski 2009, Li, Mak and Loke 2013), the significant others identified by patients in this study were most commonly blood relatives, mainly spouses (n=6, 38%), living in the same household with the patients. In circumstances of limited availability of support, such as the patient who had disagreements with family members, the patient identified the nurse navigator as her significant other, even though the nurse was not blood related. This highlights the need for patient support as from initiation of treatment.

It is interesting to note, that although patients were free in their choice of a significant other, most patients (n=12) identified a female individual as their significant other. In fact, around 66% (n=66 million) of cancer caregivers in Europe are females between 45 and 75 years old (Europe Cancer Patient Coalition and Eurocarers 2018). Therefore the traditional expectation that females are considered as 'kin-keepers and care providers' (Moen, Robison and Dempster-McClain 1995, p. 259) also presents locally. This may be due to familial experiences, traditional gender norms and societal expectations that females are emotionally and physically dedicated to care for others (Ochoa, Buchanan Lunsford and Smith 2020, Ketcher et al. 2020). Interestingly, several studies showed that female caregivers typically experience higher level of psychological distress compared to their male counterparts (Dumont et al. 2006, Li, Mak and Loke 2013, Morgan et al. 2016, Swinkels et al. 2019).

The findings generated in relation to the **first objective** of the research, showed that significant others acknowledged cancer as a common life-threatening illness. Some patients were noted to be afraid of seeking medical assistance even when experiencing symptoms suggestive of cancer. Despite the advances in technology that enabled improved sharing of information, significant others and patients had poor knowledge about treatment of colorectal cancer, fuelling misconceptions about treatment intent. The multinational study PACE (Patient Access to Cancer Care Excellence) Cancer Perception Index captured the perceptions of cancer and its management amongst patients, caregivers and the public in six countries, namely Germany, France, Italy, United Kingdom, Japan and United States (Ramers-Verhoeven, Geipel and Howie 2013). It showed that almost half of the public (48%, n=1444) did not agree with the statement that 'regardless of treatment, a cancer diagnosis will ultimately result in death'. Also, most caregivers (63%, n=421) and patients (78%, n=517) acknowledged and were satisfied with the progress made in the past 20 years with regards treatment against cancer. A recent cross-sectional questionnaire-based study in India demonstrated that 71% (n=105) and 76% (n=113) of caregivers believed that cancer can be cured and that patients with cancer can lead a normal life after treatment respectively (Nidhi and Basavareddy 2020). These findings are congruent with the findings of our study where significant others perceived treatment with antineoplastic medicines to result in cure. Our study showed that the perception of significant others towards the use of antineoplastic medicines differed along the treatment journey; with less optimism in achievement of cure as treatment progressed.

The findings in relation to the **second research objective** showed that the significant others observed limited patient involvement in the decision-making process about their treatment. Patients were noted by significant others to immediately consent to the recommended treatment proposed by the oncologist without answering any questions or hesitation. At completion of treatment, the significant others yearned for increased shared responsibility between the patient and their oncologist to decide collaboratively what is best for the patient, taking into consideration all the available options together with patient's concerns and preferences.

In contrast to the high level of adoption of shared decision-making in Western countries and its consideration as a gold standard during recent decades (Malhotra et al. 2020), the findings of this study highlighted the lack of adoption of this concept in local practice. This is indicative that a change in the current practice of decision-making about treatment is needed and calls for increased patient involvement. Major barriers for joint decision-making included the lack of explicit disclosure of prognosis by oncologists, unless they are directly questioned by patients; consideration of a single treatment option, without informing the patient about possible treatment alternatives and lack of assessment of the patient's understanding about the illness and its treatment. A similar experience was revealed in a survey carried out in Finland amongst 168 relatives of patients receiving treatment for cancer in 2001, whereby it was noted that there was little encouragement for patients to be actively involved in decisions concerning their care (Eriksson 2001). In contrast, the oncologist's behaviour with regards decision-making was described differently by the significant other of a non-Maltese patient, with the description fitting a more patient-centred approach. In this case, the patient was offered a choice of treatment and was allowed a few days to reflect about the treatment options before deciding. This could possibly indicate a cultural bias. The systematic review by Hubbard, Kidd and Donaghy (2008) showed that patients' preferences to be involved in decisions about treatment may vary based on the stage of the illness, with most patients preferring a collaborative approach and a significant minority preferring a passive one. By incorporating patients' preferences for decision-making about treatment, the healthcare system would be more sensitive to the needs and expectations of each patient (Hubbard, Kidd and Donaghy 2008). Also, patients themselves could benefit from better satisfaction with treatment, a greater sense of personal control and improved trust in their healthcare professionals (Butow et al. 2007, Stacey, Samant and Bennett 2008, Kane et al. 2014).

The significant others participating in this study remarked that they themselves were also not being involved in the decision-making. While they would have preferred to be involved, they agreed to support the patient in whatever decision was taken about treatment. The findings of our study contrasted with those of Jones et al. (2013), who described that patients with cancer were rarely alone in the decision-making process and expected to discuss their preference with persons who support their decision such as caregivers. These authors concluded that even though patients ultimately agreed with the recommended treatment option of the oncologist, patients felt involved in the decision-making process by being at least provided with treatment options (Jones et al. 2013).

The significant others seemed to have an important role in the provision of support for the management of adverse effects when the patient is at home in between treatment cycles. Although patients were receiving parenteral antineoplastic medicines at a specialised oncology centre, this study highlighted that the significant others took over the caring role whilst patients were recovering from treatment at home. The significant others expressed concern regarding their lack of knowledge and of structures to support them in this role. This was also highlighted in other studies involving pain management in cancer patients (Chi and Demiris 2017, Meeker, Finnell and Othman 2011). Supportive medicines mainly anti-diarrhoeal treatments, anti-emetics and laxatives were prescribed on an 'as required' basis and were not routinely administered. Assessment of symptoms and decisions on when to administer treatment or when to go to hospital needed to be taken by the significant others. A study by Van Ryn et al. (2011) who looked at caregivers of newly diagnosed colorectal and lung cancer patients in America highlighted that a system for routine provision of education and knowledge to caregivers did not exist, raising concerns about patients' safety and the burden on significant others. Buhr, Kuchibhatla and Clipp (2006) argued that when such tasks of symptom management were performed ineffectively, this resulted in negative outcomes to both patients (by leading to a poor quality of life) and their caregivers (with a sense of guilt and disappointment). The significant others participating in our study reported that as a result of their inexperience and uncertainty, when the patient experienced problems, they either took the patient to the hospital emergency department or phoned the nurse navigator. The latter option was generally the preferred alternative, because in spite of being told that they would get priority care, the experience of cancer patients at the hospital emergency department was very negative. In fact this was the main complaint of patients and their significant others about cancer care services. These findings further emphasise the need of support services and interventions to offer consistent effective support to significant others. Berry, Dalwadi and Jacobsen (2017) proposed a cohesive program of caregiver support focusing on assessment of the caregivers' needs together with education and training in basic medical support. This was considered to enable the caregivers to form part of the healthcare team and to proactively assist them in their duties. As highlighted in our study the patients' needs and symptoms vary over time along the treatment journey, therefore this calls for regular assessment and a more personalised approach to assist patients with cancer and their carers depending on their needs and circumstances. Hollander, Liu and Chappell (2009) reported that supporting family caregivers in Canada has become a national public health priority given their essential role in the healthcare system.

With regards the **last objective** of the research, significant others described how treatment with antineoplastic medicines resulted in considerable physical, psychological, social and financial strain on patients and their families. Patients had to adapt to the challenges faced during the treatment journey, with the support received from their significant others.

Fan, Filipczak and Chow (2007) reported that a patient with advanced cancer may experience up to 13 concurrent symptoms. Due to the increased intensity of these burdensome symptoms along the treatment journey, patients' well-being is adversely impacted. Fatigue and peripheral neuropathy were identified by significant others as the two most reported physical effects. As reported in other studies (Fan, Filipczak and Chow 2007, Beijers et al. 2015, Aapro et al. 2017, Eyl et al. 2020), the effects of fatigue and peripheral neuropathy may warrant dose reduction of treatment and therefore potentially compromise the treatment outcome. In view of its complex aetiology, healthcare professionals should educate patients and their significant others on the potential adverse effects and self-management strategies. using pharmacological or nonpharmacological interventions.

In addition to providing physical support, significant others were frequently burdened with the provision of emotional support to the patient, especially when the latter experienced distressing symptoms and adverse effects.

Significant others reported that patients went through an initial disbelief, but subsequently there was an improvement in the patients' psychological wellbeing. The patients' initial emotional turmoil changed to acceptance of the illness and expectant treatment outcome. This is consistent with the findings of the systematic review by Watts et al. (2014) whereby patients with prostate cancer were noted to suffer from anxiety which was highest pre-treatment (27%) and reduced during treatment (15%) and post-treatment (18%). Thus attention to the patients' mental health and well-being should start from the time of diagnosis. Significant others attempted to provide patients with emotional support by instilling them with hope and motivation together with support to manage anxiety. Studies show that managing patients' negative emotions is the most challenging task of caregiving (Wang et al. 2018, Niedzwiedz et al. 2019). Alongside the treatment for their physical health, referral for personalised psychological support services is warranted. The extension of these services to significant others would be of additional benefit for the patient and the significant other and would also reduce the burden on the healthcare system.

The stigma related to cancer diagnosis, the adoption of cautionary infection control measures due to the use of antineoplastic medicines and the presence of stoma in some patients were identified by the significant others as the main threats to the social well-being of patients. Similar to the findings of our study, Van Roij et al. (2019) showed that patients with advanced cancer and their caregivers experienced substantial social consequences, even though they strived to continue living their life in the same way as they did prior the diagnosis. In our study it was noted that during treatment the patients' main social encounters were the friendships which they built with other patients at the hospital ward. Van Roij et al. (2019) considered that the time which the patients spent in hospital appointments reduced the time that patients had for social engagement. Whilst Knapp, Marziliano and Moyer (2014) claimed that cancer-related stigma has become more subtle compared to the past, our study showed that in Malta the stigma related to cancer is still high. In fact, significant others highlighted that patients were reluctant to share the information about the diagnosis of cancer with their relatives and friends, particularly at initiation of treatment. It is recommended that the effect of social stigmatisation in relation to patient quality of life and treatment outcomes in cancer patients is prioritised for future research. This may warrant the need to introduce psychosocial interventions to improve the patients' wellbeing and assist significant others to deal with the stigma and social isolation. It may also require more education of the public.

While initially most significant others did not anticipate any financial impact from the treatment, healthcare-related costs were reported to be dynamic across the longitudinal continuum of the patient care. Patients experienced different degrees of direct and indirect costs due to cancer and its treatment. The significant others of young working-age patients reported higher financial burden than those of the older patients due to reduced income. This was comparable to the study by Yabroff et al. (2016) that included 1200 adult cancer survivors who reported that financial hardship, such as loans, debt and inability to pay for care was more common among cancer survivors younger than 65 years of age when compared to older age group (28.4% versus 13.8%) (Yabroff et al. 2016). As younger patients may have less savings, fewer assets and increased financial responsibilities such as caring for young children, this makes them ill-equipped to incur out-of-pocket expenses for treatment (Bradley 2019). In our study, financial burden was mainly due to purchasing of supportive medicines and the 'need' to visit the oncologist privately. This was confirmed by recent statistics demonstrating that Malta ranks amongst the highest in terms of out-of-pocket expenses for treatment in comparison to other European countries (OECD/European Observatory on Health Systems and Policies 2021). Significant others were concerned about the financial hardship that the patients may end up facing in the future.

Significant others remarked that the experience of cancer and its treatment made patients resort to their faith in God to obtain a sense of control over their feelings of helplessness. This was noted to further sustain the patients' hope for cure. In line with the recommendations of Swihart, Yarrarapu and Martin (2022), healthcare professionals should be knowledgeable about the patients' religious and spiritual beliefs and subsequently try to understand how these are linked to the patients' health to recognise the potential impact on patient care and achieve better healthcare delivery.

Nowadays, there is an increasing demand for the healthcare system to integrate patients in planning and management of their treatment, thereby taking on a professional role (Menichetti et al. 2016). As shown in this study, the significant others have more than a simple caring role in the patients' treatment journey. This study calls for more active involvement of patients and their significant others by healthcare professionals in cancer care.

5.4.3. Strengths and limitations

The main strength of Phase III of this research is that, to our knowledge, this is the first longitudinal study to collate the perspective of the significant others about the patients' experience with antineoplastic medicines for colorectal cancer. Phase III of the research was conducted in parallel to Phase II where the patients' lived experience with antineoplastic medicines was explored from the patients' perspective.

A satisfactory retention rate of significant others (n=11/16; 69%) was maintained for this Phase; with reasons for discontinuation discussed above. Two semi-structured interviews with the significant others (at initiation of patient's treatment and at completion of treatment) were adequate to capture the changes in beliefs, medicine-taking practice and burden along the patient's treatment trajectory. The use of one-to-one interviews provided the opportunity for significant others to speak openly and discuss personal confidential issues such as the challenges related to their caregiving role. Rigorousness in collection and presentation of the findings was ensured by carrying two independent analyses of data from the interviews and by holding frequent discussions within the research team.

There are some limitations to the findings of the study that must be taken in consideration. In view that the data was generated at the single national oncology centre in Malta with a tax-funded healthcare system, the findings may lack transferability to countries with a different model of health system. As recruitment of significant others for Phase III was based on patients' nominations by snowball sampling, this led to recruitment of a heterogenous sample of significant others with different relationships with the patient. The nomination of the nurse navigator as a significant other of one of the patients led to bias due to personal knowledge and direct role in the field. As the study contained a strong representation of females (n=13), this may possibly introduce a gender bias to the findings, an aspect that warrants further research. The degree and type of support provided to patients by different types of significant others (spouses, other family members, healthcare professional) may differ and this could possibly be a reason for not achieving data saturation on completion of 16 interviews with significant others.

Since two interviews were carried out with an interval of 24 weeks, this may have resulted in recall bias. Another possible limitation is that audio recording of the interviews may have hindered the openness of the significant others. Although translations of quotations from Maltese to English were checked for authenticity by a second researcher fluent in both languages, some profound meaning or metaphorical phrases may have been lost. To ensure that this did not affect the study findings, data was analysed in the original language of the transcript.

5.5. Conclusion

The patients’ lived experience with antineoplastic medicines from the perspective of significant others offered an additional valuable insight in understanding the changing needs of patients along the treatment journey. Significant others stressed the need to improve their own and the patients’ knowledge by taking the initiative to search for further information or ask questions on patients’ behalf. The establishment of the patient-significant other relationship as from initiation of treatment was recognised by patients as the essence of their support to be able to cope with the burden of illness and treatment. Significant others got progressively engaged in the patients’ cancer care to meet the growing demands of the patients’ needs, with little recognition from the healthcare system. This calls for the need of the healthcare system to foster and support the active inclusion of the significant others as this will directly and indirectly affect patients’ care.

Chapter 6

Discussion

6. Introduction to the chapter

This final chapter provides a summary of the research findings in relation to the overall aim. The contribution of these findings to the body of knowledge are highlighted, with emphasis of the key aspects of PLEM, as described by patients and significant others. Differences and similarities between the patients’ and the significant others’ perspectives with regards to the treatment journey are outlined. Further comparisons of the study findings are made with published original studies. This chapter then discusses the methodological strengths and limitations. Clinical implications are explored and suggestions for future studies are described.

6.1. Research aim and key findings

The overall aim of this doctoral research was to explore longitudinally the patients’ lived experiences with antineoplastic medicines for management of colorectal cancer during the treatment journey and beyond. The specific objectives of this research were to:

- Explore the patients’ beliefs and knowledge of antineoplastic medicines
- Explore the patient’s medicine taking practice of antineoplastic medicines
- Explore the burden experienced by patients during treatment with antineoplastic medicines
- Compare and contrast the perspectives of patients and significant others on the beliefs, practice and burden of antineoplastic medicines.

In order to be able to answer these objectives, the research was conducted in three phases. These were:

Phase I: Systematic review
Phase II: Longitudinal qualitative study involving patients
Phase III: Longitudinal qualitative study involving significant others

6.1.1. Phase I: Systematic Review

Despite the overwhelming amount of studies published on cancer and its treatment, no published systematic reviews were identified which focused specifically on patients experience with antineoplastic medicines. The aim of the systematic review was to critically appraise, synthesise and present the available evidence on patients' lived experiences with antineoplastic medicines prescribed for the management of malignant solid tumours. This systematic review identified ten studies, mainly from European countries, that focused on the holistic aspect of medicine-related belief, medicine-taking practice and medicine-related burden of antineoplastic medicines. The studies had a generally high methodological quality, with mostly following a qualitative methodology.

The key findings from this systematic review were the lack of a standard definition of PLEM and longitudinal qualitative studies exploring the beliefs, medicines taking practice and burden of antineoplastic medicines. The review recognised that patients had already pre-conceived notions and expectations about their treatment prior to its initiation. Though it provided grounds for hope of disease-free future, there was an element of fear that the burden would be worse than the illness itself. Misconceptions were particularly related to efficacy of treatment, with patients believing that oral antineoplastic medicines are indicated for less aggressive cancer types. The included studies showed that patients were highly adherent to antineoplastic medicines even though their use had profound effect on the patients' lives. Information about treatment was mainly provided to patients at initiation of treatment when patients were naïve to treatment. Despite being provided with information, patients were unable to assess the severity of adverse effects experienced with the antineoplastic medicines. This placed patients in a dilemma when to report these adverse effects.

An adapted model for the patients' lived experience with antineoplastic medicines was developed following the systematic review (Figure 3.2). A detailed interpretation of findings of this systematic review was discussed in Chapter 3.

6.1.1.1. Update of the systematic review

Since the finalisation of this systematic review in 2016, three additional studies were identified to meet the inclusion criteria with the key findings of these studies described below.

The qualitative study of Yagasaki, Komatsu and Takahashi (2015) aimed to explore the experiences of 14 Japanese patients with gastric cancer receiving oral antineoplastic medicines using Strauss and Corbin’s grounded theory approach. The study identified the patients’ inner conflict as a core category with five related categories (Rational belief, Emotional resistance, Subjective view: perceived adherence, Behaviour: partial non-adherence and Recognition of one’s role in medication therapy). Patients with cancer experienced an inner conflict between their own rational belief that antineoplastic medicines have the potential to prolong their survival and their emotional resistance casting uncertainty about efficacy of these medicines and concern over its adverse effects. Therefore, their occasional non-adherent behaviour to antineoplastic medicines was the result of outbalancing their emotional resistance with their rational belief. Also, the study revealed that patients experienced contradictions between their subjective view (perceived adherence) and their behaviour (partial non-adherence). Whilst patients acknowledged the importance of taking antineoplastic medicines and perceived themselves as adherent to treatment, they claimed to intentionally skip their medicines due to change in routine or having a special occasion (intentional non-adherence) or forgetting to take the medicine (unintentional non-adherence). When the patient actually took the medicine, there was a reduced gap between the patient’s emotional resistance and rational belief. Therefore, healthcare professionals should not solely consider non-adherence to antineoplastic medicines as irrational behaviour, but it is imperative for them to understand the patient’s compelling reasons leading to this non-adherent behaviour and provide tailored interventions accordingly.

Talens et al. (2021) explored the patients’ experience with oral antineoplastic medicines and identified barriers and facilitators related to illness and treatment. The patients’ responses were then compared with healthcare professionals’ perspectives (medical, nursing, pharmacy). This exploratory qualitative study, which took place in a Spanish hospital involved three focus groups with 23 onco-haematological patients taking oral antineoplastic medicines for a median time of 8.5 months and two nominal group discussions with 18 practising healthcare professionals with at least 5 year experience in oncology or haematology. The findings were grouped in eight categories, namely (1) beliefs about the medicine, (2) need and expectations of treatment, (3) information about treatment, (4) adverse effects from treatment, (5) social, family and professional support, (6) experience with treatment, (7) polymedication, (8) medicine errors and forgetting to take medicines. The first 5 categories were recognised by patients and healthcare professionals to have the greatest impact in patients' medicine experience. Both patients and healthcare professionals agreed that the adverse effects of oral antineoplastic medicines followed by forgetfulness were considered as the main barriers to adherence. Information about treatment and the availability of social, family and professional support acted as the main facilitators of adherence. The majority of patients, particularly those receiving positive results, believed that their treatment with oral antineoplastic medicines was effective in achieving cure. In contrast, some patients who were informed that their cancer remained latent with the use of antineoplastic medicines were doubtful about the effectiveness of treatment. Despite this and the associated adverse effects, these patients were not feeling regretful of taking this treatment. Besides taking their antineoplastic medicines, all patients claimed to be taking several other medicines, with the duration of treatment and number of medicines identified as barriers to adherence. Whilst acknowledging that their oral antineoplastic medicines were prioritised over any other treatments, patients admitted to forget treatment or not taking them exactly as prescribed. Various strategies were adopted by patients to prevent forgetfulness, with planning treatment around their routine/establishing a routine as being the commonest strategy. All patients claimed to experience substantial impact on their quality of life, adversely affecting both their work and leisure activities. Though various adverse effects were experienced by patients, fatigue was the commonest followed by difficulties in walking and cramps. Whilst the oncologists or haematologists were recognised as the main source of information about cancer and treatment, hospital pharmacists were subsequently referred to for further information about antineoplastic medicines or experiencing adverse effects. Despite this, patients complained of not being informed by healthcare professionals about the common adverse effects. Though patients admitted to occasionally seek online information about illness and/or treatment, they did not recommend such behaviour as they experienced more uncertainty and concern.

The qualitative study conducted by Zhou et al. (2022) in China explored patients' perspectives on the factors that influenced their adherence to oral targeted antineoplastic medicines using the Adherence Influencing Factor Framework proposed by WHO. Twenty one patients with lung cancer who had been prescribed oral targeted antineoplastic medicines for at least 14 days were interviewed. Participants were mainly males (n=17), >50 years (n=15) and not fully adherent to their antineoplastic treatment regimen (n=15). Data analysis led to identification of four themes, namely (1) patient-related, (2) medicine-related, (3) doctor/nurse-related and (4) society related factors. Due to beliefs that cancer is infectious or a cause of bad luck, patients felt socially rejected and ashamed of themselves. Consequently, this resulted in behavioural changes such as avoidance of taking cancer medicines in the presence of others and reluctance to disclose their medical history to healthcare professionals or talk to others about these medicines. Information about cancer and medicines was provided either by healthcare professionals or obtained by passive exposure to public or social media. Misleading information such as exaggerated efficacy of treatment such as herbal medicines might have led patients giving up their prescribed antineoplastic treatment to other medicines. Patients' varying threshold to adverse effects affected their adherence to medicines. Whilst some patients continued their treatment even when experiencing adverse effects, others gave up on experiencing mild effects. However, the latter often did not completely cease their treatment but either gave up selected medicines or sought alternative medicines for milder adverse effects. Potential factors that positively influenced adherence to medicines were patient's awareness of prolonged life expectancy (>6 months), caring for underage children, availability of accurate information, gaining opportunity to choose drugs regimens by participating in shared decision-making and positive patient-nurse relationship. Findings showed that adherence to antineoplastic medicines might have improved with adequate provision of medicine-related information to patients, encouragement through patients' participation in shared decision-making and strengthening the patient-doctor-nurse collaboration.

All three studies explored the use of oral antineoplastic medicines using cross-sectional qualitative methodology. None of the studies made use of the conceptual PLEM model developed by Mohammed, Moles and Chen (2016). One included study was underpinned by the Adherence Influencing Factor Framework proposed by WHO. This framework is composed of five interacting dimensions, namely healthcare team and system-related factors, social and economic factors, condition-related factors, patient-related factors and therapy-related factors. This contrasts with the PLEM conceptual model (Mohammed, Moles and Chen 2016) which revolves around the medicine and does not take in consideration the illness. These studies reiterated the findings of the systematic review that the use of antineoplastic medicines was predominant in the patient's lives. The patients' beliefs and burden experienced by patients affected their medicine-taking practice particularly when receiving oral treatment. Although these publications in general fit into the adapted PLEM model for the oncology setting, these studies add little new evidence to the studies included in the systematic review.

6.1.2. Phase II: Longitudinal qualitative study with patients

The findings of the systematic review identified a gap in the published knowledge on the beliefs, practice and burden in oncology patients' lived experience with antineoplastic medicines. To contribute to evidence in this area, a longitudinal qualitative study was conducted with 16 patients taking FOLFOX or XELOX for colorectal cancer, using in-depth interviews at four time-points during the patients' course of treatment at an interval of 12 weeks. The aim of Phase II of this research was to explore the patients' lived experiences with antineoplastic medicines for colorectal cancer longitudinally. The research objectives for this phase were mainly to:

- Explore the patients' beliefs and knowledge with antineoplastic medicines.

- Explore the patient’s medicine taking practice of antineoplastic medicines.
- Explore the burden experienced by patients with colorectal cancer during treatment with antineoplastic medicines and beyond.

The adapted PLEM model developed in Phase I (Figure 3.2) was used to inform the development of the interview guide for these patients. Key findings of the qualitative semi-structured interviews showed that at initiation of treatment patients had poor knowledge of the alarm symptoms for colorectal cancer and its multi-modal treatment strategy. Their knowledge about the illness improved along the treatment journey, as they became aware of the risk of metastases and recurrence of cancer, non-curative intent of their treatment with antineoplastic medicines and persistent bodily harm incurred through adverse effects of antineoplastic medicines. Initially patients considered the term ‘chemotherapy’ to encapsulate a single antineoplastic medicine that treats all cancer types leading to common misconceptions related to the inevitable occurrence of treatment-induced severe alopecia and debilitating fatigue. The patients’ negative perceptions about cancer and treatment were outweighed by their perceptions of the curative potential of antineoplastic medicines. Patients were strongly influenced by their acquaintances’ experiences with anticancer treatment irrespective of the cancer types. As treatment progressed patients’ attitude and knowledge were influenced by the experiences of other patients receiving the same treatment in the ward. Patients described that they developed various selfcare strategies as time progressed such as lifestyle changes, drinking lukewarm water, refraining from touching cold surfaces and using supportive medicines, to overcome medication-related burden. Patients described that with every treatment cycle they repeatedly experienced the same physical effects with greater intensity and duration. Psychological changes were evident throughout the treatment journey. Upon diagnosis and at initiation of treatment, fear, anxiety and uncertainty predominated. This progressed to hope particularly when receiving positive news but changed into irritability, mild anxiety and uncertainty at completion of treatment. Social and financial concerns were very specific to the patient’s age. Their need for support, particularly from their significant other, intensified throughout the duration of treatment.

Patients requested various healthcare services, such as psychological support services, illness-specific peer support programme and tailored individualised patient information, to address their evolving needs for the duration the treatment journey. A detailed interpretation of findings of this longitudinal qualitative research with patients was presented in Chapter 4.

6.1.3. Phase III: Longitudinal qualitative study with significant others

A longitudinal qualitative study was conducted with 16 significant others, one for each patient, using two in-depth interviews (one at the beginning of the treatment journey and another at the end of treatment journey at 24 weeks). The aim of Phase III was to explore longitudinally the patients' lived experiences with antineoplastic medicines for colorectal cancer from the perspective of the significant other. The research objectives for Phase III included to:

- Explore the perspective of significant others on the patients' knowledge and beliefs
- Explore the perspective of significant others on the patients' approach to medicine taking practice
- Explore the burden experienced by patients from the perspective of the significant other

Key findings from Phase III showed that significant others were aware of the patients' poor knowledge of colorectal cancer and treatment. This was evident throughout the treatment journey as significant others commented that most patients still expected to return to full health. Even though cancer was perceived as a life-threatening illness, the use of antineoplastic medicines was considered to achieve cure by both patients and significant others. Significant others noted that patients identified the oncologists to be the experts in the management of cancer with patients immediately consenting to treatment unreservedly. Most significant others criticised this passive role adopted by most patients. They expressed the need for patients to be involved in shared decision-making, considering the patients' concerns and preference for treatment. Notwithstanding the significant others' initial concerns about the patient's inability to tolerate treatment with antineoplastic medicines, all significant others noted that patients remained committed to the intake of treatment throughout the treatment journey. Significant others reported that efforts were made by patients throughout the six-month treatment period to adhere to the planned treatment schedule. By and large significant others thought patients to be mostly satisfied with the cancer services offered. Recommendations for improvement such as psychological services and community cancer care services were put forward by significant others. They reported the effects of social stigmatisation, leading to patients' reluctance to disclose their diagnosis to family members and friends. As the treatment progressed, significant others became aware of the increasing physical, social, financial, spiritual and religious needs of the patients. At the same time, psychological challenges were noted by significant others to become less prominent as patients gained familiarity with the treatment process and healthcare system. A detailed interpretation of findings was reported in Chapter 5.

6.2. Comparison of patients' and significant others' perspectives on patients' lived experience with antineoplastic medicines

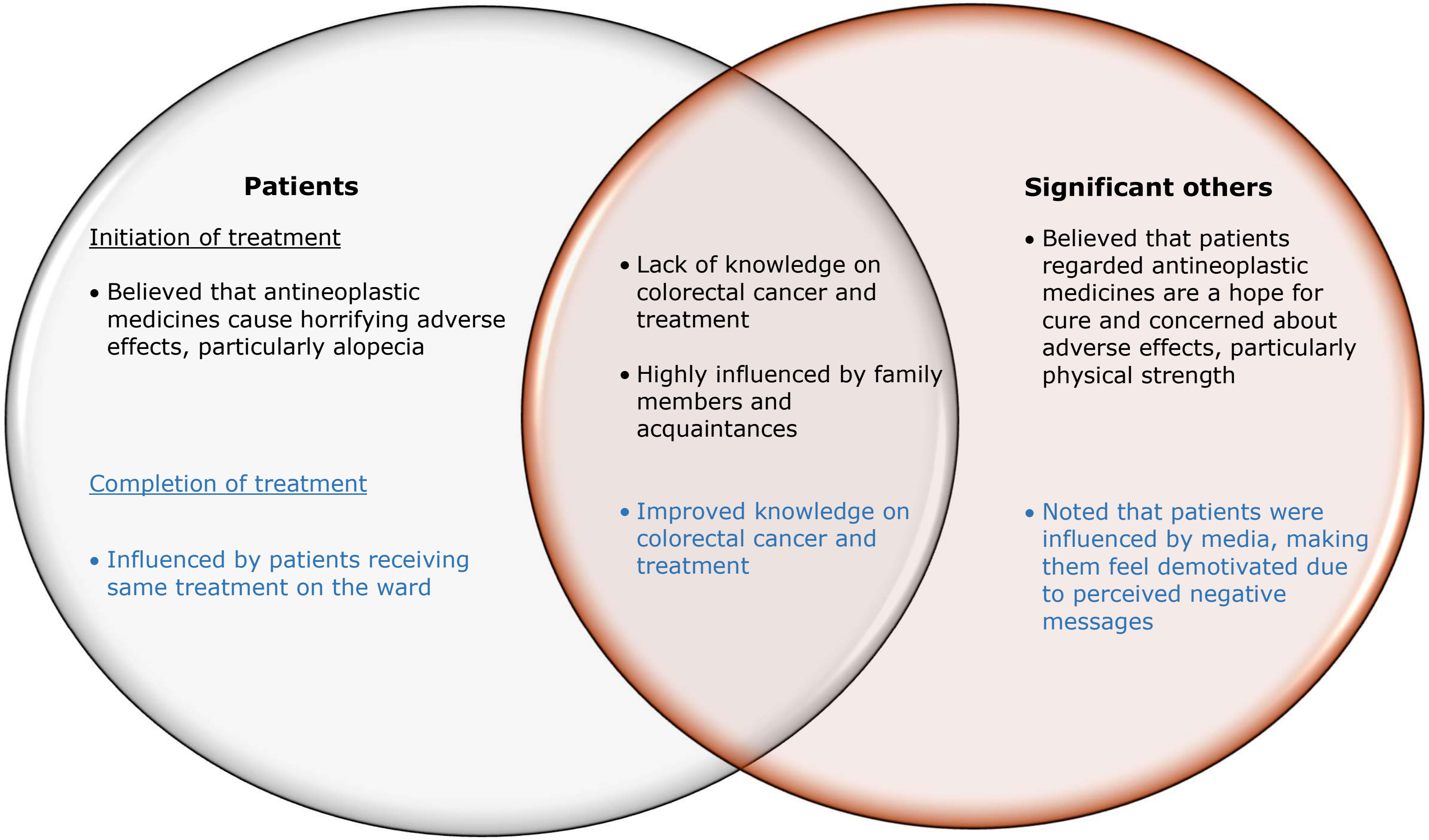
Soliciting both patients' and significant others' perspectives widens the researchers' understanding of the patients' experience with antineoplastic medicines. The longitudinal studies with patients (Phase II) and their significant others (Phase III) allowed identification of similarities and differences in their perspectives about the patients' experience with respect to beliefs, practice and burden associated with antineoplastic medicines. It is important that the significant others understand the patient's perspective to be able to empathise and provide adequate support to their patients accordingly.

6.2.1. Comparison of perspectives on beliefs and knowledge on antineoplastic medicines

At initiation of treatment, the patients' perception about antineoplastic medicines focused more on the expected adverse effects particularly those related to aesthetics. Patients were concerned about their physical appearance once experiencing hair loss and in turn making other individuals aware of their sickness. The patients' initial fear and concerns changed to relief upon realising that their antineoplastic treatment would not result in complete alopecia. Contrastingly the significant others showed greater concern about adverse effects related to the patients' physical strength, because the significant others were highly concerned about the likelihood of increasing demands on them of informal caregiving throughout the duration of the treatment. This burden would be combined to the significant others' present life challenges. The continual struggle between the desire to support the patient and the fear of the patients' loss of independence was clearly exhibited by significant others in this research. In fact, studies showed that significant others tend to experience more psychological problems, with the significant others' baseline burden and distress identified to be a risk factor for persistent distress following completion of treatment (Maguire et al. 2018, Langenberg et al. 2021). As suggested by Mosher et al. (2016) and Maguire et al. (2018), healthcare professionals should acknowledge and address the significant others' concerns as they would patients' concerns. They may be offered information and practical resources including appropriate referrals to available services.

From our study, it was evident that both patients and their significant others had a poor understanding of colorectal cancer and its management, with their main source of knowledge at initiation of treatment being the experiences of their acquaintances with cancer. This is similar to findings report in the literature (Weingart et al. 2018), where their lack of knowledge was particularly related to unique features of antineoplastic medicines such as toxicity. The patients' knowledge was noted to improve as treatment progressed because of the patients' own experience and the sharing of experiences with other patients receiving the same treatment in the ward. Therefore, the introduction of a peer-to-peer buddy scheme where a newly diagnosed patient is matched with another patient who has completed treatment for the same type of cancer was suggested. A systematic scoping review by Kowitt et al. (2019) showed that peer support is an effective strategy to increase patients' knowledge and address barriers to treatment across the cancer care continuum. Peer support may also assist patients' families to deal with their emotions particularly in palliative care (Kowitt et al. 2019).

Figure 6.1 shows similarities and differences in the perspectives of patients and significant others with regards to beliefs and knowledge on antineoplastic medicines at initiation and completion of treatment.



Patients

Initiation of treatment

- Believed that antineoplastic medicines cause horrifying adverse effects, particularly alopecia

Completion of treatment

- Influenced by patients receiving same treatment on the ward

- Lack of knowledge on colorectal cancer and treatment
- Highly influenced by family members and acquaintances

- Improved knowledge on colorectal cancer and treatment

Significant others

- Believed that patients regarded antineoplastic medicines are a hope for cure and concerned about adverse effects, particularly physical strength

- Noted that patients were influenced by media, making them feel demotivated due to perceived negative messages

Figure 6.1: Comparisons between the patients’ and significant others’ perspectives with regards to patients’ beliefs and knowledge of antineoplastic medicines at initiation and completion of treatment

6.2.2. Comparison of perspectives on the medicine-taking practice of antineoplastic medicines

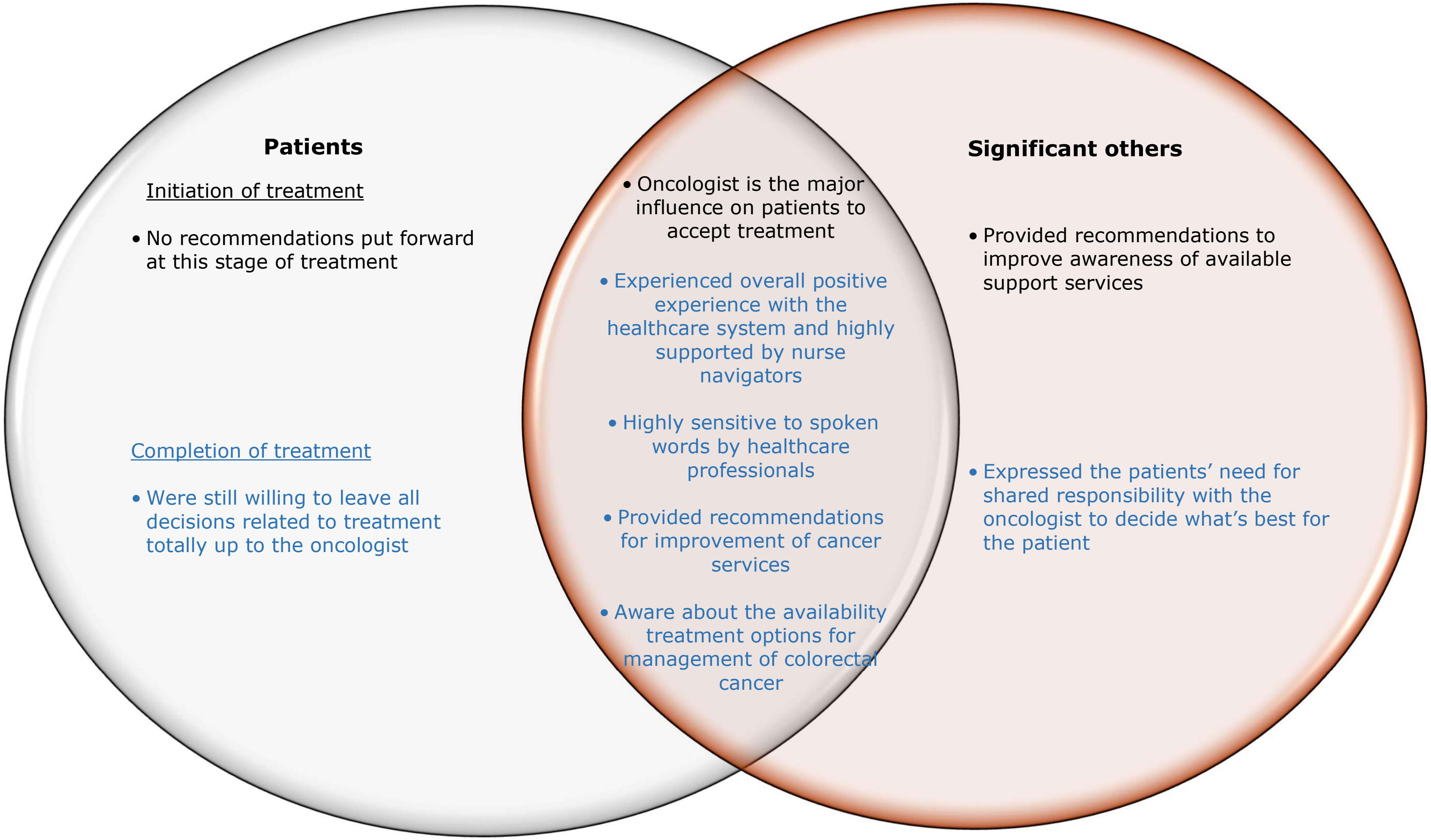
A clear difference between the patients' and significant others' perspective related to the patients' involvement in the decision-making process for treatment with antineoplastic medicines. On completion of treatment, significant others realised that there were a number of available treatment options for the management of colorectal cancer. Consequently significant others recommended the implementation of shared decision-making rather than the patient's reliance on the single option provided by the oncologist. Contrastingly patients were still willing to leave all the decisions related to treatment totally up to the oncologist. Evidence showed that patients with cancer generally preferred to be involved in decision-making process about treatment (Casarett et al. 2005, Grunfeld et al. 2006, Barry and Edgman-Levitan 2012). However, there are differing opinions as to the degree of the patients' participation in the decision-making process. For instance, previous studies amongst patients with colorectal cancer were interested to know about available treatment options but were comfortable to defer the ultimate decision to the oncologist who was the expert in the field (Beaver et al. 2005, Hirpara et al. 2016). Though patients' engagement in decision-making is listed as a priority in the Malta National Cancer Plan (Ministry for Health 2017), further research is warranted to identify patients' preference to the degree of involvement in healthcare decisions and factors that facilitate or hinder patients' involvement in the local practice.

Patients in our study were highly sensitive to the spoken words by healthcare professionals. The lack of empathy shown by some healthcare professionals particularly in the medical and nursing profession was raised by both patients and significant others in our study. A systematic review recognised a positive association between empathic behaviour shown by healthcare professionals' and patients' outcomes such as reduced psychological distress and improved satisfaction with treatment (Lelorain et al. 2012). Though further studies are warranted with healthcare professionals to evaluate factors influencing their empathy, healthcare professionals may require training to enhance their empathic skills.

Both patients and significant others were grateful to have had an overall positive experience of the healthcare system, with the service of the nurse navigator being highly praised. Though the oncologists were considered the lead in prescribing the appropriate treatment, both patients and significant others complained about the lack of accessibility to the oncologists during the treatment journey, with this gap being filled by the nurse navigators. According to patients and significant others, the nurse navigators were their first port of call for their needs and with whom they maintained ongoing communication for the duration of the treatment journey. Therefore, this showed that patients noticed and appreciated the delivery of personalised care that targeted their individual needs. As recommended by Horio et al. (2022), healthcare professionals should cooperate together as a team, by gathering an adequate history from patients, informing the respective healthcare professional from multidisciplinary team and supporting the patients according to their needs.

Whilst at the beginning of treatment significant others were very open and upcoming with listing recommendations for improvement of the services, patients did not come up with any recommendations to improve the healthcare service. In contrast, at completion of treatment, both the patient and the significant others put forward recommendations for improvement of services. This aspect of the research was in line with the findings by Okuyama, Wagner and Bijnen (2014) who concluded that hesitancy amongst patients to speak up might be due to fear of appearing rude or disrespectful, disappoint the healthcare professionals or endanger their own care. In fact, WHO recommends the gathering of patients’ and healthcare professionals’ experiences to be able to develop service improvement and promote participatory governance in public healthcare systems (WHO 2020).

Figure 6.2 shows similarities and differences in the perspectives of patients and significant others with regards to the medicine-taking practice of antineoplastic medicines at initiation and completion of treatment.



Patients

Initiation of treatment

- No recommendations put forward at this stage of treatment

Completion of treatment

- Were still willing to leave all decisions related to treatment totally up to the oncologist

- Oncologist is the major influence on patients to accept treatment
- Experienced overall positive experience with the healthcare system and highly supported by nurse navigators
- Highly sensitive to spoken words by healthcare professionals
- Provided recommendations for improvement of cancer services
- Aware about the availability treatment options for management of colorectal cancer

Significant others

- Provided recommendations to improve awareness of available support services

- Expressed the patients’ need for shared responsibility with the oncologist to decide what’s best for the patient

Figure 6.2: Comparisons between the patients’ and significant others’ perspectives with regards medicine-taking practice of antineoplastic medicines at initiation and completion of treatment

6.2.3. Comparison of perspectives on the burden of antineoplastic medicines

Whilst patients and significant others were aware of possible physical adverse effects resulting from treatment, they were unable to recognise their severity. In a prospective observational study, Horio et al. (2022) investigated the consistency between 20 pairs of patients and their respective family in recognising the occurrence and severity of adverse effects of antineoplastic medicines. Horio et al. (2022) commented that there was better congruency between patients and family members who lived in the same household. Despite this there was a high level of agreement between patients and family members with recognising visible symptoms, the latter found it difficult to detect invisible symptoms such as physical weakness, dysesthesia and emotional disturbances (Horio et al. 2022). This finding contrasts with our study where significant others were able to describe the patients' psychological changes such as anxiety and irritability during their treatment journey. This is important as significant others were taking on the role of principal caregiver when patients were recovering at home in between treatment cycles highlighting the importance of educating both patients and significant others to promote a better understanding and facilitate supportive care. This would give patients an additional sense of security.

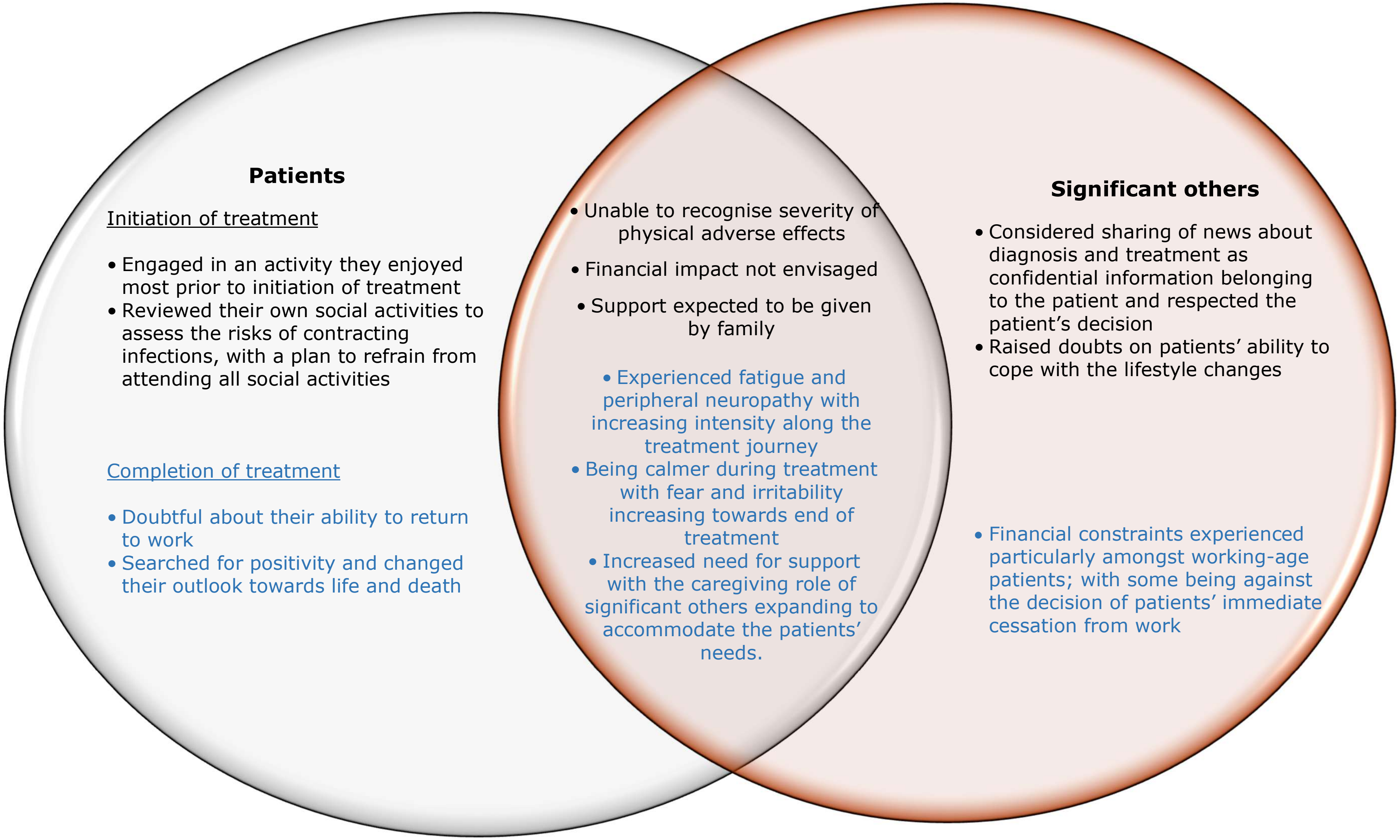
Whilst initially both patients and significant others did not envisage any major financial impact, they had contrasting views relating to patients' employment and financial burden. Upon being informed about their treatment with antineoplastic medicines, patients who were still of working age took a decision about their employment with most of these patients stopping temporarily. A patient who continued to work found support from the place of work to adapt working conditions to suit circumstances. While it seemed necessary for patients to prioritise their own needs in the acute stage, some significant others considered the long-term impact. They highlighted their disagreement with the patients' immediate decision to cease working upon initiation of treatment with antineoplastic medicines. Studies showed that cessation of work may result in profound consequences on the financial and psychological well-being of patients and their families (De Boer et al. 2009, Mehnert 2011, Rick et al. 2012, La Vecchia et al.

2015). However, patients with an ongoing employment during treatment offer them meaning, control and sense of normality during an emotionally challenging time (Blinder et al. 2012, Glare et al. 2017). Unlike the local situation where most patients decided to immediately stop working, literature showed that there is an increasing interest in maintaining employment whilst patients are receiving treatment (Yuan et al. 2021). In countries such as United Kingdom, Norway and Denmark financial incentives are offered to employers to provide adequate work conditions to patients such as flexible schedule and adaptations to the work environment. Besides this, programmes were established to involve employers in return to work planning (Clayton et al. 2012). Blinder and Gany (2020) suggested that healthcare professionals must liaise with the patients to address work-related concerns, like monitoring of physical and psychological effects.

At initiation of treatment with antineoplastic medicines, patients started resorting to self-regulation to mitigate effects from the illness and treatment with antineoplastic medicines. For instance, patients engaged in a joyful event such as enjoying a meal in their favourite restaurant, something which was not going to be possible during treatment. Some patients attempted to adopt a healthier lifestyle while others planned to ban social events because of their high risk of acquiring infections. Contrastingly significant others raised concerns about the patients' determination to restrict themselves to these planned lifestyle changes for the whole duration of the treatment journey. Despite this, significant others took a back seat whilst still supporting the patients and respected the patients' decision, even if they did not personally agree with the plan. The greatest challenge for significant others was to withhold the sharing of cancer diagnosis from other members of the family and friends in accordance with the patients' wish. By having a better understanding of how patients and their significant others interact together, healthcare professionals can assist both parties in confronting the illness and improving their quality of life (Hamidou et al. 2018).

Irrespective of age, all patients immediately established their personal support network. Most patients identified family members as their significant others, with the latter feeling they should provide their support in view of being the patient's next of kin. It emerged that the significant other was a great resource to the patient. This strong relationship has been frequently conceptualised in the literature as a single unit of care (Tolbert et al. 2018). Due to lack of formal training, the significant others felt unprepared to manage the patients' anticipated care needs in-between treatment cycles. This made significant others over-protective to patients and exhibit inquisitive behaviour such as searching online information and querying healthcare professionals. This significant others' behaviour was not always well received by patients. Along the treatment journey, patients often turned to their significant others for physical and emotional support due to effects from treatment and illness. Patients felt well-supported throughout the treatment journey, with the need of support intensifying towards completion of treatment. Similar to other studies (Wolff and Roter 2011, Badr, Bakhshaie and Chhabria 2019, Norton et al. 2019), significant others played different roles throughout the treatment journey, with their roles shifting from emotional to more physical support (symptom management, assisting with errands and household tasks). Therefore healthcare professionals should evaluate the patient's availability of personal support early on in the treatment journey. Importantly the needs of this 'single unit of care' should be considered when devising supportive care interventions (Badr, Bakhshaie and Chhabria 2019). Both the patient and the significant other should work simultaneously to alleviate the burden associated with cancer and its treatment (Arteaga Perez 2022, Howard et al. 2022). Strategies to improve communication between patients and significant others are necessary to take in consideration their preferences. Also, significant others should be supported to learn how to support the patient rather than being controlling and over-protective.

Figure 6.3 shows similarities and differences in the perspectives of patients and significant others with regards to the burden of antineoplastic medicines at initiation and completion of treatment.



Patients

Initiation of treatment

- Engaged in an activity they enjoyed most prior to initiation of treatment
- Reviewed their own social activities to assess the risks of contracting infections, with a plan to refrain from attending all social activities

Completion of treatment

- Doubtful about their ability to return to work
- Searched for positivity and changed their outlook towards life and death

- Unable to recognise severity of physical adverse effects
- Financial impact not envisaged
- Support expected to be given by family

- Experienced fatigue and peripheral neuropathy with increasing intensity along the treatment journey
- Being calmer during treatment with fear and irritability increasing towards end of treatment
- Increased need for support with the caregiving role of significant others expanding to accommodate the patients' needs.

Significant others

- Considered sharing of news about diagnosis and treatment as confidential information belonging to the patient and respected the patient's decision
- Raised doubts on patients' ability to cope with the lifestyle changes

- Financial constraints experienced particularly amongst working-age patients; with some being against the decision of patients' immediate cessation from work

Figure 6.3: Comparisons between the patients' and significant others' perspectives with regards to burden of antineoplastic medicines at initiation and completion of treatment

6.3. Strengths of the doctoral research

6.3.1. Coherent study design

This research followed a coherent study design initiating with a systematic review (Phase I) to identify gaps in knowledge and informed the development of the subsequent phases (Phases II and III). These phases followed a longitudinal study design exploring the patients' and significant others' perspectives for the entire duration of their treatment journey with antineoplastic medicines. As PLEM is considered a complex and multifaceted phenomenon, the use of longitudinal qualitative methodology allowed the in-depth exploration of the temporal dimension in the patients' lived experience with antineoplastic medicines along the treatment journey and beyond. The longitudinal design permitted the build-up of detailed information about the sequence of events over time leading to a rich and accurate picture of patients' lives. Also, this allowed the exploration of change in patients' belief, practice and burden along the treatment journey.

Additionally, the use of multiple perspectives in the study design enabled a richer understanding of the patients' experience with antineoplastic medicines. The significant others were asked about their perspectives about the patients' experience with treatment. Separate narrative accounts were generated from one-to-one interviews to offer freedom in expression of individual independent views ensuring that patients and significant others did not influence each other's responses. Similarities and differences in the perceptions of patients and significant others were elicited, further highlighting the complexity of patients' life situation.

6.3.2. The use of PLEM conceptual model

The PLEM conceptual model (Mohammed, Moles and Chen 2016) was used as a theoretical framework underpinning this research. The use of the theorical framework enabled the generation of an in-depth description, interpretation and explanation of the data. Though this conceptual model has not yet been validated with the potential that elements of the model may be disputed by further studies, it had a high degree of logical consistency and plausibility to medication experience. This provided an added value to the research process by providing a structure for this doctoral research and guided the development of data generation tools and interpretation of findings. The findings of the systematic review (Phase I) adapted the original PLEM conceptual model to the oncology setting. This conceptual model was further evaluated with the findings of Phase II and Phase III studies.

6.3.3. Trustworthiness

The quality of this longitudinal qualitative research was ensured by adopting the four criteria of trustworthiness (credibility, dependability, confirmability and transferability) created by Lincoln and Guba (1985). Various strategies were employed to address each criterion as detailed in Chapter 2 and the subsequent chapters.

6.4. Limitations of the doctoral research

Longitudinal qualitative studies are highly labour intensive (Fadyl et al. 2017). Substantial quantity of data was generated for each study (Phase II and III). This made data management and analysis very complex. Data analysis of longitudinal qualitative data was done both from a cross-sectional (at a particular time-point) and a longitudinal (across different time-points) dimension. This further compounded complexity in data analysis.

As bias is recognised as a threat to the quality of research, the research student implemented various steps to reduce the risk of bias as outlined in Chapter 2. Despite this, the findings of this research may have also been limited with biases such as social desirability bias. Repeated contact with patients and significant others made participants feel comfortable to share their private and sensitive issues. However, this made the research student emotionally engaged with the participants resulting in potential unconscious bias.

The active involvement of the researcher is recognised as important in qualitative research in the generation and interpretation of data (Finlay 2002, Mantzoukas 2004). So, there is a potential to unconsciously exert influence on these processes. Thus, reflexivity was employed throughout the research as a process of self-reflection to critically identify any potential impact of the researcher’s beliefs and biases on the study. Maintaining regular dialogue between the members of the research team allowed interpretations to remain objective.

As the aim of qualitative research is richly conceptualised to understand the phenomenon of medicine experience rather than to gain generalisability, transferability to other cancer types and settings needs to be applied with caution. The data generated in this research was limited to the geographical area of Malta in patients diagnosed with one type of cancer (colorectal cancer) and receiving first-line treatment with antineoplastic medicines (FOLFOX or XELOX) in a government-funded healthcare system. The issue of transferability was addressed by providing a detailed description of the research setting, participants and method to allow readers to assess the applicability of the findings in this research to other contexts.

6.5. Originality of the research

This research is original and novel with regards to its scientific research design in applying a longitudinal qualitative methodology to understand the patients' journey and consequently the generation of new data.

6.5.1. Novelty of study design

To the knowledge of the research team, no published literature explored the patients' experience with antineoplastic medicines in terms of beliefs, practice and burden from a longitudinal and multi-perspective approach.

The findings of the systematic review (Phase I) informed the research design of the subsequent phases of the study. In order to explore the patients' lived experience with antineoplastic medicines, the conceptual model of Mohammed, Moles and Chen (2016) showed that it was imperative to understand the complex interplay of the patients' beliefs, practice and burden about the medicines. As the original conceptual model was based on studies involving patients taking any medicine for chronic and acute illness, it was beneficial to adapt this model to the oncology setting. This was made possible with the completion of the systematic review at Phase I. With regards to the exploration of beliefs, practice, and burden of antineoplastic medicines in patients with solid tumours, limited literature was identified, with lack of employing a longitudinal qualitative study design. The resultant adapted model to the oncology setting was later used as a framework for the development of the interview guide in the longitudinal qualitative studies with patients (Phase II) and significant others (Phase III).

This research set out to longitudinally explore the patients' lived experience with antineoplastic medicines for the management of colorectal cancer. The patients' experience was captured not only from the patients themselves but also from their significant others. This provided a comprehensive understanding of the complex experiences and needs of the patients along their treatment journey. Several strategies were adopted to ascertain quality of this research as described in Chapter 2; thus promoting the study rigour and robustness.

The longitudinal qualitative studies of Phase II and III were conducted in Malta, where such studies are lacking. In fact, the recently published Malta's Smart Specialisation Strategy 2021-2027 (Government of Malta and the Malta Council for Science and Technology 2021) strongly encourages the local research community to perform longitudinal long-term research in healthcare, particularly in cancer.

6.5.2. New contribution to knowledge

Overall, this doctoral research generated original findings with regards to changes in patients' beliefs, practice and burden to the use of antineoplastic medicines along the treatment journey. These included the unrealistic patients' expectation of cure which later patients had to recognise and accept, the immediate acceptance to the oncologist's proposed treatment with lack of active involvement in decision-making and the identification of a significant other as part of their own personal support network to cater for the expected impact of treatment. The findings obtained from the longitudinal qualitative studies supported inferences relevant to development of interventions to address the patients' needs along the treatment trajectory. These include the introduction of buddy system and educational sessions with treatment-specific information at appropriate time-points in the treatment journey. Healthcare professionals may use their understanding of this complex interplay to assist patients in traversing this journey with the least impact on their quality of life.

6.5.3. Dissemination of research findings

To inform patient care, results of this study have been disseminated at several national and international conferences as oral and poster presentations as well as publications in peer-reviewed scientific journals with plans for further dissemination. These are listed in the foreword section of this doctoral research. In order to reach a larger audience, links to the peer-reviewed publications and abstracts were shared through the use of online platforms (Twitter, ResearchGate and ORCiD). Key findings will also be shared with stakeholders in Malta, including the Ministry for Health and hospital management to assist in shaping a new care service landscape for oncology patients.

6.6. Implications of findings to practice

This research provided an understanding of the experience of patients being treated with antineoplastic medicines for colorectal cancer. Patients brought about their perspective as experts from their own experience along the treatment journey with antineoplastic medicines. Therefore, this places them in a perfect position to provide the necessary recommendations to ameliorate cancer care. Several recommendations were voiced by patients and significant others, which can be forwarded to different stakeholders (healthcare professionals, hospital management, policy makers and society). Prior to implementation, these recommendations are still subject to further discussion with the relevant stakeholders to be assessed for feasibility. This approach ensures that policy priorities are in line with patients’ needs.

As highlighted in the National Cancer Plan for the Maltese Islands, the government of Malta is committed to provide person-centred healthcare service in cancer care. Person-centred care is defined by the WHO as ‘‘care approaches and practices that see the person as a whole with many levels of needs and goals, with these needs coming from their own personal social determinants of health’’ (WHO 2015 p.5). The findings of this research showed that the diagnosis of colorectal cancer resulted in a life-changing event for the patients and their significant others irrespective of age emphasising the fact that the focus of cancer care must be on the individual patient.

6.6.1. Recommendations for healthcare professionals

Recommendations put forward by patients and significant others with regards to healthcare professionals are detailed in Figure 6.4.

Improvement in healthcare professional communication skills at the point of initial diagnosis of cancer and suggested treatment were proposed by both the patients and significant others. It was emphasised that healthcare professionals should explore the patient's prior knowledge and beliefs, provide the information at the patient's own pace to allow adequate time for the patient to understand the information and its implications and elicit the patient's concerns and expectations. Most patients expected to be informed of the treatment goals. Patients looked beyond the healthcare professionals' expertise. They asked healthcare professionals to be empathetic and sensitive to their evolving needs along their treatment journey while taking into consideration the cultural and religious values. The availability of a psychologist throughout their treatment journey was also recommended.

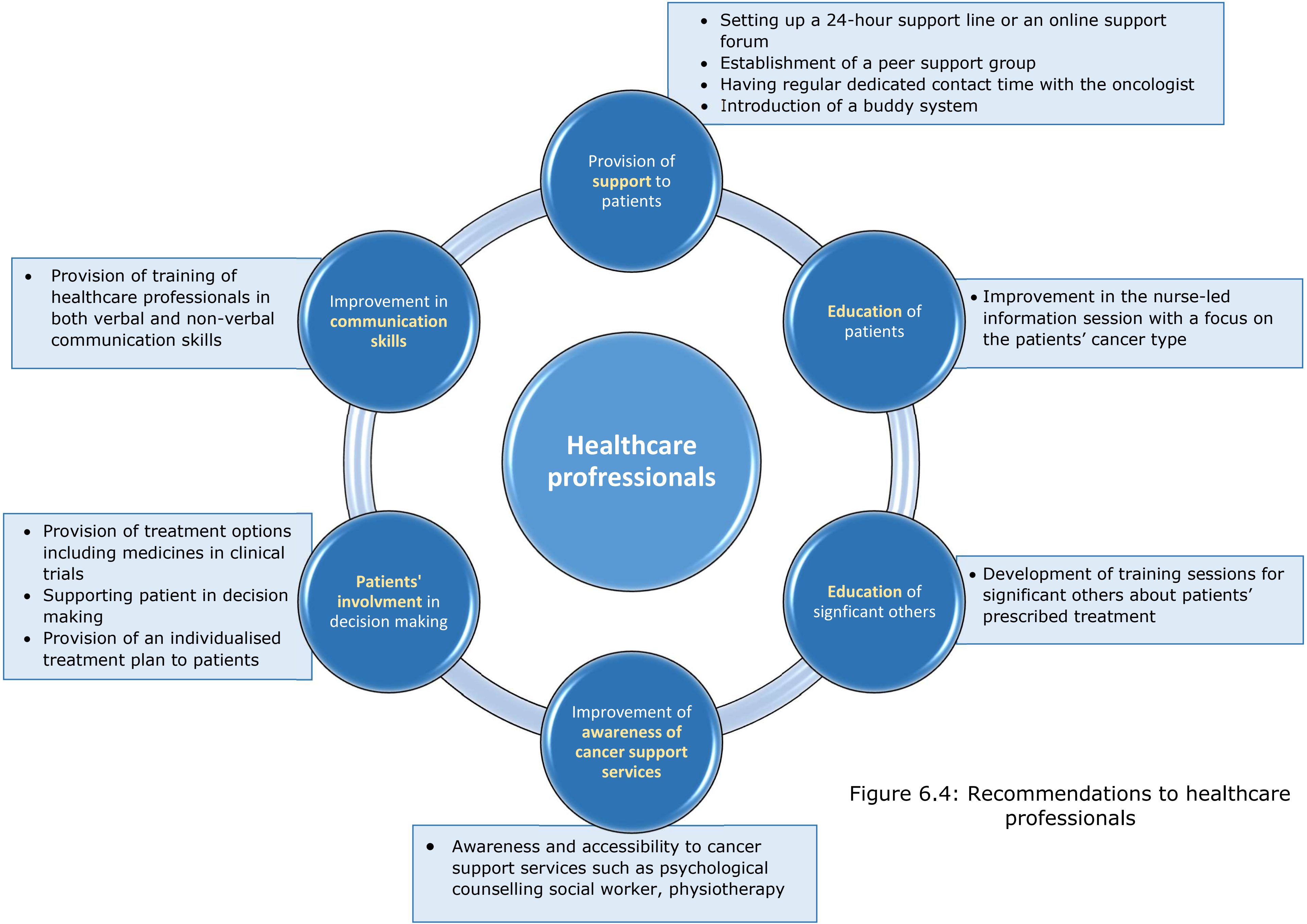
The oncologists are in a position of power having the trust of patients who believe they have the necessary experience and knowledge to treat their cancer. Significant others noted that healthcare professionals should provide patients with all available different treatment options and ultimately allow them to decide about their preferred treatment option. Healthcare professionals should therefore acknowledge that patients are ultimately in control of their own care. It is imperative to make the necessary changes to boost patients' ability to critically think about the available treatment options allowing them to make autonomous, informed decisions about their health. This is crucial in putting shared decision-making into practice.

The findings of this longitudinal study emphasised the importance of continuity of care throughout the treatment journey and beyond. This may be easily exemplified by the service of the nurse navigator, for whom patients and significant others were grateful to have the availability of an ongoing professional cancer-specific support, even in between treatment cycles. This showed that patients strived to build an ongoing relationship with a few healthcare professionals that could monitor their progress and identify their changing needs. This could be noted from their suggestions of setting up a symptom control unit, being informed about the assigned nurse taking care of the patient during hospital admission and the establishment of regular contact time with the medical team to share their difficulties rather than visiting them privately with out-of-pocket expenses. Patients also showed a desire to be individually supported by a clinical pharmacist by having a medicine review including their chronic medicines.

Improvement of the nurse-led information sessions was suggested by patients and their significant others. Recommendations included the creation of small groups of patients all with the same cancer type to be provided with specific information about treatment. The use of materials such as videos or online material based on the local context were also suggested for ease of accessibility.

Patients eased the impact of treatment by establishing their own personal support network and adopted self-regulated behaviour as from initiation of treatment. This highlighted further the need of a support system as an integral part of care. Significant others complained of not feeling recognised as a member of the patients' healthcare team despite their unique role in supporting the patient in cancer care. This highlights the need for focused training on how to adequately assist patients with cancer who are receiving treatment with antineoplastic medicines. This may include:

- the rationale behind implementation of cautionary measures
- identification of adverse effects and their severity including when to seek specialist advice
- the use, storage and disposal of supportive medicines
- handling of patients' body waste contaminated with antineoplastic medicines.



- Setting up a 24-hour support line or an online support forum
- Establishment of a peer support group
- Having regular dedicated contact time with the oncologist
- Introduction of a buddy system

- Improvement in the nurse-led information session with a focus on the patients’ cancer type

- Development of training sessions for significant others about patients’ prescribed treatment

- Awareness and accessibility to cancer support services such as psychological counselling social worker, physiotherapy

- Provision of treatment options including medicines in clinical trials
- Supporting patient in decision making
- Provision of an individualised treatment plan to patients

- Provision of training of healthcare professionals in both verbal and non-verbal communication skills

Figure 6.4: Recommendations to healthcare professionals

6.6.2. Recommendations directed to hospital management

Recommendations put forward by patients and significant others with regards to the hospital management are shown in Figure 6.5. Improvement to existing services included scheduling of transport services and better room allocation for patients during treatment cycles to facilitate the sharing of patients’ experience. Introduction of new services was also suggested and included the setting up of oncology and palliative outreach programmes, the introduction of symptom control units and provision of a survivorship care plan for each patient following completion of treatment.

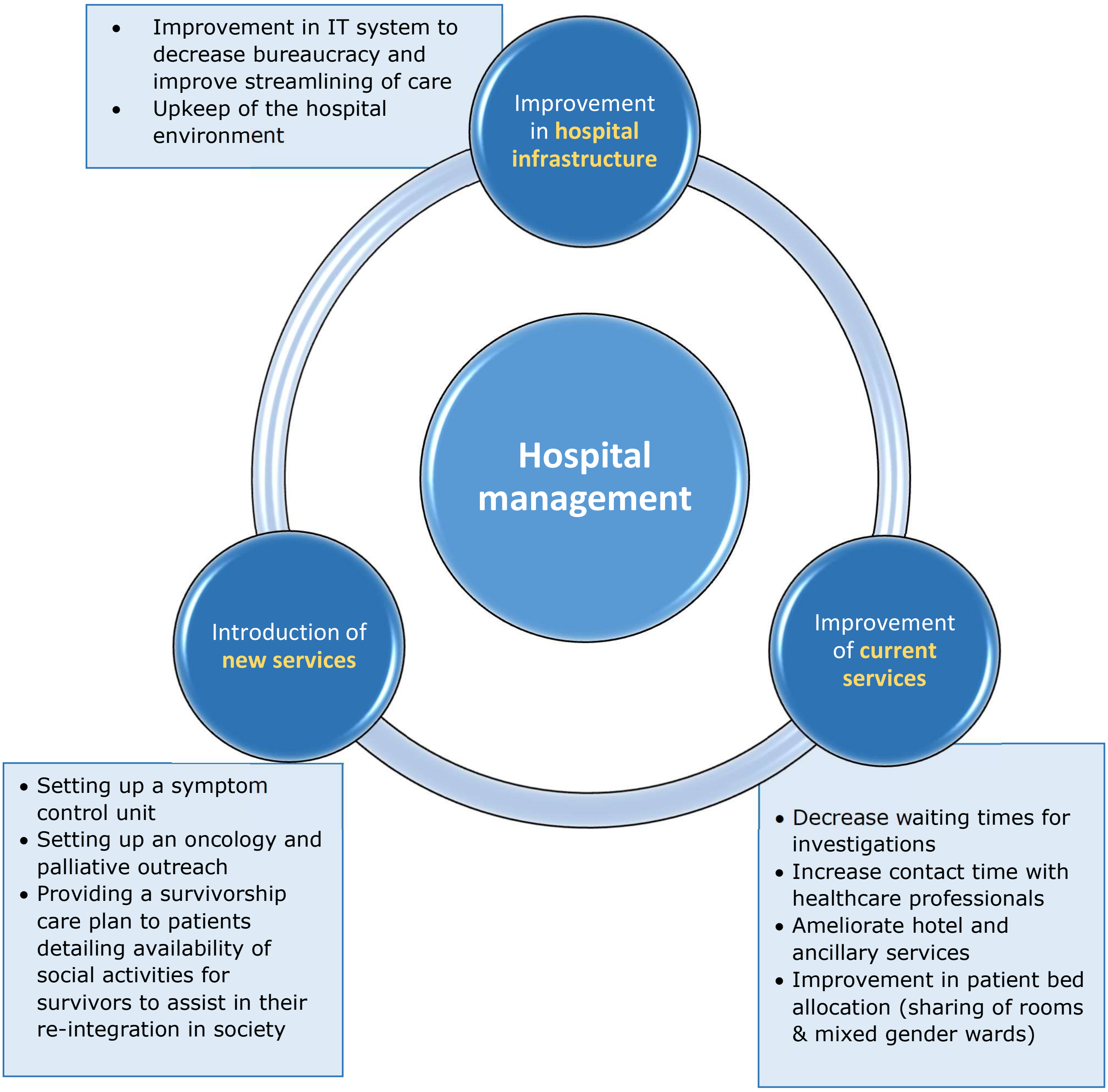
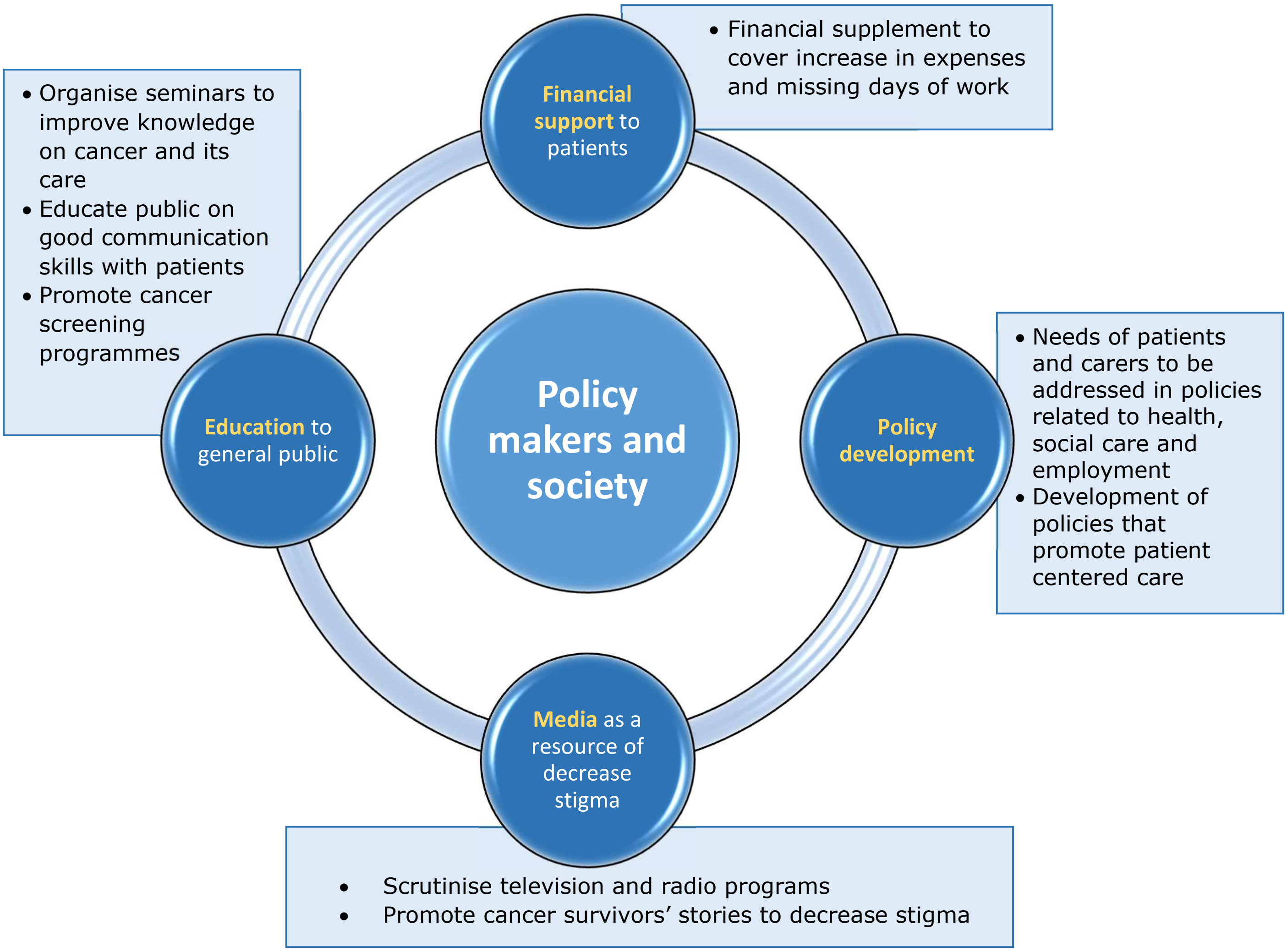


Figure 6.5: Recommendations to hospital management

6.6.3. Recommendations directed to policy makers and society

Figure 6.6 shows the recommendations directed at the policy makers and society as suggested by patients and significant others. Patients praised the role of government in providing a publicly funded healthcare system. They suggested that additional financial support should be provided to meet their needs, similar to other patients who suffer from chronic illness. Additionally, the public should be educated to improve the knowledge on cancer risk factors and alarm symptoms whilst at the same time promoting the importance of cancer screening programmes. Other suggestions included more scrutiny of the media that has the potential to worsen patient’s fear of cancer or treatment and the promotion of cancer survivor stories to address cancer-related stigma.



- Financial supplement to cover increase in expenses and missing days of work

- Organise seminars to improve knowledge on cancer and its care
- Educate public on good communication skills with patients
- Promote cancer screening programmes

- Needs of patients and carers to be addressed in policies related to health, social care and employment
- Development of policies that promote patient centered care

- Scrutinise television and radio programs
- Promote cancer survivors’ stories to decrease stigma

Figure 6.6: Recommendations to policy makers and society

6.7. Future research

This research in patients' lived experience provided a greater understanding of the beliefs, practice and burden associated with the use of antineoplastic medicines in patients with colorectal cancer. Besides contributing to the existing knowledge in medicine experience, the findings of this research identified the need of further research in the development, implementation, and assessment of the effectiveness of patient-tailored interventions in cancer care in Malta. This will continue to inform healthcare professionals about how to provide optimal care that addresses the patients' needs. Study proposals of further research stemming from the findings described in this thesis are outlined below.

6.7.1. Proposal for study 1

A pre-post study evaluating the effectiveness of a treatment-specific educational intervention in improving patients' knowledge about treatment with antineoplastic medicines

Research aim

To investigate the effect of a treatment-specific group information session on the patients' level of knowledge on illness and treatment with antineoplastic medicines and reduce treatment-related anxiety

Research philosophy

A positivist approach is suitable to assess the impact of an educational intervention on patients' self-reported knowledge and treatment-related anxiety.

Methodology and methods

A pre-post study design with a quantitative approach will be employed to identify any changes in patients' knowledge and anxiety following the implementation of a treatment-specific educational intervention.

Adult patients diagnosed with colorectal cancer who will be receiving treatment with antineoplastic medicines (FOLFOX) for the first time will be recruited to the study. They will be randomly allocated to two groups either a control group (attending nurse-led group information session, as per current system) or an intervention group (group having treatment-specific information session). Treatment-specific group information session will be conducted face-to-face for a small group of patients (not more than 5 patients) who are receiving the same treatment protocol. This education session will be carried out on two repeated occasions (at initiation of treatment and mid-treatment cycles). The material of the education intervention will be co-designed with a group of patients who had just finished treatment with antineoplastic medicines.

Prior to initiation of the study, the sample size will be calculated to detect significant difference between the two groups with 80% power and alpha 0.05.

Prior to the intervention, all the participants in both groups will complete two self-administered questionnaires. One questionnaire will be designed to collate socio-demographic data, information about the patients' knowledge to the specific antineoplastic treatment prescribed. The questionnaire will be developed based on the literature, reviewed for face and content validity by an expert panel of multidisciplinary team of healthcare professionals and pilot tested. The other questionnaire will be used to record the patients' anxiety levels using the Hospital Anxiety and Depression Scale (Zigmond and Snaith 1983). The same questionnaire will be re-administered to both groups after completion of the second session to mitigate recall bias.

Statistical analysis will be employed to compare the data before and after the intervention as well as between intervention and control groups.

6.7.2. Proposal for study 2

A study exploring the views and perceptions of patients, significant others and healthcare professionals in setting up a symptom control unit within the oncology centre: a qualitative approach

Research aim

To explore the views and perceptions of patients, significant others and healthcare professionals (oncologists, nurses and pharmacists) towards the potential development of a symptom control unit within the oncology centre in Malta

Research philosophy

An exploratory qualitative research design with an interpretivist stance will be adopted as the researcher seeks to understand the patients, significant others and healthcare professionals' point of view about the setting up of a symptom control unit for cancer patients.

Methodology and methods

A qualitative study design, using focus groups will be employed to gain a wide range of views and perceptions of patients, significant others and healthcare professionals in the setting up of a symptom control unit within the oncology centre in Malta. Challenges associated with symptom identification and assessment as well as resources needed will be explored. Participants will be recruited using purposive sampling. Four separate focus groups of 8 participants will be held for patients with cancer who completed first-line treatment with antineoplastic medicines, significant others of patients with cancer who received treatment with antineoplastic medicines, hospital management and multidisciplinary healthcare professionals working in the oncology setting including oncologists, nurses and pharmacists. A focus group topic guide will be developed based around the domains of the Consolidated Framework for Implementation Research (Damschroder et al. 2009) and the literature. Responses will be reviewed and verified at the end of each. Focus group interviews will be recorded, transcribed verbatim and anonymised. Data will be analysed using Braun and Clarke (2006) thematic analysis.

6.7.3. Proposal for study 3

A study exploring healthcare professionals' and patients' perceptions of patient involvement in decision-making and information provision in colorectal cancer care: mixed methods approach

Research aim

To explore the perceptions of patients and healthcare professionals on the involvement of patients in decision-making and information provision in colorectal cancer care

Research philosophy

This study will adopt a pragmatic approach to allow the exploration of shared decision-making in colorectal cancer care from multiple perspectives. The study will follow the definition of shared decision-making as defined by Elwyn et al. (2012 p.1361) as "an approach where physicians and patients share the best available evidence when faced with the task of making treatment decisions, and where patients are supported to consider options, to achieve informed preferences".

Methodology and methods

An explanatory sequential mixed-methods approach will be adopted; with the first phase involving a self-reported questionnaire survey followed by a second phase using in-depth interviews. The study will be underpinned by the conceptual model for shared decision-making during the surgical consultation (Leon-Carlyle et al. 2009). The participants in the study are patients with colorectal cancer who are receiving their second cycle of adjuvant antineoplastic medicines, together with practising oncologists and surgeons in managing patients with colorectal cancer.

Phase 1 of the study: Two parallel questionnaires will be used to produce quantitative data; one intended for patients and the other for healthcare professionals. The questionnaires shall gather data pertaining to the patients' and healthcare professionals' general preference for patients' participation in decision-making in the management of colorectal cancer, situation-based preferences for patients' participation in decision-making and preferences in modes of information delivery about colorectal cancer and its treatment. A literature search will be conducted to identify an appropriate instrument to examine the preferences for patients' participation in decision-making and information provision. Any available instrument will be evaluated for its suitability in collecting data with regards to the aim of the study. If the identified instruments are inadequate, a questionnaire will be developed based on the available literature about decision-making, followed by validation and piloting. The participants will also be given the option to show their interest in participating in an in-depth semi-structured interview in the second phase of the study. The questionnaire will be distributed by post to randomly selected patients, oncologists and surgeons. A reminder letter about the questionnaire will be sent after 2 weeks to increase the response rate. The appropriate sample size for the study will be determined using sample size calculations. Descriptive analysis will be used to explain the key features observed in the data.

Phase 2 of the study: Semi-structured interviews will be employed to complement the findings of the questionnaire survey (Phase 1). This will allow further exploration of the results obtained from the questionnaire. Healthcare professionals and patients will be selected using purposive sampling. The interview schedule will be guided by the responses obtained from the questionnaire with emphasis on the rationale behind their preference, facilitators and barriers to patients' involvement in decision-making about treatment. Interviews will be audio recorded with the participant's permission and transcribed verbatim prior to analysis. Recruitment of participants will continue until no further information will be produced and therefore data saturation is reached. Data will be analysed using constant comparative analysis (Ritchie and Lewis 2003).

6.8. Research Impact

The Economic and Social Research Council (UK Research and Innovation (UKRI) 2022) defined impact of research as "the demonstrable contribution that excellent research makes to society and the economy." This clearly shows that the impact from research does not only involve the creation of academic knowledge but also results in an influence on economy and society (Denicolo 2014). Whilst academic impact relates to improved understanding of scientific method and theory, the economic and societal impact reflects the benefits of research to individuals, society, economy, organisation and countries (UKRI 2022). Tools such as Pathway to Impact (Figure 6.7) were introduced to assist researchers in identification of the potential impacts that their research may have in academia, economy and society (Kearnes and Wienroth 2011).

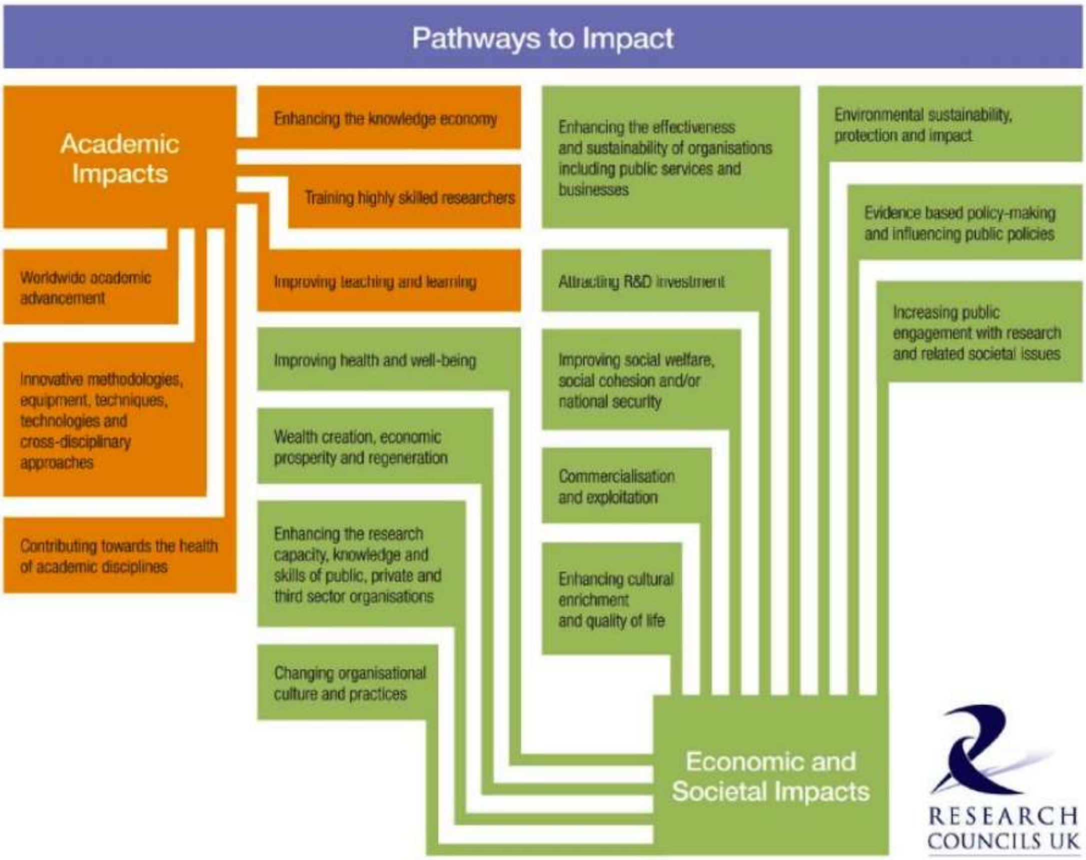


Figure 6.7: Matrix of possible pathways to achieve impact in academia, economy and society © 2011 Springer Science+Business Media B.V. (Kearnes and Wienroth 2011)

The research presented in this thesis is expected to have impact on multiple levels (as shown in Figure 6.8) and further explained below.

1. Academic impact
    - The research student developed substantial knowledge and skills in conducting research using longitudinal qualitative methodology and methods. These skills are transferable and may be used in conducting other pieces of research
    - This research also provided opportunities to the research student to build her network with other researchers and students from different countries
    - Findings from the different phases of this research were disseminated in local and international conferences to reach a wider audience. Also parts of this research were published in peer-

reviewed journals to further contribute to knowledge within the scientific community

- This research may encourage other researchers to conduct similar studies for other cancer types and in different healthcare settings
- The research also has a positive impact on the educational institution (Robert Gordon University) in being promoted to develop adequately trained skilled researchers

2. Societal impact
   - The research generated evidence that can be used to consider implementation of patients' involvement in shared decision-making, which is still lacking on a local level
   - This research will result in the potential development and implementation of patient-tailored interventions which in turn affect the local practice and improve patients' satisfaction
   - This research identified the important role of significant other and promoted their involvement in patients' care
   - This research will help improve wellbeing of patients with colorectal cancer and significant others both in Malta and beyond through effective dissemination
   - This research will influence local management policies, procedures and training (which can be shared internationally) resulting in potential improvements in current healthcare services

3. Economic impact
   - The findings of this research will help to provide better utilisation of resources and potentially lead to the development of cost saving interventions. Adequate services as recommended by the patients and significant others themselves will be provided at the right time during their treatment journey, based on the patients' needs and preferences rather than the convenience of the healthcare provider resulting in better value for money

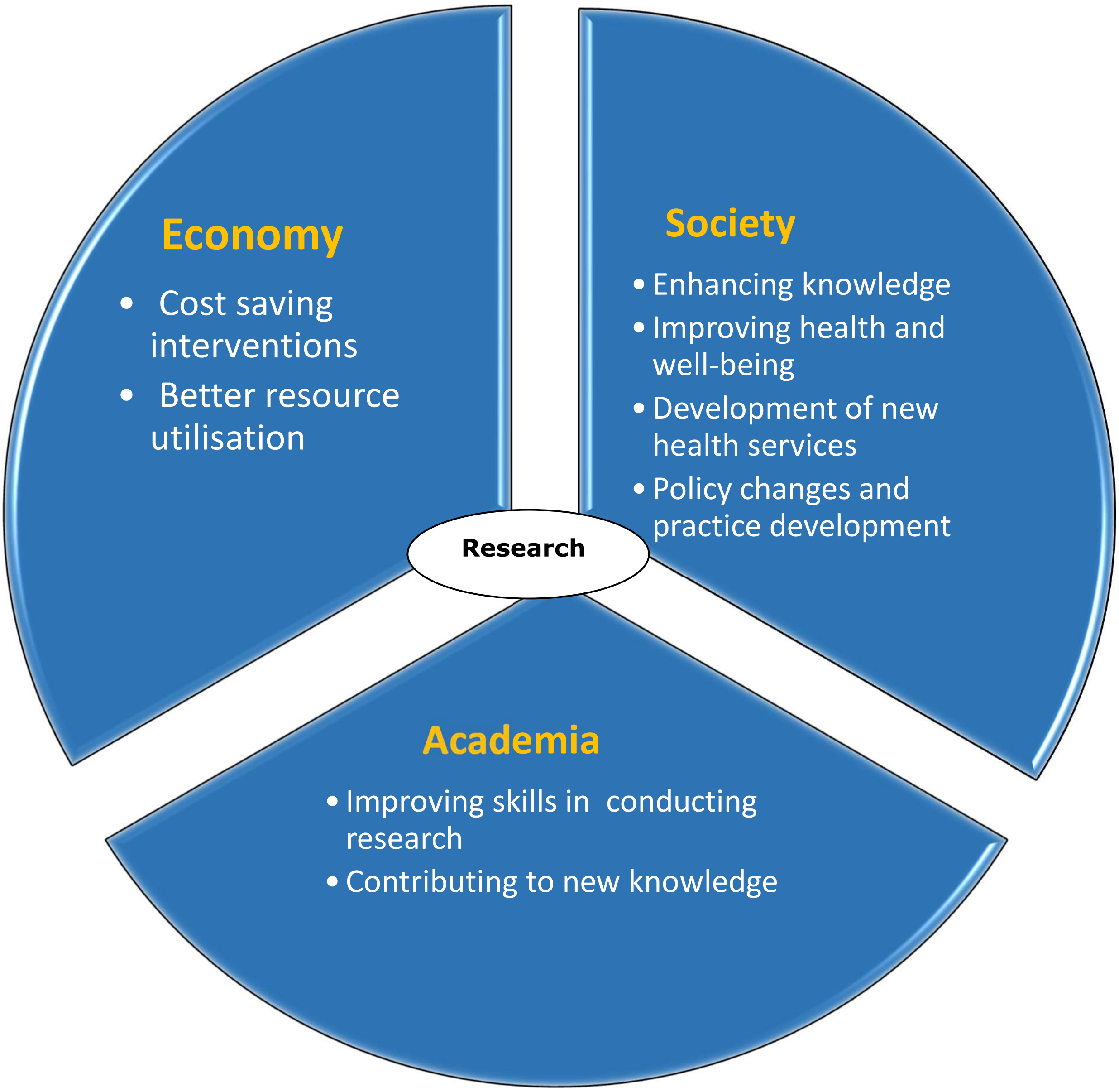


Figure 6.8: Impact of research on economy, society and academia

6.9. Conclusion

Despite the wealth of studies published on cancer and its treatment, there were only a limited number of publications focusing on the patients' experience with antineoplastic medicines. The use of antineoplastic medicines is a mainstay treatment for most common cancers including colorectal cancer. Due to population growth and an aging population that further promotes the incidence of cancer, there is an anticipated increase in the demand for antineoplastic medicines. Therefore, this calls for the need to explore the patients' experience with antineoplastic medicines.

According to the original model by Mohammed, Moles and Chen (2016), PLEM is a complex interplay between medicines-related beliefs, practice and burden. As this model was not based on studies receiving antineoplastic medicines, its applicability to the oncology setting was limited. The systematic review (Phase I) showed that this model captured well the patients' lived experience with antineoplastic medicines and may be adapted to the oncology setting with minor modifications. This adapted model was used to inform the subsequent studies of this research.

Prior to conducting this research, there was no published research that sought to longitudinally explore the patients' belief, practice and burden with respect to the use of antineoplastic medicines in colorectal cancer from the patients' perspective (Phase II). The temporal dimension employed in this research was necessary to identify the changes in the patients' beliefs, practice, and burden in relation to the use of antineoplastic medicines with progression of treatment. An additional perspective to PLEM was obtained from the significant others through a parallel longitudinal study (Phase III). Overall, this research presented an original contribution to knowledge, with the findings obtained from a robust study design underpinned by the PLEM conceptual model (Mohammed, Moles and Chen 2016) and phenomenology approach.

This study showed that patients' initial beliefs were fuelled by their lack of knowledge and generalising the symptoms of cancer and antineoplastic medicines into one type of illness and treatment. Knowledge was noted to be gained by patients throughout their treatment because of their own experience as well as that of others receiving the same treatment in the ward. This emphasised the need for improved knowledge about cancer and treatment in the public domain to address patients’ misconceptions.

In relation to medicine taking practice, this research demonstrated the lack of patients’ involvement in their decision for cancer treatment. It also demonstrated that whilst patients were indifferent to their own cancer treatment, the significant others yearned for shared decision-making. This calls for the need of treatment-specific information provision that matches patient’s needs and improved patient-healthcare professional relationship based on empathy.

This research showed that antineoplastic medicines adversely affected the patients’ physical and psychosocial wellbeing characterised by gradual reduction in function. The increasing effects of physical weakness, social isolation and financial impact were amongst the challenges encountered by patients along the treatment journey. These highlighted the importance of strengthening a personalised care and support services that cater for the broader individual needs in addition to the provision of medicines. With the increasing number of individuals surviving cancer due to progress in prevention, early detection, and treatment of cancer, it is important that patients can develop coping strategies to adapt to changes in their daily and social life. Additionally, the patients’ constant support provided by the significant others throughout the treatment journey should be acknowledged. So, the integration of significant others as part of the patients’ care team should be considered to improve the patients’ delivery of cancer care.

In conclusion, this research showed that the patients’ lived experience with antineoplastic medicines is complex and challenging long-term. This research has highlighted aspects within the patients’ medicine experience (availability and awareness of patients support services, specific information provision, empathic behaviour) that warrants attention from healthcare professionals, hospital management and policy makers. It can also support the development of specific patient-tailored interventions provided at appropriate time-points during the treatment journey such that the central focus of care should always be the person rather than the illness or the medicine.

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Appendices

Appendix 3.1: CASP Tool

A. CASP Tool for qualitative study

CASP
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Summertown Pavilion, Middle
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CASP Checklist: 10 questions to help you make sense of a **Qualitative** research

How to use this appraisal tool: Three broad issues need to be considered when appraising a qualitative study:

- Are the results of the study valid? (Section A)
- What are the results? (Section B)
- Will the results help locally? (Section C)

The 10 questions on the following pages are designed to help you think about these issues systematically. The first two questions are screening questions and can be answered quickly. If the answer to both is "yes", it is worth proceeding with the remaining questions. There is some degree of overlap between the questions, you are asked to record a "yes", "no" or "can't tell" to most of the questions. A number of italicised prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

About: These checklists were designed to be used as educational pedagogic tools, as part of a workshop setting, therefore we do not suggest a scoring system. The core CASP checklists (randomised controlled trial & systematic review) were based on JAMA 'Users' guides to the medical literature 1994 (adapted from Guyatt GH, Sackett DL, and Cook DJ), and piloted with health care practitioners.

For each new checklist, a group of experts were assembled to develop and pilot the checklist and the workshop format with which it would be used. Over the years overall adjustments have been made to the format, but a recent survey of checklist users reiterated that the basic format continues to be useful and appropriate.

Referencing: we recommend using the Harvard style citation, i.e.: *Critical Appraisal Skills Programme (2018). CASP (insert name of checklist i.e. Qualitative) Checklist. [online] Available at: URL. Accessed: Date Accessed.*

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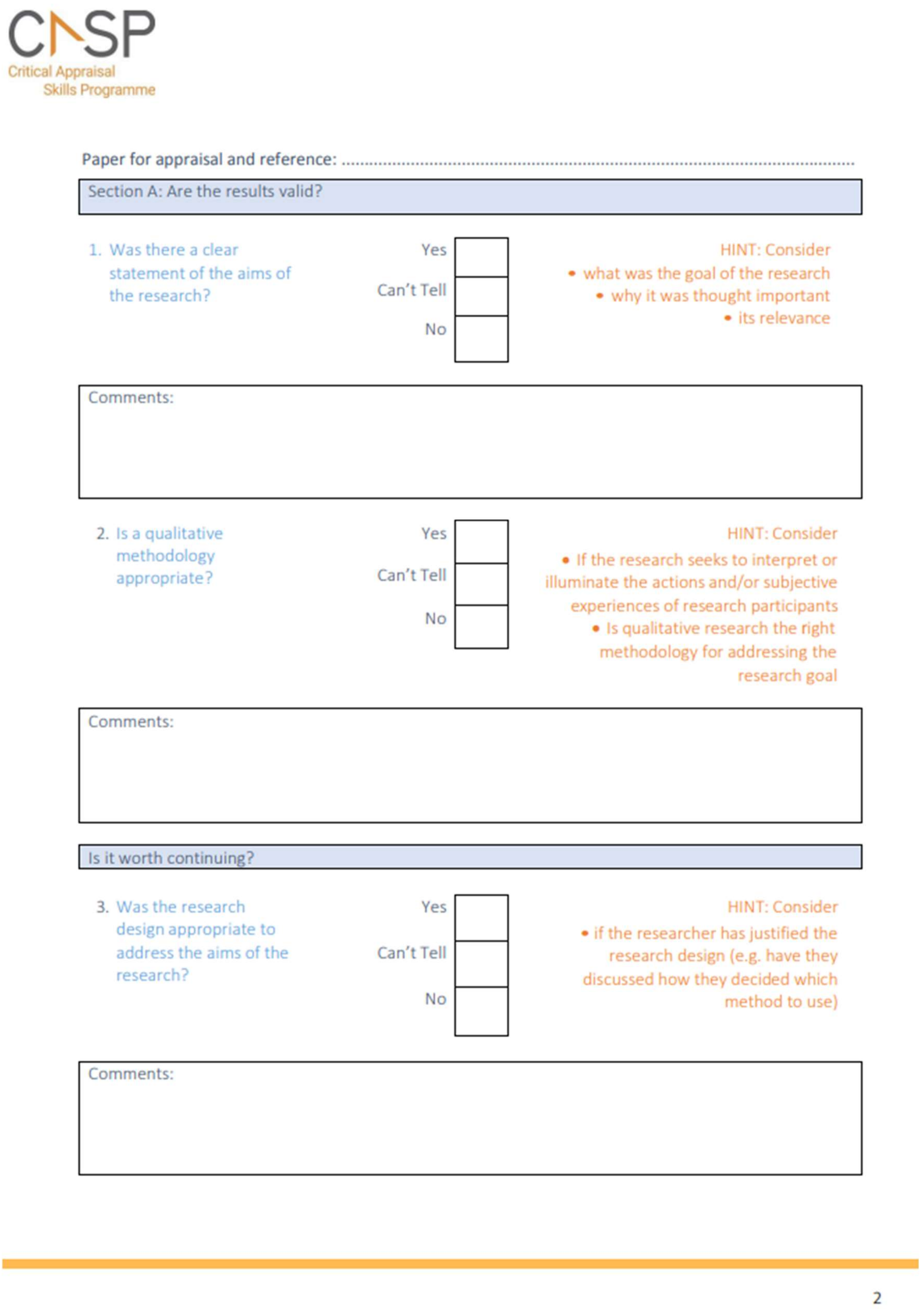

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Paper for appraisal and reference: ....

Section A: Are the results valid?

1. Was there a clear statement of the aims of the research?	Yes ☐ Can't Tell ☐ No ☐	HINT: Consider • what was the goal of the research • why it was thought important • its relevance

Comments:

2. Is a qualitative methodology appropriate?	Yes ☐ Can't Tell ☐ No ☐	HINT: Consider • If the research seeks to interpret or illuminate the actions and/or subjective experiences of research participants • Is qualitative research the right methodology for addressing the research goal

Comments:

Is it worth continuing?

3. Was the research design appropriate to address the aims of the research?	Yes ☐ Can't Tell ☐ No ☐	HINT: Consider • if the researcher has justified the research design (e.g. have they discussed how they decided which method to use)

Comments:

4. Was the recruitment strategy appropriate to the aims of the research?

Yes ☐
Can't Tell ☐
No ☐

HINT: Consider

- If the researcher has explained how the participants were selected
- If they explained why the participants they selected were the most appropriate to provide access to the type of knowledge sought by the study
- If there are any discussions around recruitment (e.g. why some people chose not to take part)

Comments:

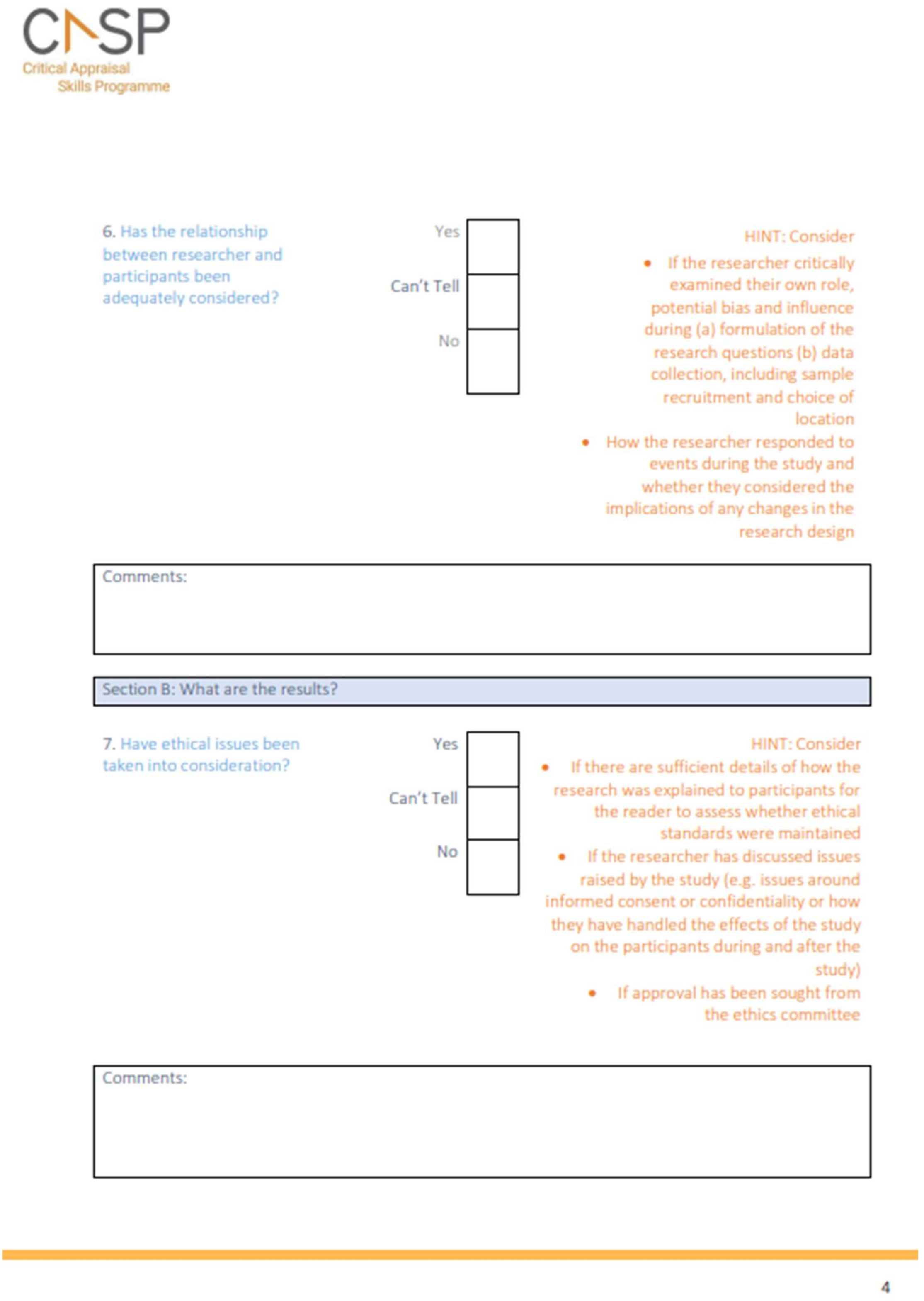
5. Was the data collected in a way that addressed the research issue?

Yes ☐
Can't Tell ☐
No ☐

HINT: Consider

- If the setting for the data collection was justified
- If it is clear how data were collected (e.g. focus group, semi-structured interview etc.)
- If the researcher has justified the methods chosen
- If the researcher has made the methods explicit (e.g. for interview method, is there an indication of how interviews are conducted, or did they use a topic guide)
- If methods were modified during the study. If so, has the researcher explained how and why
- If the form of data is clear (e.g. tape recordings, video material, notes etc.)
- If the researcher has discussed saturation of data

Comments:



6. Has the relationship between researcher and participants been adequately considered?

Yes ☐
Can't Tell ☐
No ☐

HINT: Consider
- If the researcher critically examined their own role, potential bias and influence during (a) formulation of the research questions (b) data collection, including sample recruitment and choice of location
- How the researcher responded to events during the study and whether they considered the implications of any changes in the research design

Comments:

Section B: What are the results?

7. Have ethical issues been taken into consideration?

Yes ☐
Can't Tell ☐
No ☐

HINT: Consider
- If there are sufficient details of how the research was explained to participants for the reader to assess whether ethical standards were maintained
- If the researcher has discussed issues raised by the study (e.g. issues around informed consent or confidentiality or how they have handled the effects of the study on the participants during and after the study)
- If approval has been sought from the ethics committee

Comments:

4

8. Was the data analysis sufficiently rigorous?

Yes ☐

Can't Tell ☐

No ☐

HINT: Consider
- If there is an in-depth description of the analysis process
- If thematic analysis is used. If so, is it clear how the categories/themes were derived from the data
- Whether the researcher explains how the data presented were selected from the original sample to demonstrate the analysis process
- If sufficient data are presented to support the findings
- To what extent contradictory data are taken into account
- Whether the researcher critically examined their own role, potential bias and influence during analysis and selection of data for presentation

Comments:

9. Is there a clear statement of findings?

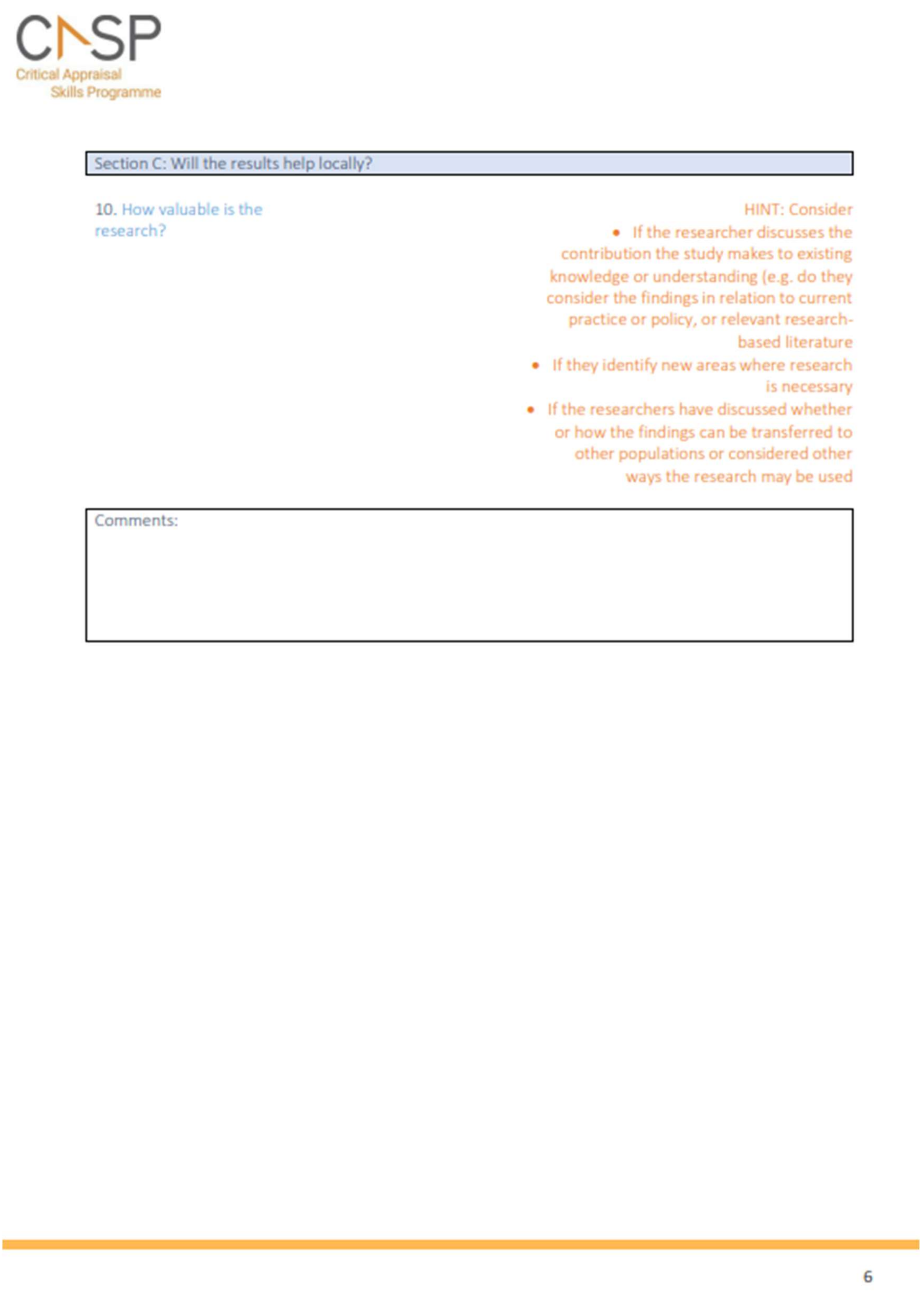
Yes ☐

Can't Tell ☐

No ☐

HINT: Consider whether
- If the findings are explicit
- If there is adequate discussion of the evidence both for and against the researcher's arguments
- If the researcher has discussed the credibility of their findings (e.g. triangulation, respondent validation, more than one analyst)
- If the findings are discussed in relation to the original research question

Comments:



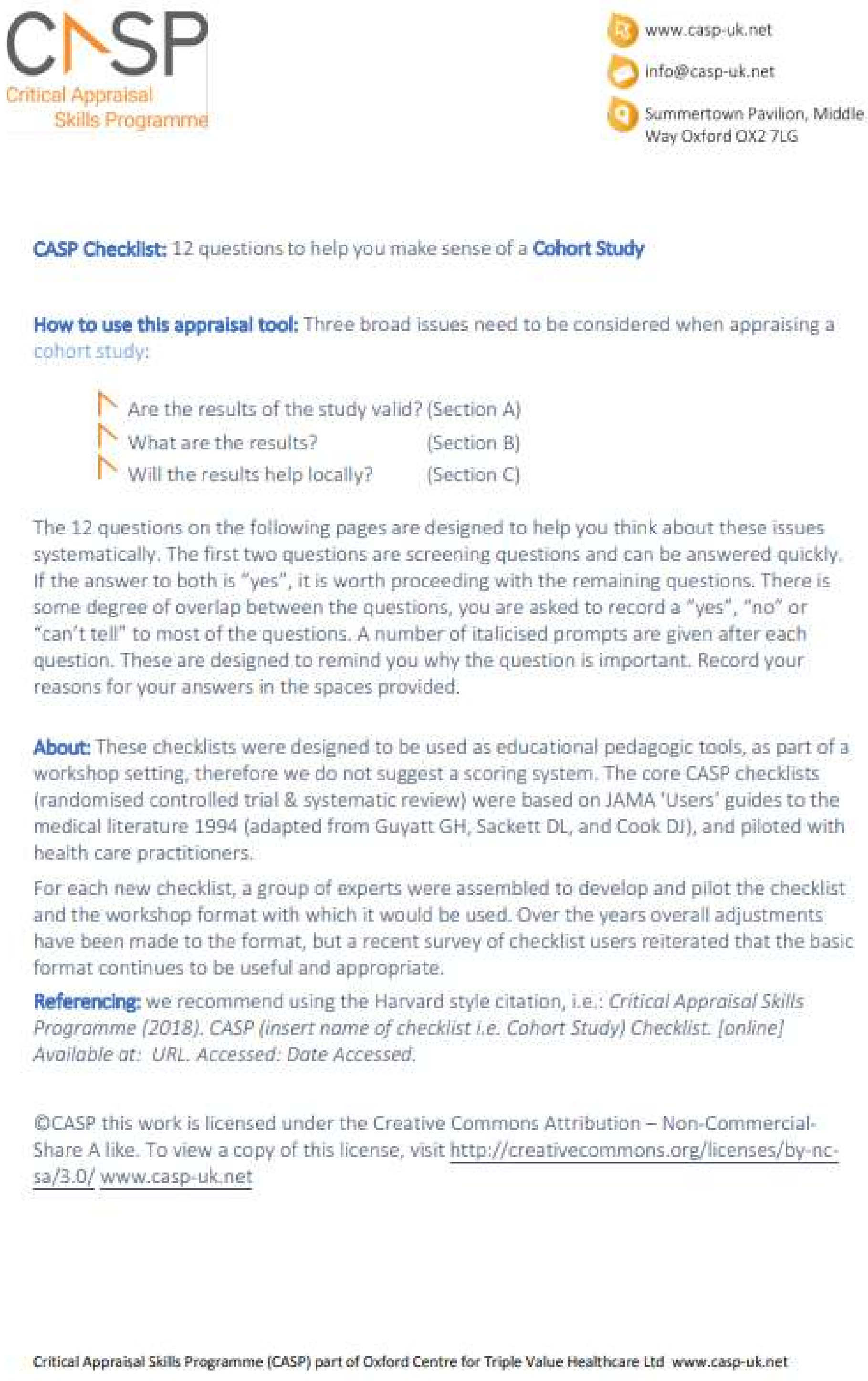
Section C: Will the results help locally?

10. How valuable is the research?

HINT: Consider
- If the researcher discusses the contribution the study makes to existing knowledge or understanding (e.g. do they consider the findings in relation to current practice or policy, or relevant research-based literature
- If they identify new areas where research is necessary
- If the researchers have discussed whether or how the findings can be transferred to other populations or considered other ways the research may be used

Comments:

B. CASP Tool for cohort study



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CASP Checklist: 12 questions to help you make sense of a **Cohort Study**

How to use this appraisal tool: Three broad issues need to be considered when appraising a cohort study:

- Are the results of the study valid? (Section A)
- What are the results? (Section B)
- Will the results help locally? (Section C)

The 12 questions on the following pages are designed to help you think about these issues systematically. The first two questions are screening questions and can be answered quickly. If the answer to both is "yes", it is worth proceeding with the remaining questions. There is some degree of overlap between the questions, you are asked to record a "yes", "no" or "can't tell" to most of the questions. A number of italicised prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

About: These checklists were designed to be used as educational pedagogic tools, as part of a workshop setting, therefore we do not suggest a scoring system. The core CASP checklists (randomised controlled trial & systematic review) were based on JAMA 'Users' guides to the medical literature 1994 (adapted from Guyatt GH, Sackett DL, and Cook DJ), and piloted with health care practitioners.

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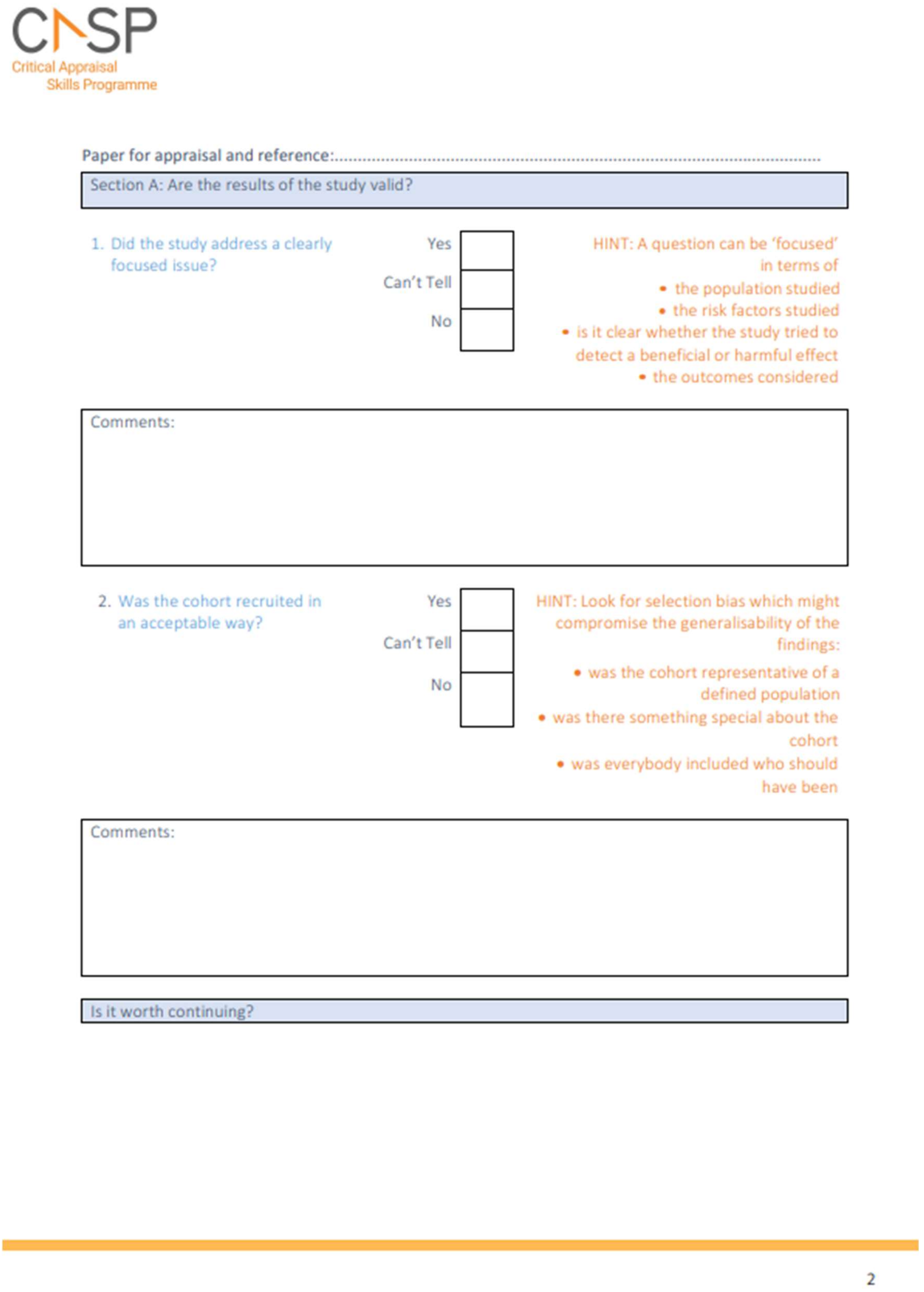

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Paper for appraisal and reference:...

Section A: Are the results of the study valid?

1. Did the study address a clearly focused issue?

Yes ☐
Can't Tell ☐
No ☐

HINT: A question can be 'focused' in terms of
- the population studied
- the risk factors studied
- is it clear whether the study tried to detect a beneficial or harmful effect
- the outcomes considered

Comments:

2. Was the cohort recruited in an acceptable way?

Yes ☐
Can't Tell ☐
No ☐

HINT: Look for selection bias which might compromise the generalisability of the findings:
- was the cohort representative of a defined population
- was there something special about the cohort
- was everybody included who should have been

Comments:

Is it worth continuing?

3. Was the exposure accurately measured to minimise bias?

Yes ☐
Can't Tell ☐
No ☐

HINT: Look for measurement or classification bias:
- did they use subjective or objective measurements
- do the measurements truly reflect what you want them to (have they been validated)
- were all the subjects classified into exposure groups using the same procedure

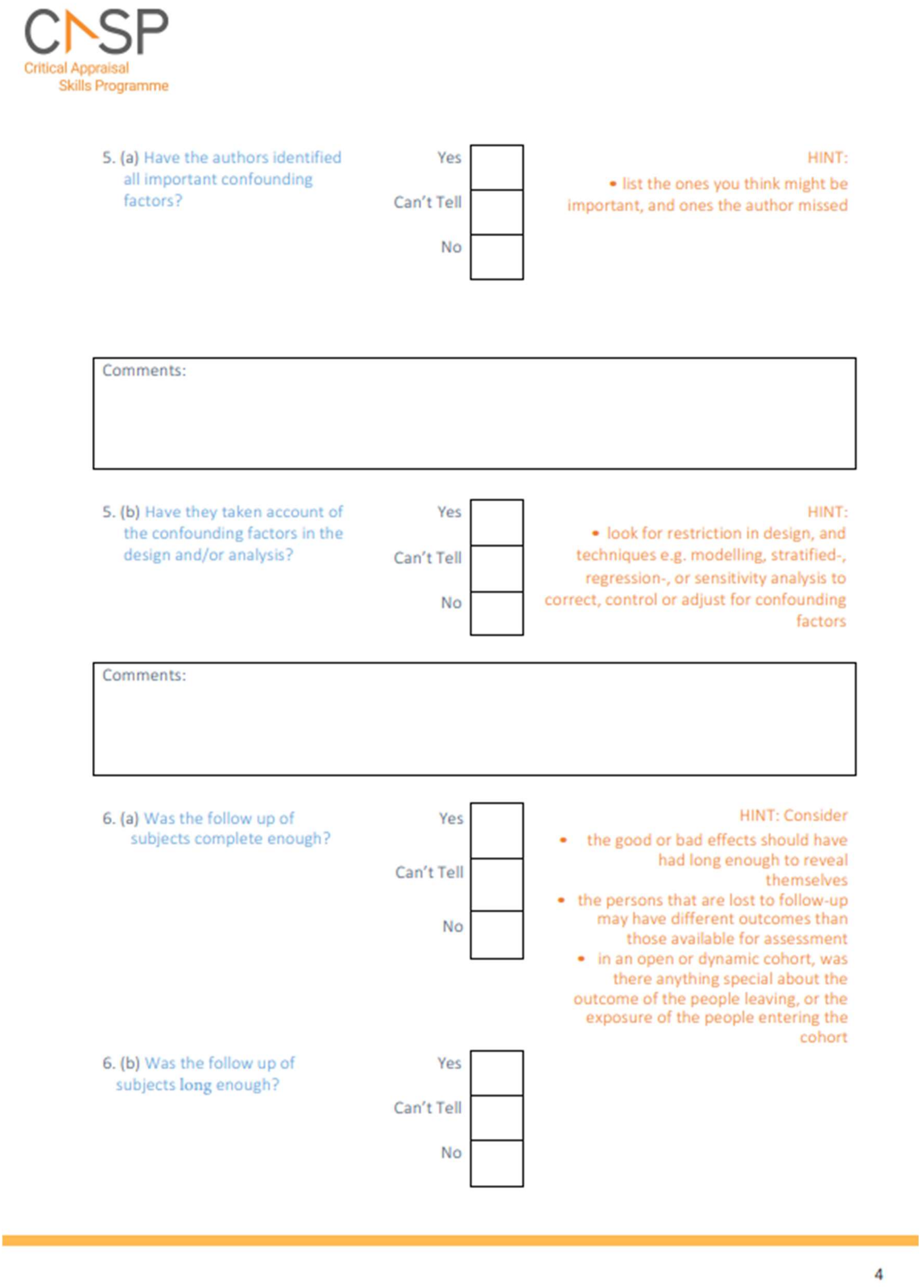
Comments:

4. Was the outcome accurately measured to minimise bias?

Yes ☐
Can't Tell ☐
No ☐

HINT: Look for measurement or classification bias:
- did they use subjective or objective measurements
- do the measurements truly reflect what you want them to (have they been validated)
- has a reliable system been established for detecting all the cases (for measuring disease occurrence)
- were the measurement methods similar in the different groups
- were the subjects and/or the outcome assessor blinded to exposure (does this matter)

Comments:



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5. (a) Have the authors identified all important confounding factors?	Yes ☐ Can't Tell ☐ No ☐	HINT: • list the ones you think might be important, and ones the author missed

Comments:

5. (b) Have they taken account of the confounding factors in the design and/or analysis?	Yes ☐ Can't Tell ☐ No ☐	HINT: • look for restriction in design, and techniques e.g. modelling, stratified-, regression-, or sensitivity analysis to correct, control or adjust for confounding factors

Comments:

6. (a) Was the follow up of subjects complete enough?	Yes ☐ Can't Tell ☐ No ☐	HINT: Consider • the good or bad effects should have had long enough to reveal themselves • the persons that are lost to follow-up may have different outcomes than those available for assessment • in an open or dynamic cohort, was there anything special about the outcome of the people leaving, or the exposure of the people entering the cohort
6. (b) Was the follow up of subjects long enough?	Yes ☐ Can't Tell ☐ No ☐	

Comments:

Section B: What are the results?

7. What are the results of this study?

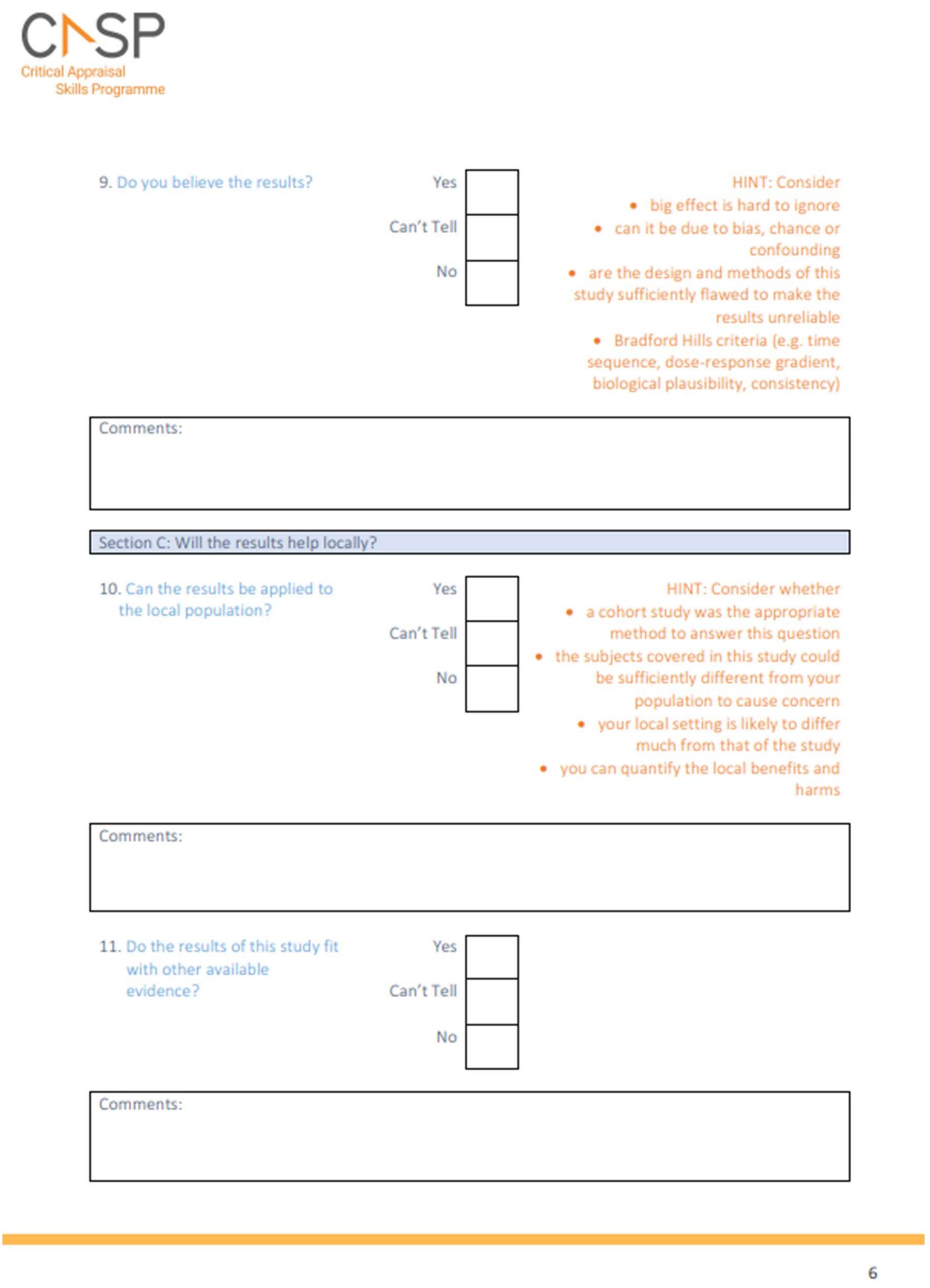
HINT: Consider
- what are the bottom line results
- have they reported the rate or the proportion between the exposed/unexposed, the ratio/rate difference
- how strong is the association between exposure and outcome (RR)
- what is the absolute risk reduction (ARR)

Comments:

8. How precise are the results?

HINT:
- look for the range of the confidence intervals, if given

Comments:



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9. Do you believe the results?

Yes ☐
Can't Tell ☐
No ☐

HINT: Consider
- big effect is hard to ignore
- can it be due to bias, chance or confounding
- are the design and methods of this study sufficiently flawed to make the results unreliable
- Bradford Hills criteria (e.g. time sequence, dose-response gradient, biological plausibility, consistency)

Comments:

Section C: Will the results help locally?

10. Can the results be applied to the local population?

Yes ☐
Can't Tell ☐
No ☐

HINT: Consider whether
- a cohort study was the appropriate method to answer this question
- the subjects covered in this study could be sufficiently different from your population to cause concern
- your local setting is likely to differ much from that of the study
- you can quantify the local benefits and harms

Comments:

11. Do the results of this study fit with other available evidence?

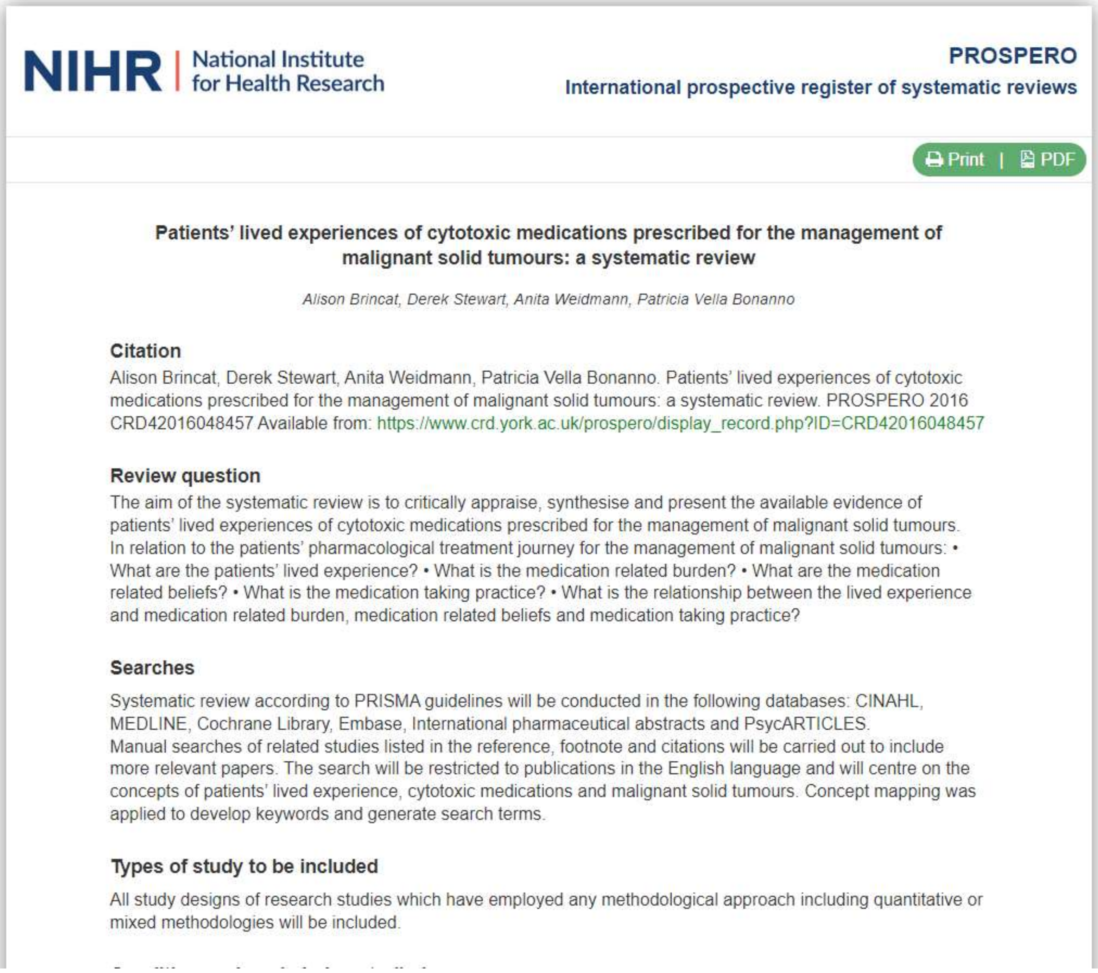
Yes ☐
Can't Tell ☐
No ☐

Comments:

12. What are the implications of this study for practice?	Yes ☐ Can't Tell ☐ No ☐	HINT: Consider • one observational study rarely provides sufficiently robust evidence to recommend changes to clinical practice or within health policy decision making • for certain questions, observational studies provide the only evidence • recommendations from observational studies are always stronger when supported by other evidence

Comments:

Appendix 3.2: Screenshot of the systematic review protocol



Patients' lived experiences of cytotoxic medications prescribed for the management of malignant solid tumours: a systematic review

Alison Brincat, Derek Stewart, Anita Weidmann, Patricia Vella Bonanno

Citation

Alison Brincat, Derek Stewart, Anita Weidmann, Patricia Vella Bonanno. Patients' lived experiences of cytotoxic medications prescribed for the management of malignant solid tumours: a systematic review. PROSPERO 2016 CRD42016048457 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42016048457

Review question

The aim of the systematic review is to critically appraise, synthesise and present the available evidence of patients' lived experiences of cytotoxic medications prescribed for the management of malignant solid tumours.
In relation to the patients' pharmacological treatment journey for the management of malignant solid tumours: • What are the patients' lived experience? • What is the medication related burden? • What are the medication related beliefs? • What is the medication taking practice? • What is the relationship between the lived experience and medication related burden, medication related beliefs and medication taking practice?

Searches

Systematic review according to PRISMA guidelines will be conducted in the following databases: CINAHL, MEDLINE, Cochrane Library, Embase, International pharmaceutical abstracts and PsycARTICLES.
Manual searches of related studies listed in the reference, footnote and citations will be carried out to include more relevant papers. The search will be restricted to publications in the English language and will centre on the concepts of patients' lived experience, cytotoxic medications and malignant solid tumours. Concept mapping was applied to develop keywords and generate search terms.

Types of study to be included

All study designs of research studies which have employed any methodological approach including quantitative or mixed methodologies will be included.

Appendix 3.3: Key findings of each included study in the systematic review with respect to review questions

Medicine-related beliefs				
Quantitative studies				
Study	**Theme**	**Main findings in relation to theme**	**Theme**	**Main findings in relation to theme**
Yokoyama dos Anjos and Zago, 2005	**Influence of family members**	• Influenced by her sister who died of cancer and other acquaintances • Other persons who had had cancer and survived	**Patients belief on treatment adverse effects**	• Expected treatment to make you feel weak, sick, vomiting, hair loss
	Influence of culture	• Disease is seen as a consequence of moral behaviour in Latin American culture. • Patient refer to cancer using a soft voice and terms such as this, the disease, that showing the associated stigma	**Patients belief on treatment efficacy**	• Chemotherapy is the treatment of the present that can lead to a future without disease and to survival • The uncertainty of the treatment
	Influence of media	• Knowledge about cancer and its treatment acquired from social group, media and other patients in outpatient clinic • Social groups portray the potential physical reactions to chemotherapy as standardised	**Preconceived notion of treatment**	• Treatment expected to cause suffering
			Patient belief on treatment cycle	• With every treatment cycle, patients' expectations of adverse effects got worse
	Influence of healthcare professionals	• Patient's trust in healthcare professional in accepting treatment	**Patients belief regarding post treatment**	• Making plans for trips following completion of treatment to regain strength • Expecting a better future post treatmen •
Bergkvist and Wengstrom, 2006	**Influence of media**	• Patients expected treatment effects as seen on TV	**Preconceived notion of treatment**	• A feeling of not wanting to share or talk about the diagnosis and treatments they were going through with anyone outside the immediate family.
			Patients belief regarding post treatment	• After treatment – looking forward to normal life • Worries about needing more treatment, and wondered if the treatment had been successful or whether they would have to continue and change treatment? Thoughts also concerned follow-up visits and monitoring the symptoms related to cancer
			Patients belief on treatment efficacy	• Worried about needing more treatment, and wondered if the treatment had been successful or whether they would have to continue and change treatment

Browall, Gaston-Johansson and Danielson, 2006	**Influence of media**	• Influenced by experience of others	**Preconceived notion of treatment**	• Expressed more fear about treatment than the illness itself • Constantly aware of the fact that they were dealing with and fighting a serious illness, even though they feeling healthy
			Patient belief on treatment cycle	• Dependency on the intake of medicine
			Patients belief on treatment adverse effects	• Expected chemotherapy to be horrible and makes patients very sick. They were also afraid of what the treatment would do to their looks (eg, loss of their hair), and this made them feel even sicker.
			Patients belief regarding post treatment	• They could never feel secure of a healthy and long life; they could only hope for it
Bell, 2009	**Influence of media**	• Influenced by media and support groups - statements were uncontested and accepted either as hypotheses about the mechanism of action of chemotherapy or as simple statements of fact	**Patients belief on treatment efficacy**	• Side effects perceived as a way of monitoring the overall effectiveness of chemotherapy • Dose reductions or treatment delays may reduce the efficacy of adjuvant chemotherapy • Participants who received oral chemotherapy generally perceived it to be less powerful than the intravenous form • Cancer could not have been ‚‚as bad'' because she received oral rather than intravenous chemotherapy.
	Influence of culture	• Chemotherapy considered as "source of suffering"	**Patients belief on treatment adverse effects**	• Cumulative and worsening adverse effects over time • Wonders whether chemotherapy is actually effective as patient is not experiencing many side effects and expecting that the more side effects you have, the better it is working
			Preconceived notion of treatment	• "Hurting the good cells & really hurting cancer cells" • Treatment is worse than cancer itself
Regnier Denois et al, 2011	**Influence of culture**	• patients feel uncomfortable to talk about certain side effects, such as vaginal dryness	**Patients belief on treatment efficacy**	• Afraid that the oncologist will change their treatment due to reported side effects and thus reduce the possibility of a response. • Side effects considered as a sign of treatment efficacy or the 'price to pay' for treatment efficacy
Gerber et al, 2012	**Influence of healthcare professionals**	• Trust in healthcare professionals' opinion as a driving force in their potential decision.	**Preconceived notion of treatment**	• Survival benefits, disease control and "buying time"

				• Maintenance treatment giving them a chance to be eligible for future treatments
	Influence of family members	• Feeling obliged to take treatment to prolong survival and be more with their family	**Patient belief on treatment cycle**	• Breaks between treatment provided an opportunity for recovery from adverse effects
Gassmann, Kolbe and Brenner, 2016	**Influence of family members**	• Feeling responsible towards their family: feeling obliged to survive even if this was associated with suffering and restrictions	**Patients' belief on treatment efficacy**	• Strong belief in the efficacy of oral chemotherapy
			Patient belief on treatment cycle	• Perceived the administration of chemotherapy in cycles to allow patients to be relieved from adverse effects. Additionally, they compared the interruptions to "holidays"
Komatsu et al, 2016			**Patients' belief regarding post treatment**	• Determined to enjoy their lives after treatment and acknowledged life priorities
Quantitative studies				
Timmers et al, 2015			**Preconceived notion of treatment**	• Most patients (55%, n=34) receiving erlotinib were "ambivalent" regarding this treatment in view of considering treatment to be of high necessity and high concern
			Patients' belief on treatment efficacy	• The mean score for treatment control at baseline in patients who will be receiving erlotinib was found to be 6.4±2.3
Timmers et al, 2016			**Preconceived notion of treatment**	• In accordance to beliefs gathered in Medicines Questionnaire (BMQ), half of the participants (50%, n=46) have accepted treatment with capecitabine as they considered these medicines to be of high necessity with low concern
			Patients' belief on treatment efficacy	• Quantitative data showed that in accordance to the Brief Illness perception questionnaire, with a response scale from 0 (minimum) to 10 (maximum), patients believed that capecitabine will achieve control of their disease with a score of 7.8±1.8 at baseline and slightly improved to 8.0±1.6 at week 2 of cycle 5
Medicine-related practice				

Qualitative studies				
Study	**Theme**	**Main findings in relation to theme**	**Theme**	**Main findings in relation to theme**
Yokoyama dos Anjos and Zago, 2005	**Patient feelings on treatment along the treatment journey**	• Being offered treatment led to hope		
	Network of support	• Support by family, close friends and other patients met at outpatients' clinic • Religion and spiritual groups as a coping mechanism		
Bergkvist and Wengstrom, 2006	**Patient feelings on treatment along the treatment journey**	• Experienced anxiety and stress days prior to treatment • Experienced relief when starting treatment • Patient felt lonely with no guidance on treatment		
	Coping with medicine	• Patients learned how to change eating habits		
	Network of support	• Family members supported patients by helping them to cook and also pushed them to eat and drink		
Browall, Gaston-Johansson and Danielson, 2006	**Patient feelings on treatment along the treatment journey**	• Felt chemotherapy as an assault on the body.		
	Coping with medicine	• Took time to adjust • Diverted negative thoughts and learning on how to prevent symptoms • Taking personal responsibility to feel physically and mentally better, example being more physically and socially active • Take a day at a time to be able to enjoy life a bit more • Learnt not to take anything for granted.		
	Network of support	• Relatives giving time and support to help patients • Lack of support lead to an imbalance in the relationships		
Bell, 2009	**Patient feelings on treatment along the treatment journey**	• Most patients seek certainty over indeterminacy • Delays in treatment caused marked distress during treatment and following the successful completion of treatment. Patients' accounts of dosage reductions or treatment delays showed that they continued to experienced doubts about its efficacy despite assured by oncologist.that such treatment changes did not reduce efficacy	**Dosing regimen adjustment by healthcare professionals**	• Strives to get full dose • Often do not receive their scheduled number of chemotherapy treatments
	Network of support	• Support groups	**Missing dose**	• Results from complications (low blood counts) and treatment side effects
Regnier Denois et al, 2011	**Coping with medicine**	• Strategies used to make treatment easier, to avoid forgetfulness and reduce anxiety: writing the dates of the cycles on a support, such as a calendar so that they organise their activities around the predicable side effects, the involvement of family and close friends in checking that the tablets are taken daily and the treatment cycles are respected	**Self alteration of treatment regimen**	• Most claimed that they had never forgotten their treatment • Variations in the timing for taking the treatment in terms of meal times, which has a real effect on the efficacy and toxicity of capecitabine • Associated with a change in their routine such as outing in town, visiting friends or going on holiday

				• under dosing by mistake because they had not understood their prescriptions. • Over dosing -take the forgotten treatment at the end of the cycle and a patinet did not always respect the break between cycles.
			Dosing regimen adjustment by health care providers	• Dose adjustment on advice given by the oncologist when the side effects were felt to be too severe or unsupportable to continue taking the medicine (e.g. severe digestive problems, bleeding)
Gerber et al, 2012	**Patient feelings on treatment along the treatment journey**	• Maintenance therapy as a chance to keep ‘‘doing something’’ instead of taking a wait-and see approach. • Maintenance therapy with an opportunity to keep up the ‘‘fight’’ against cancer • Reliance on treatment and fear of recurrence during a treatment break. • Patients with few side effects from their current chemotherapy were more enthusiastic about maintenance therapy • The limited survival benefit not worth undergoing treatment if patient quality of life likely to be poor		
Gassmann, Kolbe and Brenner, 2016	**Patient feelings on treatment along treatment journey**	• Felt highly responsible to adhere to their oral chemotherapy depending on the perceived severity of the illness. • Fearful of the cancer and ready to assume the considerable burden of therapy side effects. • Experienced emotional reluctance against the intake of up to four pills. Compared the pills with a toxic chemical mix:	**Missing dose**	• None of the patients reported to ever have missed a dose despite months of treatment
	Coping with medicine	• Developing coping strategies to integrate therapy into everyday life to ensure strict adherence: Counting pills, preparing them for the next day, programming an acoustic sign on their mobile phone and storing the packages in a clearly visible prominent place contributed to fulfill the prescribed regime.		
	Network of support	• Patients supported by their family	**Self-alteration of treatment regimen**	• The maximum deviation from the medication regimen was forgetting to take pills at the exact time but still within the time window for medicine intake • Sometimes uncertain if they had taken the correct number of pills or if they had missed the exact time for intake • Self alteration of treatment in view of running out of pills.

Komatsu et al, 2016	**Coping with medicine**	• Physically, they saved their energy by restricting their activities described as 'hibernating' • Emotionally, they concentrated on what they were able to do in their daily lives • Gained confidence in their ability to exert control over their lives by maintaining daily routines and completing tasks • Felt that life was worth living when they did something for someone else		
	Network of support	• Family members were asked to help patients or arrange a helper service		
Quantitative studies				
Timmers et al, 2015			**Self-alteration of treatment regimen**	the patients' mean adherence to erlotinib for the treatment of non-small cell lung cancer was 96.8% ± 4.0% using data from Medication Event Monitoring System (MEMS)
			Dosing regimen adjustment by healthcare professionals	Discontinuation of treatment was experienced amongst 26 patients from 62 patients receiving erlotinib (42%). Reasons for discontinuation of treatment with antineoplastic medicines were identified to be: • Occurrence of adverse effect (31% of 26 patients – erlotinib) • Progression of the disease (69% of 26 patients – erlotinib) Most of the patients (88% of 26 patients – erlotinib) discontinued treatment on the oncologists' instructions.
Timmers et al, 2016			**Self-alteration of treatment regimen**	The pill count method used also showed a high adherence rate with capecitabine amongst patients being treated, with a mean adherence rate of 99.3%. Only 8% (n=7) of the patients had less than 95% of treatment whilst one patient took "*more than 105% of the prescribed dose*"
			Dosing regimen adjustment by healthcare professionals	At least one variation in the initial dosing regimen of capecitabine was recorded amongst 62% (n=57) of the patients. This being manifested by decreasing (30%, n=28) or increasing (13%, n =12) the dose, delaying the next treatment cycle (35%, n=32) or shorten the number of treatment cycles (21%, n=19). Multivariate analysis identified emotional response to the disease (OR 1.32, 95% CI: 1.10–1.59) and the number of co-medications (OR 1.19, 95% CI: 1.03–1.39) as factors associated with variation of dosing regimen. Several symptoms were frequently reported by

				patients during treatment, with depression (p=0.025) and skin problems (p=0.004) being the commonest in the first two cycles of treatment with capecitabine and which also warrants variation in dosing regimen

Medicine-related burden

Qualitative studies

Study	Theme	Main findings in relation to theme	Theme	Main findings in relation to theme	Theme	Main findings in relation to theme
Yokoyama dos Anjos and Zago, 2005					**Physical adverse effects**	• Feeling sick • Sore throat • Vomiting • Bad taste • Worsening of adverse following the third cycle
Bergkvist and Wengstrom, 2006	**Medicine characteristics**	• Effected by the colour of chemotherapy • Feeling chained to the infusion set • Effected by the nurse wearing protective equipment to administer chemotherapy			**Physical adverse effects**	• Nausea • Vomiting • Lethargy • Alopecia • Neutropenic infections • Anaemia • Diarrhoea • Skin reactions • Constipation • Bad smell • Weight loss • Metallic tase Insomnia
					Psychological adverse effects	• Degrading anxiety-provoking experience • Fear of inability to recognise self due to sickness and chance in aesthetics
Browall, Gaston-Johansson and Danielson, 2006					**Physical adverse effects**	• Change in smell and taste • Alopecia • Constipation • Fatigue • Change in appearance
					Psychological adverse effects	• Deteriorated memory • Difficulties with concentration • Mental fatigue
Bell, 2009	**Medication characteristics**	Oral vs intravenous formulations			**Physical adverse effects**	• Peripheral neuropathy – even in post treatment survivors • Some patients remained symptom-free throughout their full course of treatment

						• Others had severe adverse effects that required hospitalisation
Regnier Denois et al, 2011			**Adherence to prescribed dose and schedule**	• Patients considered it important to take their treatment exactly as prescribed. • Multiplicity of previous treatments results in lower adherence to treatment	**Reporting of adverse events**	• Delayed reporting of side effects even for months with worsening of side effects
Gerber et al, 2012					**Physical adverse effects**	• Shortness of breath • Acute diarrhoea • Oral mucus and gingivitis • Hairloss • Lethargy
Gassmann, Kolbe and Brenner, 2016	**Medication characteristics**	• Fear of gelatin coating of pills staying in his stomach. • Intake of pills associated with dependency. • Size of the pills caused physical revulsion (difficult to swallow and metallic after-taste) • Other pills do not have this vital importance and thus can be more easily forgotten.	**Barriers to adherence**	• Feeling torn between necessity of adhering to oral chemotherapy and the practical as well as emotional difficulties of everyday life • Interruptions of daily routine were challenging, as participants felt the risk of forgetting their pills or not taking them in advance • Some of them left the house only if absolutely necessary; avoided visiting friends or stopped going out in the evening because changes in daily routine always had to be planned according to the complicated oral chemotherapy regimen. They described how they had to get up between five and seven o'clock in the morning every day in order to comply with the time lag between pill intake and nutrition intake.	**Psychological adverse effects**	• The pills dominate the mind • Lack of concentration • Preoccupied with adherence to oral chemotherapy • The mere thought of the pills was enough to trigger vomiting
					Physical adverse effects	• Exhaustion hindering enjoyable social activity • Cold and painful tingling in the hands and feet • Skin changes – rash • Dysesthesia. • Mild alopecia - thin and curlier hair structure. • Brittle nails • Physical effects had an impact on participants' body image
					Reporting of adverse events	• Invisible treatment toxicities led to underreporting of side effects for weeks later or until their next scheduled appointment
Komatsu et al, 2016					**Physical effects**	• loss of appetite • fatigue • nausea • numbness

					Psychological adverse effects	• loss of control • overwhelmed • sad • depression • feeling lonely and tearful. • Empty head and fog causing lack of concentration
Quantitative studies						
Timmers et al, 2015					**Physical effects**	In the quantitative analysis, rash (86.4%), fatigue (82.6%) and cough (75%) were the most common patient-reported symptoms after 2 months of initiation of treatment with erlotinib
					Psychological adverse effects	The baseline score of the mental component of SF-12 Health Survey was similar (47.7±8.2) in patients diagnosed with non-small cell lung cancer
Timmers et al, 2016					**Physical effects**	Fatigue was the most reported adverse event with capecitabine at baseline (78.7%) and increased to 91.1% at cycle 5. The commonest patient-reported symptoms with capecitabine at cycle 5 were hand and foot syndrome (94.5%), fatigue (91.1%) and flatulence (67.9%). Thirty three percent of patients blamed side effects for the discontinuation of treatment with capecitabine prior to completion of the 5th cycle
					Psychological adverse effects	As treatment cycles progressed, patients remarked feeling calmer and more peaceful (mean value of the mental component of SF-12 Health Survey improved from 47.1±7.5 at baseline to 50.4±5.4 at cycle 5

Medicine-related burden (continuation)

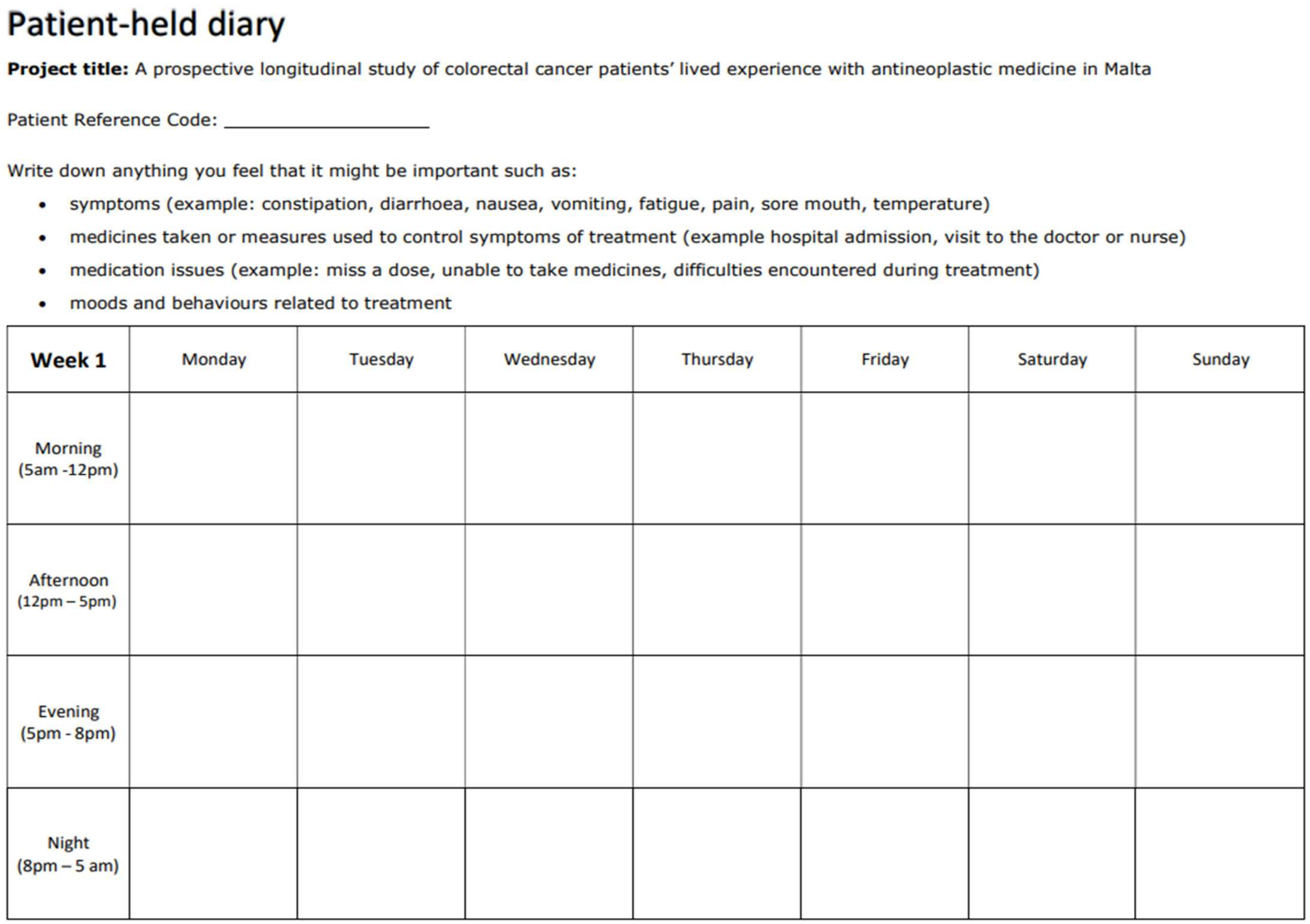
Qualitative studies

Study	Theme	Main findings in relation to theme	Theme	Main findings in relation to theme
Yokoyama dos Anjos and Zago, 2005	**Effect on daily routine**	• Experiencing periods that effects of treatment made it impossible to work		
	Effect on relationships	• Strengthening the relationship with her father • Difficulty with maintaining good affective relationship with children and worried with young son who required more attention • Increased friendship • Relationships help her to express herself		
	Effect on financial status	• Adverse effects made patient stop working for some periods with a consequence reduction of her financial resources. • Able to continue working and overcome financial difficulties		
Bergkvist and Wengstrom, 2006			**Healthcare support and provision of information**	•Lack of information provision on side effects • Lack of a soothing environment at the hospital •Lack of support from healthcare staff on an individual level
			Logistics	•Being admitted in a four-bedded room Negative (experienced by seeing other cancer patients dying) and positive interactions (companionship and support) experienced with healthcare staff and fellow patients
Browall, Gaston-Johansson and Danielson, 2006	**Effect on daily routine**	• Developing a new normalcy and identity	**Health care support and provision of information**	•The experience of variation between different professionals' attitude, knowledge and empathy
	Effect on financial status	• Felt pressured by society and healthcare professionals to get back to work • Other patients experienced difficulties going back to work • Patients who continued working considered the illness being a part of life and work provided some distance from the illness		
	Effect on relationship	• Had to hold back their own fear and not show that they were sad, so not to be a burden their relatives • Losing friends as they consistently spoke about cancer • Withdrawing from friends to avoid bad reaction from others and the fact that cancer was regarded with horror		
Bell, 2009			**Research associated burden**	•Still using same treatment that has been around for 20 years
Regnier Denois et al, 2011			**Health care support and**	•Provided patients little information about the treatment

			provision for information	
Gerber et al, 2012			**Research-associated burden**	•Lack of available lung cancer treatments with an enthusiasm for maintenance treatment for prolonging of life until new treatment emerge
			Logistics problem	•Clinic time weighed against the potential benefits of treatment •Transportation and distance as logistic barriers to treatment
Gassmann, Kolbe and Brenner, 2016	**Effect on daily routine**	• Medication regimen and side effects determine everyday life • Oral chemotherapy is omnipresent by determining the participants' thinking and daily lives • Being adherent required restrictions in daily life. Some participants gave up their hobbies because of side effects	**Health care support and provision for information**	•Patients feeling insecure about not having professional counselling at home to help them solving practical problems
Komatsu et al, 2016	**Effects on daily routine**	• Patients' lives were suddenly disturbed and became uncertain with the diagnosis of cancer • Severity of symptoms restricted their daily activities and experienced loss of control		
	Relationships with others	• Patients felt isolated as they experienced changes in their daily lives and relationships with others		
Quantitative studies				
Timmers et al, 2015				
Timmers et al, 2016				

Appendix 4.1: Patient diary

A. English version



Patient-held diary

Project title: A prospective longitudinal study of colorectal cancer patients’ lived experience with antineoplastic medicine in Malta

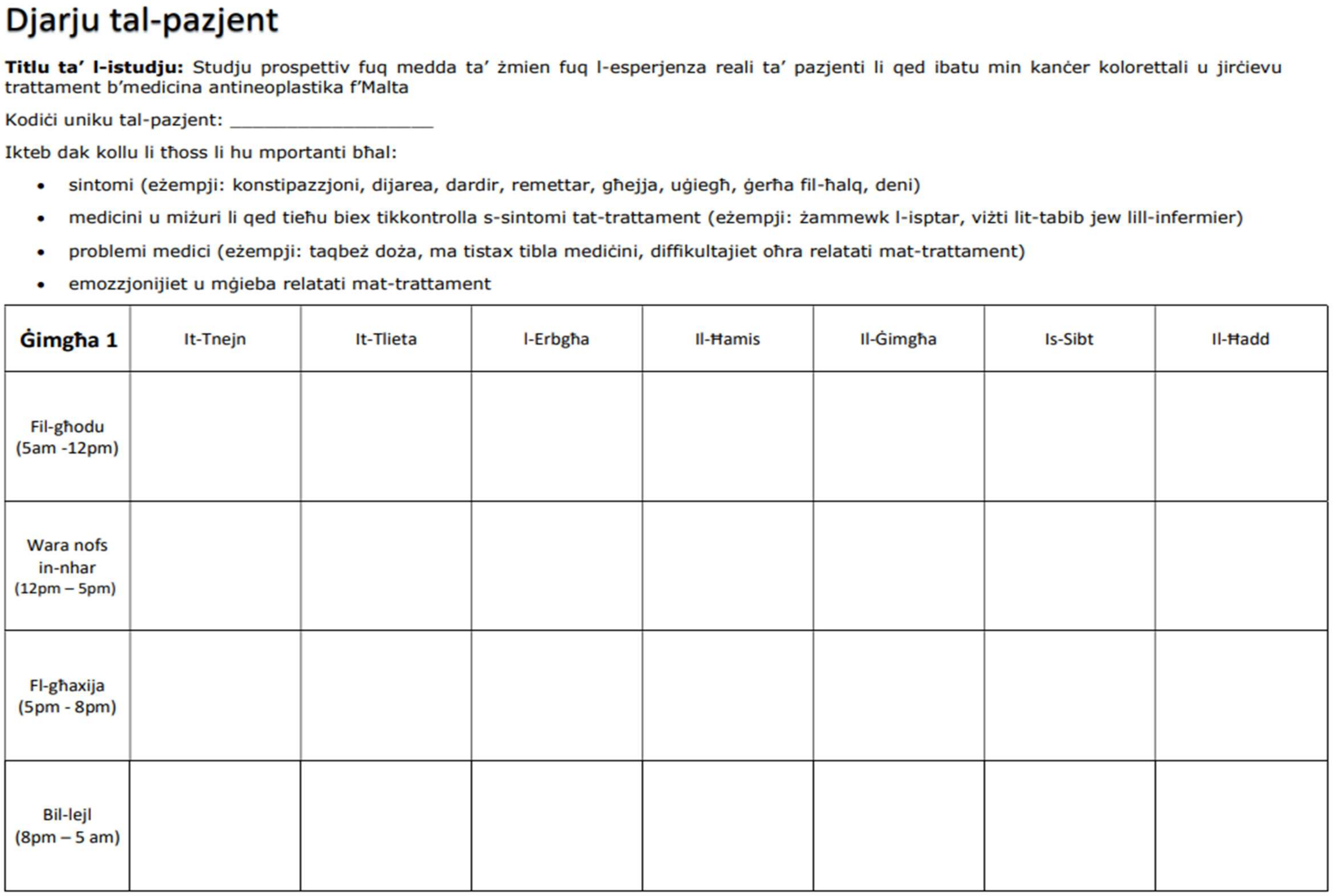
Patient Reference Code: ___________________

Write down anything you feel that it might be important such as:

- symptoms (example: constipation, diarrhoea, nausea, vomiting, fatigue, pain, sore mouth, temperature)
- medicines taken or measures used to control symptoms of treatment (example hospital admission, visit to the doctor or nurse)
- medication issues (example: miss a dose, unable to take medicines, difficulties encountered during treatment)
- moods and behaviours related to treatment

Week 1	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Morning (5am -12pm)							
Afternoon (12pm – 5pm)							
Evening (5pm - 8pm)							
Night (8pm – 5 am)							

B. Maltese language



Djarju tal-pazjent

Titlu ta' l-istudju: Studju prospettiv fuq medda ta' żmien fuq l-esperjenza reali ta' pazjenti li qed ibatu min kanċer kolorettali u jirċievu trattament b'medicina antineoplastika f'Malta

Kodiċi uniku tal-pazjent: ___________________

Ikteb dak kollu li tħoss li hu mportanti bħal:

- sintomi (eżempji: konstipazzjoni, dijarea, dardir, remettar, għejja, uġiegħ, ġerħa fil-ħalq, deni)
- medicini u miżuri li qed tieħu biex tikkontrolla s-sintomi tat-trattament (eżempji: żammewk l-isptar, viżti lit-tabib jew lill-infermier)
- problemi medici (eżempji: taqbeż doża, ma tistax tibla mediċini, diffikultajiet oħra relatati mat-trattament)
- emozzjonijiet u mġieba relatati mat-trattament

Ġimgħa 1	It-Tnejn	It-Tlieta	l-Erbgħa	Il-Ħamis	Il-Ġimgħa	Is-Sibt	Il-Ħadd
Fil-għodu (5am -12pm)							
Wara nofs in-nhar (12pm – 5pm)							
Fl-għaxija (5pm - 8pm)							
Bil-lejl (8pm – 5 am)							

Appendix 4.2: Information sheet to patients

A. English version

RESEARCH TEAM: Alison Brincat Dr Anita E Weidmann
Professor Derek Stewart Dr Patricia Vella Bonanno

27th February 2018

Participant Information Sheet for patient

Project title: A prospective longitudinal study of colorectal cancer patients' lived experience with antineoplastic medicine in Malta

We would like to invite you to participate in a research study entitled 'A prospective longitudinal study of colorectal cancer patients' lived experience with antineoplastic medicine in Malta'. Whilst thanking you for taking the time to read this information carefully, do not hesitate to clarify anything that is not clear or if you would like further information.

What is the purpose of the study?
The purpose of the study is to explore the medication related beliefs, medication taking practice and medication related burden of patients suffering from gastrointestinal cancer planned to receive anticancer medicines.

Why have I been chosen?
Patients suffering from gastrointestinal cancer and planned to receive anti-cancer medicines (either capecitabine and oxaliplatin infusion (XELOX) or fluorouracil infusion and oxaliplatin infusion (FOLFOX)) are selected. If you stop the planned FOLFOX or XELOX treatment and initiate another treatment, you will be stopped from further participation in the study.

Do I have to take part?
Participation in the study is voluntary and you have no obligation to participate. All information provided is confidential. A decision to withdraw, or a decision not to take part, will not affect the standard of care you receive now or in the future. Anonymised data collected until the point of completion of the study may be utilised for research purposes.

What do I have to do if I take part?
If you agree to take part in the study, you will be asked to take part in four (4) interviews to ask you some questions about your experiences with medicines along your treatment journey. The interviews will last approximately thirty (30) to forty-five (45) minutes up to a maximum of 60 minutes each. The interviews will be scheduled at a time and place that is mutually convenient. These will only be conducted on one-to-one basis after you have given your consent. The first interview will take place at the beginning of treatment and then every 12 weeks. The conversation will be audiotaped to ensure that your responses are captured accurately and will be used so that the researcher can later transcribe the data. You

may also be invited to keep a diary to record any event you deem to be important and share it with the research team at your own discretion. Your hospital records may be accessed for further information regarding your treatment.

If you are willing to participate in this study, we would also like you to provide us with the name of a person highly involved in your care and provide him/her the permission to talk about your treatment in two (2) interviews:

- name of nominee
- relationship to the nominee
- e-mail address or telephone number

These details may be provided directly to the researcher during the interview or via e-mail: a.brincat@rgu.ac.uk

What are the possible benefits of taking part?
There is no direct benefit to you from taking part. Participation in the study will help to understand the needs of cancer patients and identify initiatives which may support cancer patients during treatment with antineoplastic medicines.

Will my contribution to this study be kept confidential?
Yes. Information provided will be kept strictly confidential. Names of participants will not appear in any publication as unique patient reference codes will be used. Recordings of the interview will be destroyed after transcribing. Hard copies of documents are kept for 5 years in a locked drawer before shredding, in line with standard operating procedures of Robert Gordon University. Data is also secured in password protected documents in the computer for 5 years.

What will happen to the results of the research study?
The findings will be presented at international conferences and submitted for publication in a peer reviewed journal. A copy of publication or report may be requested.

Who is organising and funding the research?
This project is organised by the Robert Gordon University in Scotland as part of MRes/PhD study and will be partially funded by the Get Qualified Scheme.

Who has reviewed the study?
The study has been reviewed by academic experts, the Robert Gordon Ethics Committee and Health Ethics Committee within the Ministry for Health, Malta.

What do I do now?
If you are interested in taking part in this study you should complete the attached consent form and contact the research team to participate.

We would also like you to provide us with the name of a person highly involved in your care and provide him/her the permission to talk about your treatment:

- name of nominee
- relationship to the nominee
- e-mail address or telephone number

If you have any questions or would like further information, please do not hesitate to contact Alison Brincat via e-mail a.brincat@rgu.ac.uk or phone 79933433.

B. Maltese version

Tim tar-riċerka: Alison Brincat
Professor Derek Stewart
Dr Anita E Weidmann
Dr Patricia Vella Bonanno

27 ta’ Frar 2018

Karta ta’ Informazzjoni ghall-Parteċipant bħala pazjent

Titlu ta’ l-istudju: Studju prospettiv fuq medda ta’ żmien fuq l-esperjenza reali ta’ pazjenti li qed ibatu minn kanċer kolorettali u jirċievu trattament b’mediċina antineoplastika f’Malta

Aħna nixtiequ nistiednuk biex tipparteċipa fi studju bit-titlu ‘Studju prospettiv fuq medda ta’ żmien fuq l-esperjenza reali ta’ pazjenti li qed ibatu minn kanċer kolorettali u jirċievu trattament b’mediċina antineoplastika f’Malta’. Filwaqt li nirringrazzjawk tal-ħin tiegħek biex taqra din l-informazzjoni bil-galbu, toqgħodx lura milli tiċċara xi punti jew tistaqsi għal iktar informazzjoni.

X’inhu l-għan tal-istudju?
L-għan tal-istudju huwa li jesplora it-twemmin, il-prattika tat-teħied u r-riperkussjoni li l-pazjent qed jieħu parti mill-kura kontra l-kanċer kolorettali.

Għaliex intagħżilt jien?
Il-pazjenti li ntagħżlu għall-istudju qed ibatu mil-kanċer kolorettali u huwa pjanat li ser tirċievi mediċini kontra l-kanċer (capecitabine u infużjoni ta’ oxaliplatin (XELOX) jew infużjoni ta’ fluorouracil u infużjoni ta’ oxaliplatin (FOLFOX)). Jekk inti ma tieħux dan it-trattament pjanat u ser tibda trattament ieħor, inti mitlub li tieqaf tipparteċipa f’dan l-istudju.

Għandi nieħu sehem?
Din il-karta ta’ informazzjoni ma ġġor l-ebda obligu min-naħa tiegħek u l-parteċipazzjoni tiegħek hija biss volontarja. Kull informazzjoni provduta hija kunfidenzjali. Id-deċizjoni li tieqaf mill-istudju jew li ma tiehux sehem ma taffetwax il-kura tas-saħħa tiegħek li qed tieħu issa jew fil-futur. L-informazzjoni anonima li tkun nġabret sat-tlestijja ta’ l-istudju tista’ tintuża għal għanijiet ta’ riċerka.

Kif nagħmel biex nipparteċipa?
Jekk taqbel li tipparteċipa f’dan l-istudju, inti ser tkun mitlub li tieħu sehem f’erbgħa (4) intervisti fejn tiġi mistoqsi dwar l-esperjenza tiegħek b’dawn il-mediċini matul il-vjaġġ tiegħek bit-trattament. Kull intervista ddum madwar tletin (30) sa ħamsa u erbgħin (45) minuta. L-intervisti jkunu skedati f’post u ħin li jkun konvenjenti għalina tnejn. Dawn l-intervisti one-to-one isiru wara li inti tagħti il-kunsens ta’ parteċipazzjoni. L-ewwel intervista ssir fil-bidu tat-trattament u mbagħad kull tnax-il ġimgħa. Id-diskursata ser tiġi rekordjata biex naċċertaw li r-risposti ġew meħuda korrettament u jintużaw mir-riċerkatur biex tinkiteb ir-riċerka. Inti ser tkun wkoll mistieden li żżomm djarju fejn tindika xi avveniment important u jekk tkun trid

taqsam din l-esperjenza mat-tim tar-riċerka. Ir-records mediċi tiegħek jistgħu wkoll jigu aċċessati għal aktar informazzjoni dwar it-trattament.

Jekk inti mħajjar tippartecipa f'dan l-istudju, nitolbuk tipprovdilna isem ta' persuna li l-aktar involuta fil-kura tiegħek u provdi permess lilu/lilha biex titkellem fuq il-kura tiegħek f'żewġ (2) intervisti:

- isem ta' min qed tinnomina
- relazzjoni ma' din il-persuna
- e-majl jew numru ta' telefon

Dawn id-dettalji jistghu jiġu provduti direttament lir-riċerkatur waqt l-intervista jew b'e-majl: a.brincat@rgu.ac.uk

X'inhuma l-benefiċċji possibli jekk nieħu sehem?
Il-parteċipazzjoni tiegħek f'dan l-istudju ma tirriżultax f'benefiċċju dirett imma twassal biex nifhmu aħjar il-bżonnijiet ta' pazjenti li jbatu bil-kanċer u jgħina nagħrfu inizzjativi u jinħolqu servizzi addattati għall-persuni morda bil-kanċer u qed jieħdu trattament b'mediċina antineoplastika.

L-informazzjoni li ser nipprovdi jien ser tibqa' kunfidenzjali?
Iva. L-informazzjoni mgħotija hija kunfidenzjali. L-ismijiet tal-parteċipanti mhux ser jidhru fl-ebda publikazzjoni għax ser tintuża sistema ta' kodiċi uniċi. L-intervista rekordjata ser tiġi meqruda wara li tiġi transkritta. Kopji stampati tad-dokumenti ser jinżammu ġo kexxun msakkar għal-ħames snin qabel it-tqattigħ, f'konformità ma 'standard operating procedures' tal-Universita' ta' Robert Gordon. L-informazzjoni ser tinżamm ukoll f'dokumenti protetti minn kodiċi sigrieti fil-kompjuter għal-ħames snin.

X'jigri bir-riżultati ta' din ir-riċerka?
Ir-riżultati ikunu preżentati f'konferenzi internazzjonali u ppublikati f'ġurnali xjentifiċi. Jekk tkun tixtieq kopja tal-publikazzjoni jew tar-rapport, din tista' tiġi pprovduta lilek.

Min qed jorganizza u jħallas din ir-riċerka?
Dan l-istudju huwa organizzat mill-Universita' ta' Robert Gordon ġewwa l-Iskozja bħala parti minn studju ta' MRes/PhD u se jkun iffinanzjat parzjalment mill-iskema 'Get Qualified'.

Għaliex għandi nafda dan l-istudju?
Dan l-istudju ġie rivedut min esperti akkademiċi, mill-kumitat ta' l-Etika mill-Universita' ta' Robert Gordon u l-kumitat ta' l-Etika tas-Saħħa fi ħdan il-Ministeru tas-Saħħa f'Malta.

X'għandi nagħmel issa?
Jekk inti nteressat li tippartecipa f'dan l-istudju, imla' il-karta ta' kunsens u nforma lit-tim tar-riċerka.

Aħna nistiednuk ukoll li tipprovidilna isem ta' persuna li hija nvoluta direttament fil-kura tiegħek u tgħati il-kunsens tiegħek lil din il-persuna biex titkellem fuq it-trattament tiegħek:

- isem ta' min qed tinnomina
- relazzjoni ma' din il-persuna
- e-majl jew numru ta' telefon

Jekk għandek xi mistoqsijiet jew tixtieq iktar informazzjoni, tista' ssaqsi lil Alison Brincat permezz ta' e-majl a.brincat@rgu.ac.uk jew cempel fuq 79933433.

Appendix 4.3: Consent form of patients

A. English version

ROBERT GORDON UNIVERSITY ABERDEEN

27th February 2018

Consent form for patient

Project title: A prospective longitudinal study of colorectal cancer patients' lived experience with antineoplastic medicine in Malta

Once you read the Information sheet, please initialise the following statements and sign underneath to give your consent to participate in the study.

1. I confirm that I have read and understood the information sheet dated 27th February 2018 for the above study. Initials:_______
2. I confirm that I have had the opportunity to ask questions about the study and have had these answered satisfactorily. Initials:_______
3. I understand that my participation is voluntary and that I am free to withdraw at any time without my medical care or legal rights being affected. Anonymised data collected until the point of completion of the study may be utilised for research purposes. Initials:_______
4. I understand that the research team may wish to review my hospital records. Initials:_______
5. I understand that I will be asked to take part in an audiorecorded in-depth interview. Initials:_______
6. I agree that the audio recordings will be stored on password protected network file storage space provided by Robert Gordon University and destroyed after data is transcribed or on my withdrawal from participation. Initials:_______
7. I agree to the use of my direct quotes in any reports or publications, if they are used in such a way that I will not be identified. Initials:_______
8. I understand that the findings will be utilised for research purposes. Initials:_______
9. I understand that relevant data collected during the study may be looked at by responsible individuals from Robert Gordon University. I give permission to these individuals to have access to this data. Initials:_______
10. I understand that hard copies of documents are kept for 5 years in a locked drawer before shredding, in line with standard operating procedures of Robert Gordon University. Data is also secured in password protected documents in the computer for 5 years. Initials:_______
11. I hereby assign the copyright for my research contribution to Robert Gordon University. Initials:_______
12. I agree to participate in this study. Initials:_______

I, the patient who have nominated __________________________ as significant other(s) and providing permission to disclose sensitive and confidential information in line with the statements mentioned above.

Name of participant: ___________________________________

Signature of participant: ________________________________

Date: ____________

Name of researcher: Alison Brincat

Signature of researcher: ______________________

Contact details of researcher: Email: a.brincat@rgu.ac.uk or contact number: 79933433

B. Maltese version

ROBERT GORDON UNIVERSITY ABERDEEN

27 ta’ Frar 2018

Il-formola ta’ kunsens għall-pazjent

Titlu ta’ l-istudju: Studju prospettiv fuq medda ta’ żmien fuq l-esperjenza reali ta’ pazjenti li qed ibatu minn kanċer kolorettali u jirċievu trattament b’mediċina antineoplastika f’Malta

Wara li inti qrajt il-karta ta’ informazzjoni dwar dan l-istudju, inti mistenni li timmarka dawn is-sentenzi bl-inizjali tiegħek u tiffirma fl-aħħar tal-formola biex tagħti il-kunsens tiegħek biex tipparteċipa f’dan l-istudju.

1. Jiena nikkonferma li qrajt u fhimt il-karta ta’ informazzjoni dwar l-istudju msemmi hawn fuq bid-data 27 ta’ Frar 2018. Inizjali:_______
2. Jiena nikkonferma li kelli l-opportunita li nsaqsi mistoqsijiet dwar l-istudju u dawn ġew imwieġba b’mod sodisfaċenti. Inizjali:_______
3. Jiena nifhem li il-parteċipazzjoni tiegħi hija wahda volontarja u li nista’ nieqaf nipparteċipa fl-istudju meta nixtieq mingħajr ma tiġi mittifsa il-kura medika u d-drittijiet legali tiegħi. L-informazzjoni anonima li tkun nġabret sat-tlestijja ta’ l-istudju tista’ tintuża għal għanijiet ta’ riċerka. Inizjali:_______
4. Jiena nifhem li t-tim tar-riċerka jkunu jixtiequ jaraw ir-records mediċi tiegħi. Inizjali:_______
5. Jiena nifhem li ser niġi mistoqsi biex nipparteċipa f’intervista fit-tul li tiġi rrekordjata. Inizjali: ________
6. Jiena naqbel li l-intervista rrekordjata tiġi miżmuma fi spazju provdut mil-Universita’ ta’ Robert Gordon li hu protett minn kodiċi u tiġi meqruda wara li tiġi transkritta jew wara li nwaqqaf il-parteċipazzjoni tiegħi. Inizjali:___________
7. Jiena naqbel li jkun hemm użu ta’ kwotazzjonijiet diretti f’rapporti u publikazzjonijiet sakemm jiena ma niġix identifikata. Inizjali:_______
8. Jiena nifhem li r-riżultati tal-istudju se jintużaw għal-għanijiet mediċi u xjentifiċi. Inizjali:_______
9. Jiena nifhem li l-informazzjoni relevanti miġbura fl-istudju tista’ tiġi analizata b’mod responsabbli minn individwi oħra mill-Universita’ ta’ Robert Gordon. Jien nagħti kunsens lil dawn l-individwi li jkollhom aċċess ghall-informazzjoni. Inizjali:_______
10. Jiena nifhem li kopji stampati tad-dokumenti ser jinzammu ġo kexxun msakkar għall-ħames snin qabel it-tqattigħ, f'konformità ma 'standard operating procedures’ tal-Universita’ ta’ Robert Gordon. L-informazzjoni ser tinżamm ukoll f’dokumenti protetti minn kodici sigrieti fil-kompjuter għal-ħames snin. Inizjali:_______
11. Jiena nagħti id-dritt tal-copyright għal għanijiet ta riċerka lil Universita’ ta Robert Gordon. Inizjali:_______

12. Jiena naqbel li nipparteċipa f’dan l-istudju. Inizjali:_______

Jiena, il-pazjent qed ninomina lil ___________________________ bħala persuna importanti fil-kura tiegħi u qed nagħti il-permess tiegħi biex tipprovdi informazzjoni sensittiva u kunfidenzjali li huma konformi mas-sentenzi msemmija hawn fuq.

Isem il-parteċipant: ____________________________________

Firma tal-parteċipant: __________________________________

Data: ____________

Isem ir-riċerkatur: Alison Brincat

Firma tar-riċerkatur: ______________________

Dettalji biex tagħmel kuntatt mar-riċerkatur:
Emajl a.brincat@rgu.ac.uk jew telefon 79933433

Appendix 4.4: Robert Gordon University Ethics Approval

ROBERT GORDON
UNIVERSITY ABERDEEN

SCHOOL OF PHARMACY & LIFE SCIENCES
Robert Gordon University
Sir Ian Wood Building
Garthdee Road
Aberdeen
AB10 7GJ
United Kingdom
Tel: 01224 262500/2800
www.rgu.ac.uk

Ref: S131

09 May 2018

Dear Alison,

Re.: A prospective longitudinal study of colorectal cancer patients' lived experience with antineoplastic medicines in Malta.

The School Research Ethics Committee has assessed the amendments you submitted and the overall decision is that there are no ethical issues with your project.

I can now confirm that you are able to proceed with your research and any further ethics applications.

Should there be any further amendments to this project during the research we would advise you to consult with the convener of the ethics committee as to whether a further ethical review would be required.

We wish you success with your project.

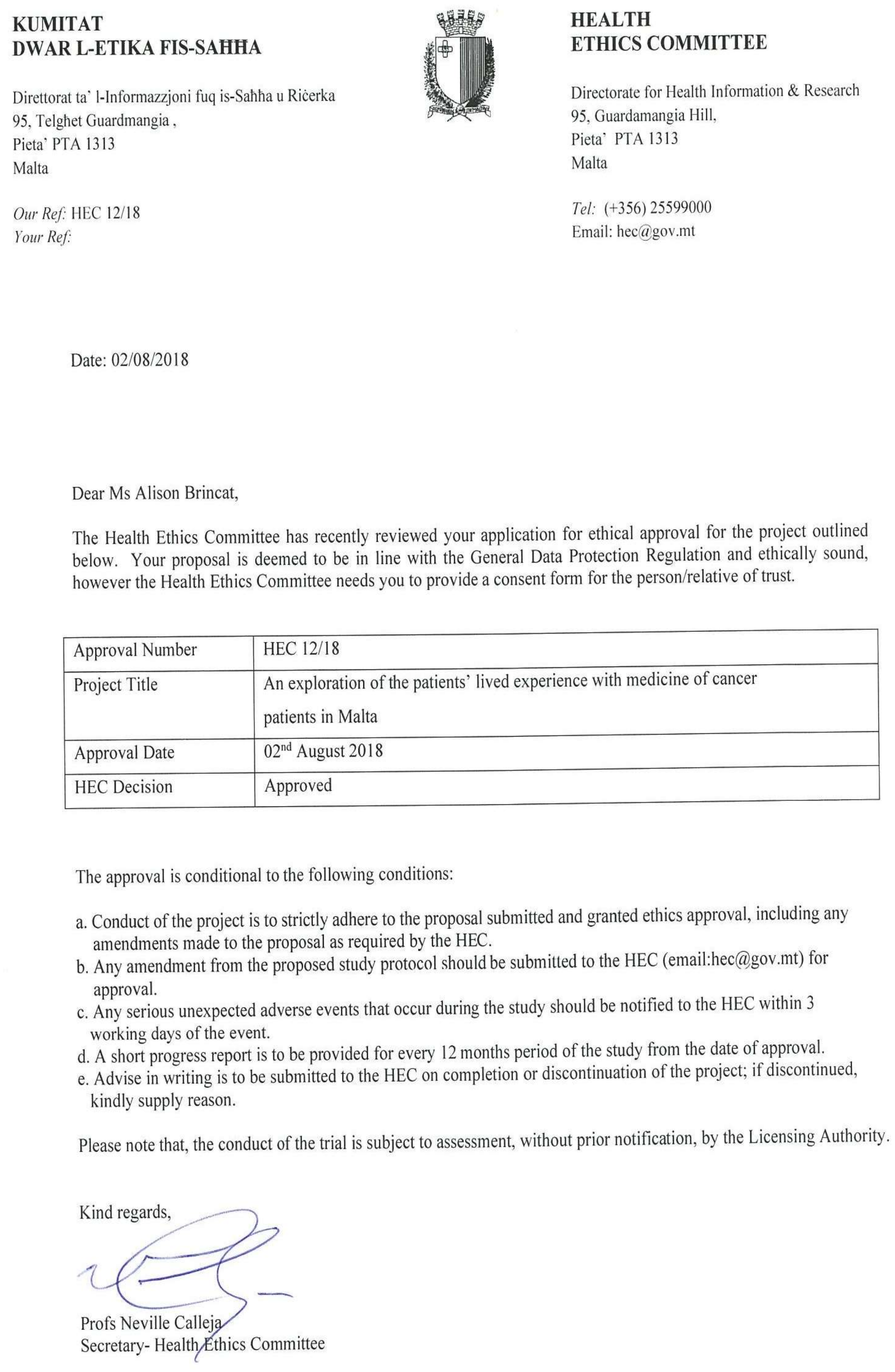
Regards

Convener of the School Ethics Review Panel

INVESTOR IN PEOPLE

Robert Gordon University, a Scottish charity registered under charity number SC013781

Appendix 4.5: Health Ethics Committee Approval



KUMITAT
DWAR L-ETIKA FIS-SAĦĦA

Direttorat ta' l-Informazzjoni fuq is-Saħħa u Riċerka
95, Telgħet Guardmangia ,
Pieta' PTA 1313
Malta

HEALTH
ETHICS COMMITTEE

Directorate for Health Information & Research
95, Guardamangia Hill,
Pieta' PTA 1313
Malta

Tel: (+356) 25599000
Email: hec@gov.mt

Our Ref: HEC 12/18
Your Ref:

Date: 02/08/2018

Dear Ms Alison Brincat,

The Health Ethics Committee has recently reviewed your application for ethical approval for the project outlined below. Your proposal is deemed to be in line with the General Data Protection Regulation and ethically sound, however the Health Ethics Committee needs you to provide a consent form for the person/relative of trust.

Approval Number	HEC 12/18
Project Title	An exploration of the patients' lived experience with medicine of cancer patients in Malta
Approval Date	02nd August 2018
HEC Decision	Approved

The approval is conditional to the following conditions:

a. Conduct of the project is to strictly adhere to the proposal submitted and granted ethics approval, including any amendments made to the proposal as required by the HEC.
b. Any amendment from the proposed study protocol should be submitted to the HEC (email:hec@gov.mt) for approval.
c. Any serious unexpected adverse events that occur during the study should be notified to the HEC within 3 working days of the event.
d. A short progress report is to be provided for every 12 months period of the study from the date of approval.
e. Advise in writing is to be submitted to the HEC on completion or discontinuation of the project; if discontinued, kindly supply reason.

Please note that, the conduct of the trial is subject to assessment, without prior notification, by the Licensing Authority.

Kind regards,

Profs Neville Calleja
Secretary- Health Ethics Committee

Appendix 4.6: Approval from the Hospital

RE: Request for approval to conduct study

Falzon Ivan at Health-MDH <ivan.falzon@gov.mt>
Mon 18/06/2018, 17:22
Brincat Alison at Health-SAMOC <alison.brincat@gov.mt>; Data Protection at MDH

Proceed in line with hospital policies regulating such.

Ivan Falzon
Chief Executive Officer | TeaMDH

T +356 2545 4102
M +356 9995 0393
E ivan.falzon@gov.mt

Mater Dei Hospital, Triq tal-Qroqq, Msida, Malta MSD 2090 | Tel +356 2545 0000 | [www.materdeihospital.org.mt]www.careandcure.gov.mt

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From: Brincat Alison at Health-SAMOC
Sent: 09 June 2018 12:08
To: Falzon Ivan at Health-MDH <ivan.falzon@gov.mt>
Cc: Data Protection at MDH <datapro.mdh@gov.mt>
Subject: Request for approval to conduct study

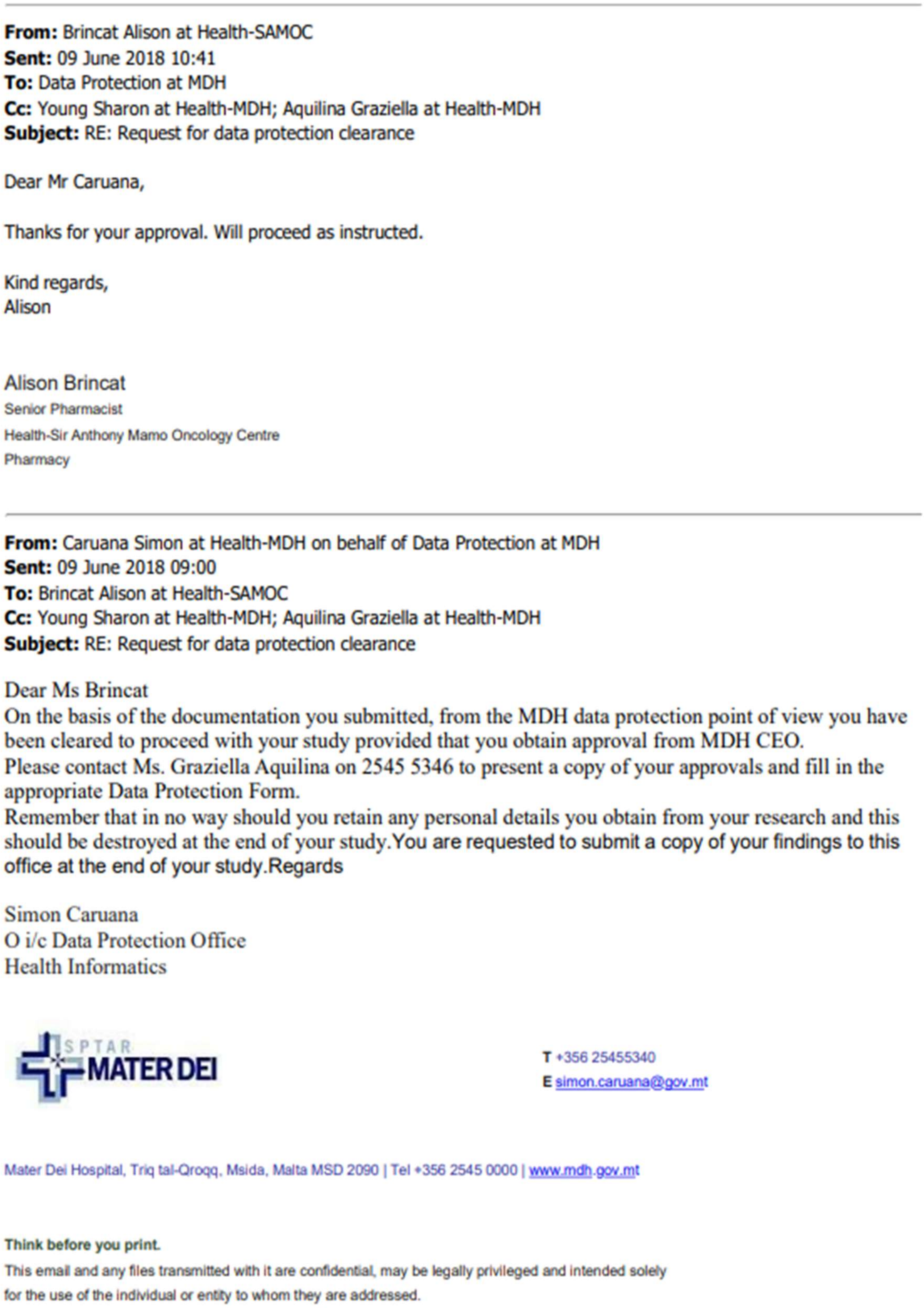
Dear Mr Falzon,

I am currently reading for an MRes/PhD at the Robert Gordon University whereby a research project needs to be presented. The proposed project is entitled *'A prospective longitudinal study of colorectal cancer patients' lived experience with antineoplastic medicines in Malta'*. In summary, the research studywill explore longitudinally the patients' lived experience with medicines (PLEM) of colorectal cancer patients receiving antineoplastic medicines and their significant others.

The research protocol has been approved by the Robert Gordon University' Research Ethics Committee and MDH Data Protection Office as per below correspondence. Henceforth, I would like to kindlyrequest your approval to undertake this research project within Sir Anthony Mamo Oncology Centre.

I look forward to hearing from you.Thank you in advance.

Kind regards,
Alison Brincat
Senior Pharmacist
Health-Sir Anthony Mamo Oncology Centre
Pharmacy



From: Brincat Alison at Health-SAMOC
Sent: 09 June 2018 10:41
To: Data Protection at MDH
Cc: Young Sharon at Health-MDH; Aquilina Graziella at Health-MDH
Subject: RE: Request for data protection clearance

Dear Mr Caruana,

Thanks for your approval. Will proceed as instructed.

Kind regards,
Alison

Alison Brincat
Senior Pharmacist
Health-Sir Anthony Mamo Oncology Centre
Pharmacy

From: Caruana Simon at Health-MDH on behalf of Data Protection at MDH
Sent: 09 June 2018 09:00
To: Brincat Alison at Health-SAMOC
Cc: Young Sharon at Health-MDH; Aquilina Graziella at Health-MDH
Subject: RE: Request for data protection clearance

Dear Ms Brincat
On the basis of the documentation you submitted, from the MDH data protection point of view you have been cleared to proceed with your study provided that you obtain approval from MDH CEO.
Please contact Ms. Graziella Aquilina on 2545 5346 to present a copy of your approvals and fill in the appropriate Data Protection Form.
Remember that in no way should you retain any personal details you obtain from your research and this should be destroyed at the end of your study.You are requested to submit a copy of your findings to this office at the end of your study.Regards

Simon Caruana
O i/c Data Protection Office
Health Informatics

SPTAR MATER DEI

T +356 25455340
E simon.caruana@gov.mt

Mater Dei Hospital, Triq tal-Qroqq, Msida, Malta MSD 2090 | Tel +356 2545 0000 | www.mdh.gov.mt

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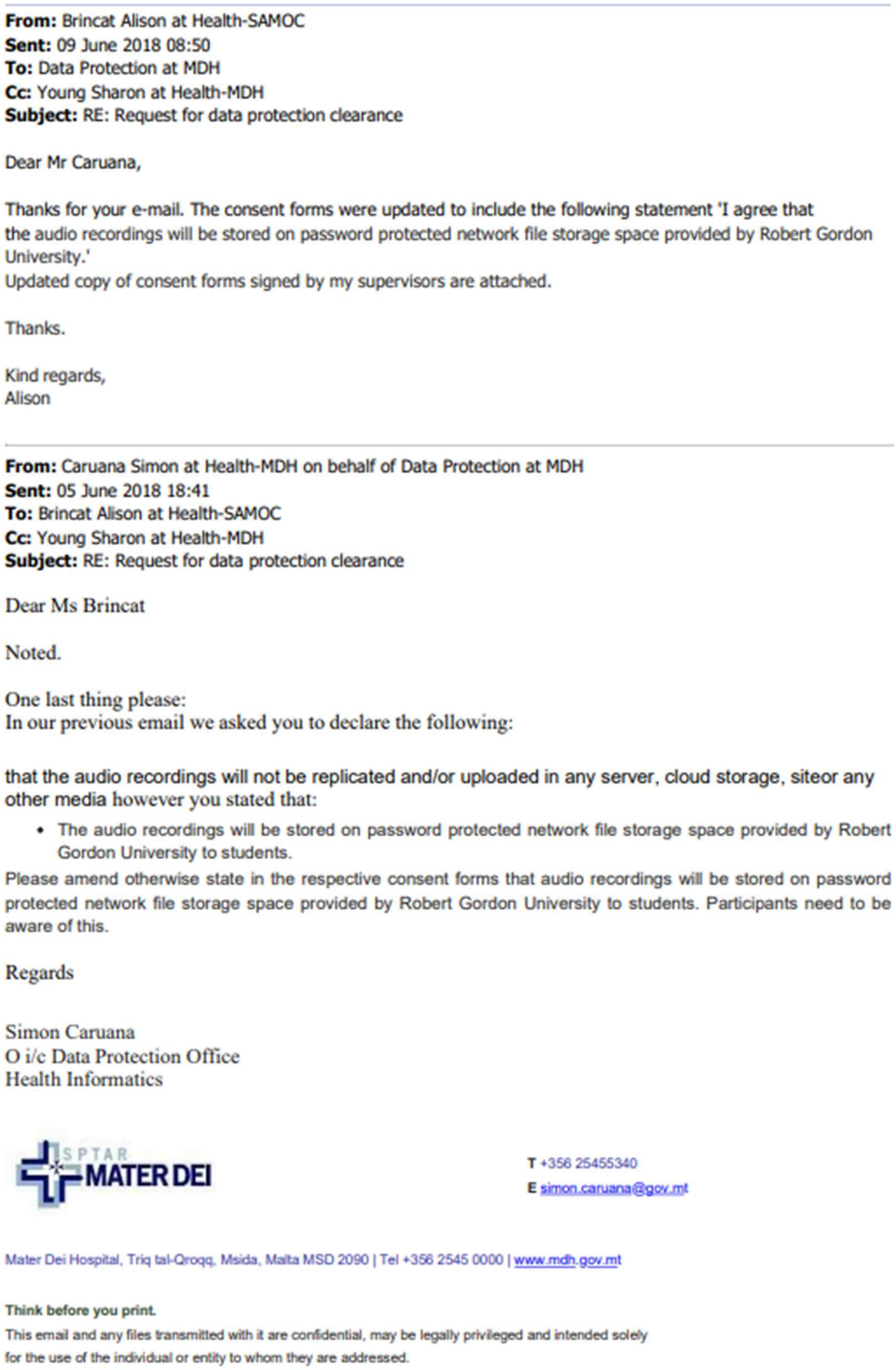

From: Brincat Alison at Health-SAMOC
Sent: 09 June 2018 08:50
To: Data Protection at MDH
Cc: Young Sharon at Health-MDH
Subject: RE: Request for data protection clearance

Dear Mr Caruana,

Thanks for your e-mail. The consent forms were updated to include the following statement 'I agree that the audio recordings will be stored on password protected network file storage space provided by Robert Gordon University.'
Updated copy of consent forms signed by my supervisors are attached.

Thanks.

Kind regards,
Alison

From: Caruana Simon at Health-MDH on behalf of Data Protection at MDH
Sent: 05 June 2018 18:41
To: Brincat Alison at Health-SAMOC
Cc: Young Sharon at Health-MDH
Subject: RE: Request for data protection clearance

Dear Ms Brincat

Noted.

One last thing please:
In our previous email we asked you to declare the following:

that the audio recordings will not be replicated and/or uploaded in any server, cloud storage, siteor any other media however you stated that:

- The audio recordings will be stored on password protected network file storage space provided by Robert Gordon University to students.

Please amend otherwise state in the respective consent forms that audio recordings will be stored on password protected network file storage space provided by Robert Gordon University to students. Participants need to be aware of this.

Regards

Simon Caruana
O i/c Data Protection Office
Health Informatics

SPTAR MATER DEI

T +356 25455340
E simon.caruana@gov.mt

Mater Dei Hospital, Triq tal-Qroqq, Msida, Malta MSD 2090 | Tel +356 2545 0000 | www.mdh.gov.mt

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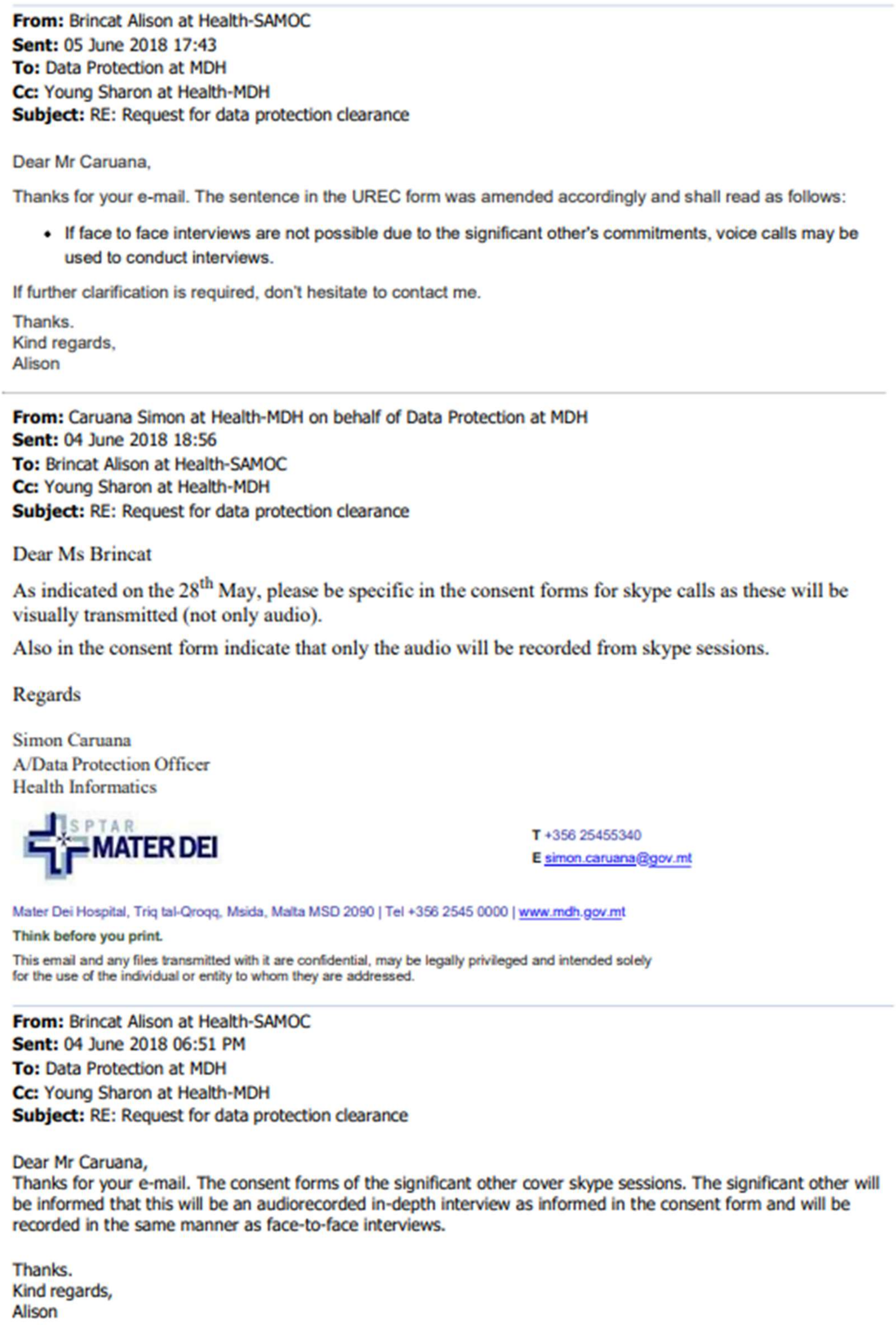

From: Brincat Alison at Health-SAMOC
Sent: 05 June 2018 17:43
To: Data Protection at MDH
Cc: Young Sharon at Health-MDH
Subject: RE: Request for data protection clearance

Dear Mr Caruana,

Thanks for your e-mail. The sentence in the UREC form was amended accordingly and shall read as follows:

- If face to face interviews are not possible due to the significant other's commitments, voice calls may be used to conduct interviews.

If further clarification is required, don't hesitate to contact me.

Thanks.
Kind regards,
Alison

From: Caruana Simon at Health-MDH on behalf of Data Protection at MDH
Sent: 04 June 2018 18:56
To: Brincat Alison at Health-SAMOC
Cc: Young Sharon at Health-MDH
Subject: RE: Request for data protection clearance

Dear Ms Brincat

As indicated on the 28th May, please be specific in the consent forms for skype calls as these will be visually transmitted (not only audio).

Also in the consent form indicate that only the audio will be recorded from skype sessions.

Regards

Simon Caruana
A/Data Protection Officer
Health Informatics

SPTAR MATER DEI

T +356 25455340
E simon.caruana@gov.mt

Mater Dei Hospital, Triq tal-Qroqq, Msida, Malta MSD 2090 | Tel +356 2545 0000 | www.mdh.gov.mt

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From: Brincat Alison at Health-SAMOC
Sent: 04 June 2018 06:51 PM
To: Data Protection at MDH
Cc: Young Sharon at Health-MDH
Subject: RE: Request for data protection clearance

Dear Mr Caruana,
Thanks for your e-mail. The consent forms of the significant other cover skype sessions. The significant other will be informed that this will be an audiorecorded in-depth interview as informed in the consent form and will be recorded in the same manner as face-to-face interviews.

Thanks.
Kind regards,
Alison

From: Caruana Simon at Health-MDH on behalf of Data Protection at MDH
Sent: 04 June 2018 14:59
To: Brincat Alison at Health-SAMOC
Cc: Young Sharon at Health-MDH
Subject: RE: Request for data protection clearance

Dear Ms Brincat

Please can you indicate me which consent forms cover skype sessions? Also confirm if these will be recorded.

Regards

Simon Caruana
O i/c Data Protection Office
Health Informatics

T +356 25455340
E simon.caruana@gov.mt

Mater Dei Hospital, Triq tal-Qroqq, Msida, Malta MSD 2090 | Tel +356 2545 0000 | www.mdh.gov.mt

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From: Brincat Alison at Health-SAMOC
Sent: 04 June 2018 14:54
To: Data Protection at MDH

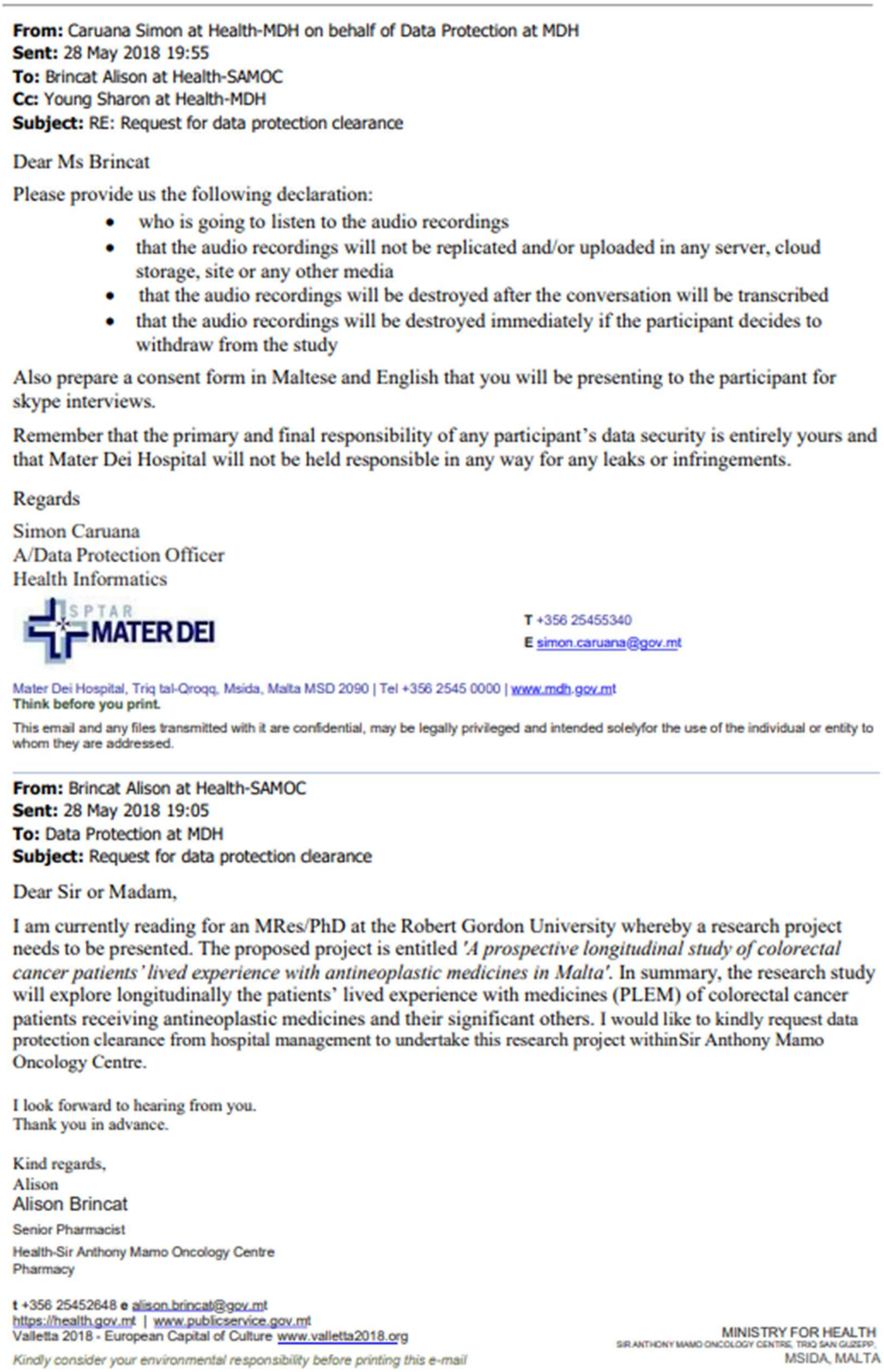
Dear Mr Caruana,
Thanks for your e-mail. Kindly find below declarations in response to below e-mail. These were also included in the UREC form.

- The audio recordings will be listened to by the researchers and transcribed verbatim. The participant will provide informed consent that relevant data with a participant unique code collected during the study may be looked at by responsible individuals from Robert Gordon University.
- The audio recordings will be stored on password protected network file storage space provided by Robert Gordon University to students.
- The audio recordings will be destroyed after the conversation is transcribed and when the participant decides to withdraw from the study. Transcribed data collected from previous interviews prior to withdrawal may be utilised for research purposes.
- The findings will be utilised for research purposes and the use of any direct quotes in any reports or publications will be anonymised.
- If face to face interviews are not possible due to the significant other's commitments, other communication media may be used to conduct interviews such as telephone or skype calls. However the researcher will still meet the significant other in person to be provided with detailed information about the study and to sign the consent form. The same consent form as for those who will undergo face to face interviews will be utilised.

If further clarification is required, don't hesitate to contact me.

Thanks.

Kind regards,
Alison



From: Caruana Simon at Health-MDH on behalf of Data Protection at MDH
Sent: 28 May 2018 19:55
To: Brincat Alison at Health-SAMOC
Cc: Young Sharon at Health-MDH
Subject: RE: Request for data protection clearance

Dear Ms Brincat

Please provide us the following declaration:

- who is going to listen to the audio recordings
- that the audio recordings will not be replicated and/or uploaded in any server, cloud storage, site or any other media
- that the audio recordings will be destroyed after the conversation will be transcribed
- that the audio recordings will be destroyed immediately if the participant decides to withdraw from the study

Also prepare a consent form in Maltese and English that you will be presenting to the participant for skype interviews.

Remember that the primary and final responsibility of any participant's data security is entirely yours and that Mater Dei Hospital will not be held responsible in any way for any leaks or infringements.

Regards

Simon Caruana
A/Data Protection Officer
Health Informatics

T +356 25455340
E simon.caruana@gov.mt

Mater Dei Hospital, Triq tal-Qroqq, Msida, Malta MSD 2090 | Tel +356 2545 0000 | www.mdh.gov.mt
Think before you print.

This email and any files transmitted with it are confidential, may be legally privileged and intended solelyfor the use of the individual or entity to whom they are addressed.

From: Brincat Alison at Health-SAMOC
Sent: 28 May 2018 19:05
To: Data Protection at MDH
Subject: Request for data protection clearance

Dear Sir or Madam,

I am currently reading for an MRes/PhD at the Robert Gordon University whereby a research project needs to be presented. The proposed project is entitled *'A prospective longitudinal study of colorectal cancer patients' lived experience with antineoplastic medicines in Malta'*. In summary, the research study will explore longitudinally the patients' lived experience with medicines (PLEM) of colorectal cancer patients receiving antineoplastic medicines and their significant others. I would like to kindly request data protection clearance from hospital management to undertake this research project withinSir Anthony Mamo Oncology Centre.

I look forward to hearing from you.
Thank you in advance.

Kind regards,
Alison
Alison Brincat
Senior Pharmacist
Health-Sir Anthony Mamo Oncology Centre
Pharmacy

t +356 25452648 **e** alison.brincat@gov.mt
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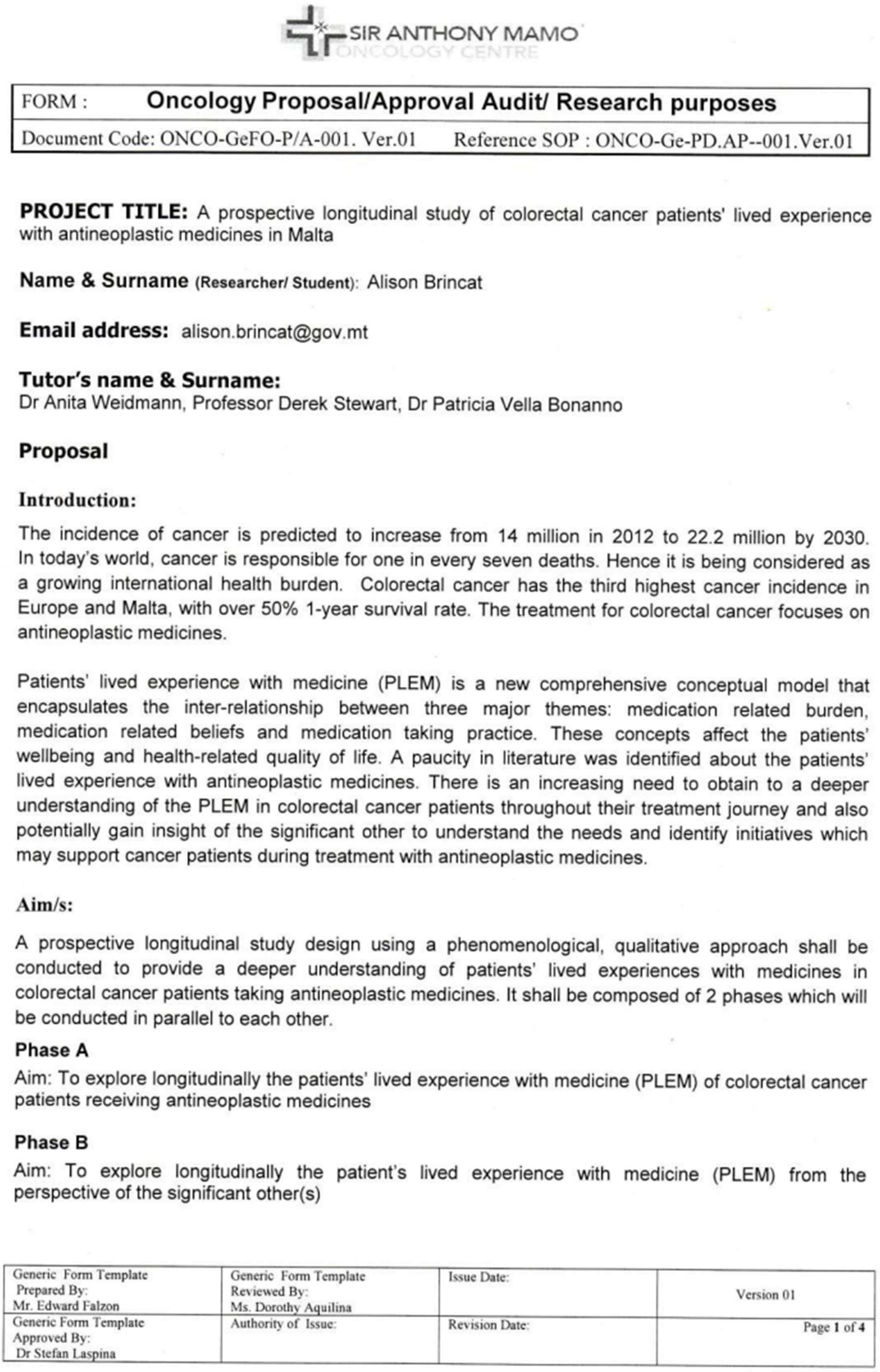
MINISTRY FOR HEALTH
SIR ANTHONY MAMO ONCOLOGY CENTRE, TRIQ SAN GUZEPP,
MSIDA, MALTA



FORM :	**Oncology Proposal/Approval Audit/ Research purposes**
Document Code: ONCO-GeFO-P/A-001. Ver.01	Reference SOP : ONCO-Ge-PD.AP--001.Ver.01

PROJECT TITLE: A prospective longitudinal study of colorectal cancer patients' lived experience with antineoplastic medicines in Malta

Name & Surname **(Researcher/ Student)**: Alison Brincat

Email address: alison.brincat@gov.mt

Tutor's name & Surname:
Dr Anita Weidmann, Professor Derek Stewart, Dr Patricia Vella Bonanno

Proposal

Introduction:

The incidence of cancer is predicted to increase from 14 million in 2012 to 22.2 million by 2030. In today's world, cancer is responsible for one in every seven deaths. Hence it is being considered as a growing international health burden. Colorectal cancer has the third highest cancer incidence in Europe and Malta, with over 50% 1-year survival rate. The treatment for colorectal cancer focuses on antineoplastic medicines.

Patients' lived experience with medicine (PLEM) is a new comprehensive conceptual model that encapsulates the inter-relationship between three major themes: medication related burden, medication related beliefs and medication taking practice. These concepts affect the patients' wellbeing and health-related quality of life. A paucity in literature was identified about the patients' lived experience with antineoplastic medicines. There is an increasing need to obtain to a deeper understanding of the PLEM in colorectal cancer patients throughout their treatment journey and also potentially gain insight of the significant other to understand the needs and identify initiatives which may support cancer patients during treatment with antineoplastic medicines.

Aim/s:

A prospective longitudinal study design using a phenomenological, qualitative approach shall be conducted to provide a deeper understanding of patients' lived experiences with medicines in colorectal cancer patients taking antineoplastic medicines. It shall be composed of 2 phases which will be conducted in parallel to each other.

Phase A

Aim: To explore longitudinally the patients' lived experience with medicine (PLEM) of colorectal cancer patients receiving antineoplastic medicines

Phase B

Aim: To explore longitudinally the patient's lived experience with medicine (PLEM) from the perspective of the significant other(s)

FORM :	**Oncology Proposal/Approval Audit/ Research purposes**
Document Code: ONCO-GeFO-P/A-001. Ver.01	Reference SOP : ONCO-Ge-PD.AP--001.Ver.01

Method (include the sample size)

Phase A

Eligible patients will be identified by the researcher with the aid of the oncology department's appointment book. The first 4 consecutive patients planned to initiate treatment on FOLFOX or XELOX each month and in accordance to the inclusion/exclusion criteria will be recruited in the study until a sample size of 12 patients is reached. Detailed information about the study including the information sheet and the consent form will then be supplied by the researcher and the patient will be allowed a minimum of 24 hours to consider the decision.

Inclusion criteria

- patients aged 18 years and older
- diagnosed with colorectal cancer
- planned to receive either capecitabine and oxaliplatin infusion (XELOX) or fluorouracil infusion and oxaliplatin infusion (FOLFOX)
- being fully aware of the diagnosis and treatment
- able to communicate in English or Maltese
- able to provide consent

Exclusion criteria

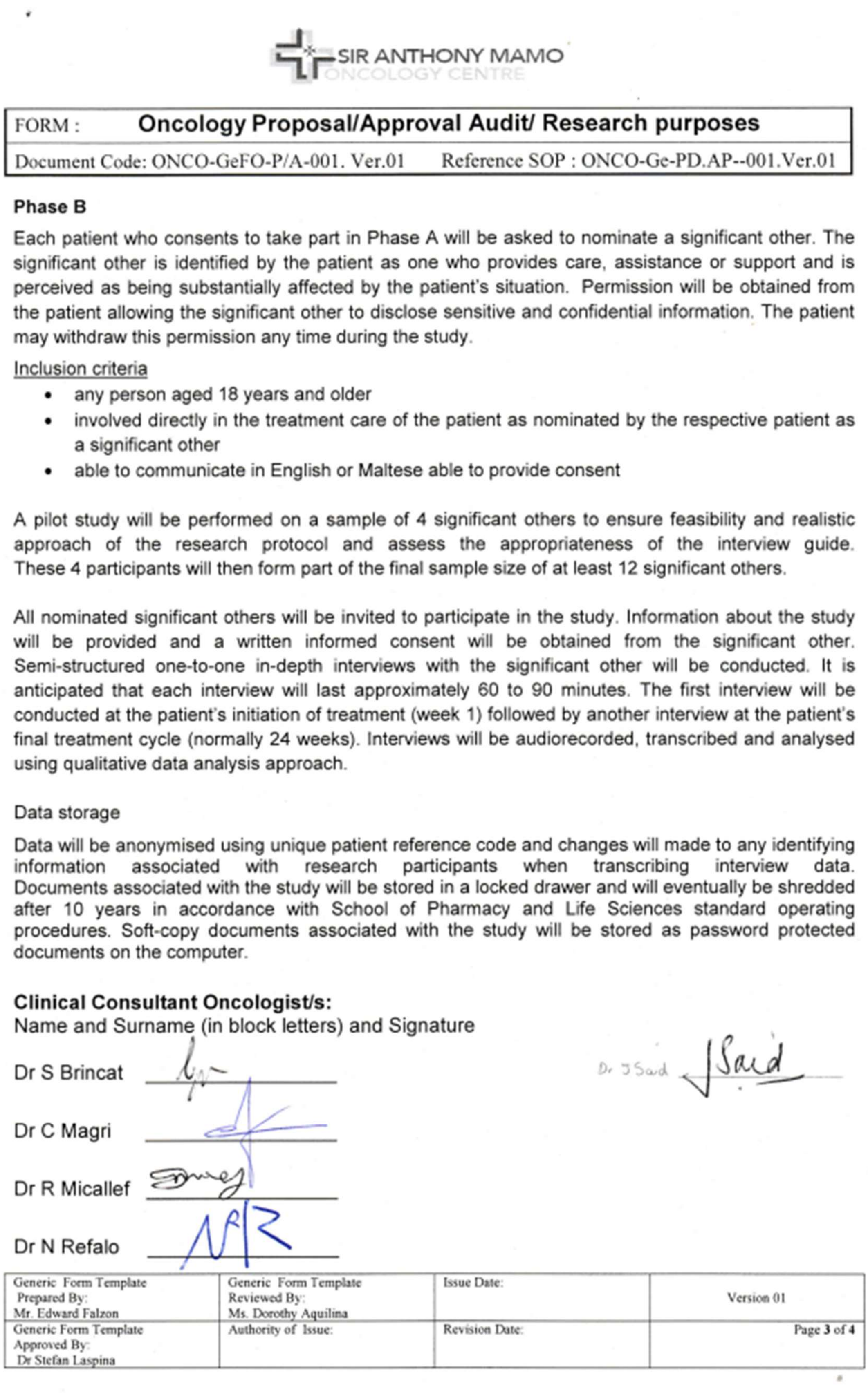
- receiving antineoplastic medicine other than capecitabine and oxaliplatin infusion (XELOX) or fluorouracil infusion and oxaliplatin infusion (FOLFOX) during time of study
- experiencing difficulty in speaking clearly due to medical reasons

A pilot study will be performed on a sample of 4 patients to ensure feasibility and realistic approach of the research protocol and assess the appropriateness of the interview guide.

Semi-structured one-to-one in-depth interviews with cancer patients will be conducted every 12 weeks from initiation of treatment at time points of 1, 12, 24 and 36 weeks. It is anticipated that each interview will last approximately 30 to 45 minutes, up to maximum of 60 minutes.

Patients will be assured confidentiality, anonymity and will be free to terminate the interviews at any time. If the patient gets tired during the interview, this will be suspended and completed during another agreed occasion. A decision to withdraw from the study will not affect their subsequent treatment. Patients who discontinue the FOLFOX or XELOX treatment and initiate another treatment will be stopped from further participation in the study.

Interviews will be audiorecorded, transcribed and analysed using qualitative data analysis approach. The patients' medical files will be accessed to supplement each interview with information regarding dose modification or occurrence of adverse effects. In addition, patients will be invited to keep a diary to record any event that they deem to be important. Patients who accept to participate will be asked to provide information from the diary at their own discretion.



SIR ANTHONY MAMO
ONCOLOGY CENTRE

FORM : **Oncology Proposal/Approval Audit/ Research purposes**	
Document Code: ONCO-GeFO-P/A-001. Ver.01	Reference SOP : ONCO-Ge-PD.AP--001.Ver.01

Phase B

Each patient who consents to take part in Phase A will be asked to nominate a significant other. The significant other is identified by the patient as one who provides care, assistance or support and is perceived as being substantially affected by the patient's situation. Permission will be obtained from the patient allowing the significant other to disclose sensitive and confidential information. The patient may withdraw this permission any time during the study.

Inclusion criteria

- any person aged 18 years and older
- involved directly in the treatment care of the patient as nominated by the respective patient as a significant other
- able to communicate in English or Maltese able to provide consent

A pilot study will be performed on a sample of 4 significant others to ensure feasibility and realistic approach of the research protocol and assess the appropriateness of the interview guide. These 4 participants will then form part of the final sample size of at least 12 significant others.

All nominated significant others will be invited to participate in the study. Information about the study will be provided and a written informed consent will be obtained from the significant other. Semi-structured one-to-one in-depth interviews with the significant other will be conducted. It is anticipated that each interview will last approximately 60 to 90 minutes. The first interview will be conducted at the patient's initiation of treatment (week 1) followed by another interview at the patient's final treatment cycle (normally 24 weeks). Interviews will be audiorecorded, transcribed and analysed using qualitative data analysis approach.

Data storage

Data will be anonymised using unique patient reference code and changes will made to any identifying information associated with research participants when transcribing interview data. Documents associated with the study will be stored in a locked drawer and will eventually be shredded after 10 years in accordance with School of Pharmacy and Life Sciences standard operating procedures. Soft-copy documents associated with the study will be stored as password protected documents on the computer.

Clinical Consultant Oncologist/s:
Name and Surname (in block letters) and Signature

Dr S Brincat ____________

Dr C Magri ____________

Dr R Micallef ____________

Dr N Refalo ____________

Dr J Said J Said

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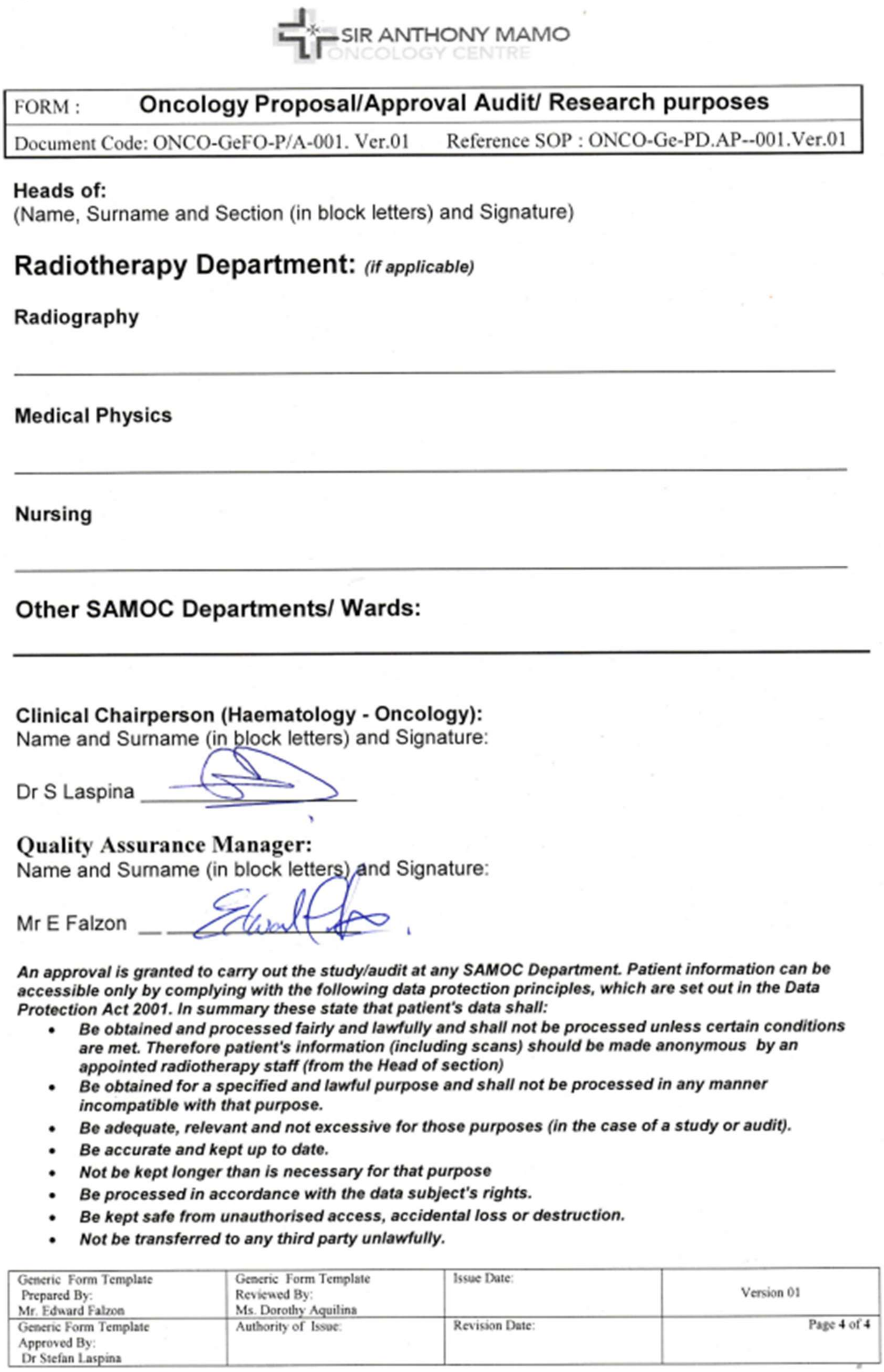
Generic Form Template Approved By: Dr Stefan Laspina	Authority of Issue:	Revision Date:	Page 3 of 4



SIR ANTHONY MAMO
ONCOLOGY CENTRE

FORM :	**Oncology Proposal/Approval Audit/ Research purposes**
Document Code: ONCO-GeFO-P/A-001. Ver.01	Reference SOP : ONCO-Ge-PD.AP--001.Ver.01

Heads of:
(Name, Surname and Section (in block letters) and Signature)

Radiotherapy Department: *(if applicable)*

Radiography

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Medical Physics

____

Nursing

____

Other SAMOC Departments/ Wards:

____

Clinical Chairperson (Haematology - Oncology):
Name and Surname (in block letters) and Signature:

Dr S Laspina ____________________

Quality Assurance Manager:
Name and Surname (in block letters) and Signature:

Mr E Falzon ____________________

An approval is granted to carry out the study/audit at any SAMOC Department. Patient information can be accessible only by complying with the following data protection principles, which are set out in the Data Protection Act 2001. In summary these state that patient's data shall:

- ***Be obtained and processed fairly and lawfully and shall not be processed unless certain conditions are met. Therefore patient's information (including scans) should be made anonymous by an appointed radiotherapy staff (from the Head of section)***
- ***Be obtained for a specified and lawful purpose and shall not be processed in any manner incompatible with that purpose.***
- ***Be adequate, relevant and not excessive for those purposes (in the case of a study or audit).***
- ***Be accurate and kept up to date.***
- ***Not be kept longer than is necessary for that purpose***
- ***Be processed in accordance with the data subject's rights.***
- ***Be kept safe from unauthorised access, accidental loss or destruction.***
- ***Not be transferred to any third party unlawfully.***

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Generic Form Template Approved By: Dr Stefan Laspina	Authority of Issue:	Revision Date:	Page 4 of 4

Appendix 5.1: Information sheet to significant others

A. English version

Dr Anita E Weidmann
Dr Patricia Vella Bonanno

27th February 2018

Participant Information Sheet for significant other

Project title: A prospective longitudinal study of colorectal cancer patients' lived experience with antineoplastic medicine in Malta

We would like to invite you to participate in a research study entitled 'A prospective longitudinal study of colorectal cancer patients' lived experience with antineoplastic medicine in Malta'. Whilst thanking you for taking the time to read this information carefully, do not hesitate to clarify anything that is not clear or if you would like further information.

What is the purpose of the study?
The purpose of the study is to explore the medication related beliefs, medication taking practice and medication related burden of patients suffering from gastrointestinal cancer planned to receive anticancer medicines.

Why have I been chosen?
You have been nominated by a patient suffering from gastrointestinal cancer. You are considered as the patient's significant other as you are highly involved in his/her care.

Do I have to take part?
This information sheet carries no obligation on your part to participate and participation in the study is voluntary. All information provided is confidential. A decision to withdraw, or a decision not to take part, will not affect the standard of care the patient receive now or in the future. Anonymised data collected until the point of completion of the study may be utilised for research purposes.

What do I have to do if I take part?
If you agree to take part in the study, you will be asked to take part in two (2) interviews to ask you some questions about the patient's experiences with medicines. The interviews will last approximately sixty (60) to ninety (90) minutes each. The interviews will be scheduled at a time and place that is mutually convenient. These one-to-one interviews will only be conducted after you have given your consent. The two interviews will take place as follows; the first interview will take place at the beginning of the patient's treatment and then at the end of the treatment (24 weeks). The conversation will be audiotaped to ensure that your responses are captured accurately and will be used so that the researcher can later transcribe the data.

What are the possible benefits of taking part?
There is no direct benefit to you from taking part. Participation in the study will help to understand the needs of cancer patients and identify initiatives which may support cancer patients during treatment with antineoplastic medicines.

Will my contribution to this study be kept confidential?
Yes. The patient who nominated you will grant permission to provide information about his/her care. Information provided will be kept strictly confidential. Names of participants will not appear in any publication as unique patient reference codes will be used. Recordings of the interview will be destroyed after transcribing. Hard copies of documents are kept for 5 years in a locked drawer before shredding, in line with standard operating procedures of Robert Gordon University. Data is also secured in password protected documents in the computer for 5 years.

What will happen to the results of the research study?
The findings will be presented at international conferences and submitted for publication in a peer reviewed journal. A copy of publication or report may be requested.

Who is organising and funding the research?
This project is organised by the Robert Gordon University in Scotland as part of MRes/PhD study and will be partially funded by the Get Qualified Scheme.

Who has reviewed the study?
The study has been reviewed by academic experts, the Robert Gordon Ethics Committee and Health Ethics Committee within the Ministry for Health, Malta.

What do I do now?
If you are interested in taking part in this study, you should complete the attached consent form and contact the research team to participate.

If you have any questions or would like further information, please do not hesitate to contact Alison Brincat via e-mail a.brincat@rgu.ac.uk or phone 79933433.

B. Maltese version

Tim tar-riċerka: Alison Brincat
Professor Derek Stewart
Dr Anita E Weidmann
Dr Patricia Vella Bonanno

27 ta’ Frar 2018

Karta ta’ Informazzjoni għall-Parteċipant bħala persuna importanti fil-kura tal-pazjent

Titlu ta’ l-istudju: Studju prospettiv fuq medda ta’ żmien fuq l-esperjenza reali ta’ pazjenti li qed ibatu minn kanċer kolorettali u jirċievu trattament b’mediċina antineoplastika f’Malta

Aħna nixtiequ nistiednuk biex tipparteċipa fi studju bit-titlu ‘Studju prospettiv fuq medda ta’ żmien fuq l-esperjenza reali ta’ pazjenti li qed ibatu minn kanċer kolorettali u jirċievu trattament b’mediċina antineoplastika f’Malta’. Filwaqt li nirringrazzjawk tal-ħin tiegħek biex taqra din l-informazzjoni bil-galbu, toqgħodx lura milli tiċċara xi punti jew tistaqsi għal iktar informazzjoni.

X’inhu l-għan tal-istudju?
L-għan tal-istudju huwa li jesplora it-twemmin, il-prattika tat-teħied u r-riperkussjoni li l-pazjent qed jieħu parti mill-kura kontra il-kanċer kolorettali.

Għaliex intagħżilt jien?
Inti gejt innominat mingħand pazjent li qed ibati mill-kanċer kolorettali. Inti gejt ikkunsidrat bħala persuna importanti fil-kura ta’ dan il-pazjent u meqjus bħala nvolut fil-kura tiegħu.

Għandi nieħu sehem?
Din il-karta ta’ informazzjoni ma ġġor l-ebda obligu min-naħa tiegħek u l-parteċipazzjoni tiegħek hija biss volontarja. Kull informazzjoni provduta hija kunfidenzjali. Id-deċiżjoni li tieqaf mill-istudju jew li ma tieħux sehem ma taffetwax il-kura tas-saħħa tal-pazjent li qed jieħu issa jew fil-futur. L-informazzjoni anonima li tkun nġabret sat-tlestijja ta’ l-istudju tista’ tintuża għal għanijiet ta’ riċerka.

Kif nagħmel biex nipparteċipa?
Jekk taqbel li tipparteċipa f’dan l-istudju, inti ser tkun mitlub li tieħu sehem f’żewġ (2) intervisti fejn tiġi mistoqsi dwar l-esperjenza tal-pazjent bil-mediċini. Kull intervista ddum madwar sittin (60) sa disgħin (90) minuta. L-intervisti jkunu skedati f’post u ħin li jkun konvenjenti għalina tnejn. Dawn l-intervisti one-to-one isiru wara li inti tagħti il-kunsens ta’ parteċipazzjoni. Dawn l-intervisti ser iseħħu kif ġej: l-ewwel intervista issir fil-bidu tat-trattament tal-pazjent u mbagħad isseħħ oħra fl-aħħar tat-trattament (wara 24 ġimgħa). Id-diskursata ser tiġi rekordjata biex naċċertaw li r-risposti ġew meħuda korrettament u jintużaw mir-riċerkatur biex tinkiteb ir-riċerka.

X'inhuma l-benefiċċji possibli jekk nieħu sehem?
Il-parteċipazzjoni tiegħek f'dan l-istudju ma tirriżultax f'benefiċċju dirett imma twassal biex nifhmu aħjar il-bżonnijiet ta' pazjenti li jbatu bil-kanċer u jgħina nagħrfu inizzjattivi u jinħolqu servizzi addattati għall-persuni morda bil-kanċer u qed jieħdu trattament b'mediċina antineoplastika.

L-informazzjoni li ser nipprovdi jien ser tibqa' kunfidenzjali?
Iva. Il-pazjent li nnominak tak il-permess li tipprovdi informazzjoni dwar il-kura tiegħu/tagħha. L-informazzjoni mogħtija hija kunfidenzjali. L-ismijiet tal-parteċipanti mhux ser jidhru fl-ebda publikazzjoni għax ser tintuża sistema ta' kodiċi uniċi. L-intervista rekordjata ser tiġi meqruda wara li tiġi transkritta. Kopji stampati tad-dokumenti ser jinżammu ġo kexxun msakkar għal-ħames snin qabel it-tqattigħ, f'konformità ma' 'standard operating procedures' tal-Universita' ta' Robert Gordon. L-informazzjoni ser tinżamm ukoll f'dokumenti protetti minn kodiċi sigrieti fil-kompjuter għal-ħames snin.

X'jiġri bir-riżultati ta' din ir-riċerka?
Ir-riżultati ikunu preżentati f'konferenzi nternazzjonali u ppublikati f'ġurnali xjentifiċi. Jekk tixtieq kopja tal-publikazzjoni jew tar-rapport, din tkun tista' tiġi pprovduta lilek.

Min qed jorganizza u jħallas din ir-riċerka?
Dan l-istudju huwa organizzat mill-Universita' ta' Robert Gordon ġewwa l-Iskozja bħala parti minn studju ta' MRes/PhD u se jkun iffinanzjat parzjalment mill-iskema 'Get Qualified'.

Għaliex għandi nafda dan l-istudju?
Dan l-istudju gie rivedut min esperti akkademiċi, mill-kumitat ta' l-Etika mill-Universita' ta' Robert Gordon u l-kumitat ta' l-Etika tas-Saħħa fi hdan il-Ministeru tas-Saħħa f'Malta.

X'għandi nagħmel issa?
Jekk inti nteressat li tipparteċipa f'dan l-istudju, imla' il-karta ta' kunsens u nforma lit-tim tar-riċerka.

Jekk għandek xi mistoqsijiet jew tixtieq iktar informazzjoni, tista' ssaqsi lil Alison Brincat permezz ta' e-majl a.brincat@rgu.ac.uk jew ċempel fuq 79933433.

Appendix 5.2: Consent form of significant others

A. English version

27th February 2018

Consent form for significant other

Project title: A prospective longitudinal study of colorectal cancer patients' lived experience with antineoplastic medicine in Malta

Once you read the Information sheet, please initialise the following statements and sign underneath to give your consent to participate in the study.

1. I confirm that I have read and understood the information sheet dated 27th February 2018 for the above study. Initials:_______
2. I confirm that I have had the opportunity to ask questions about the study and have had these answered satisfactorily. Initials:_______
3. I understand that my participation is voluntary and that I am free to withdraw at any time without the patient's medical care or legal rights being affected. Anonymised data collected until the point of completion of the study may be utilised for research purposes. Initials:_______
4. I understand that I will be asked to take part in an audiorecorded in-depth interview. Initials:_______
5. I agree that the audio recordings will be stored on password protected network file storage space provided by Robert Gordon University and destroyed after data is transcribed or on my withdrawal from participation. Initials:_______
6. I agree to the use of my direct quotes in any reports or publications, if they are used in such a way that both the patient and I will not be identified. Initials:_______
7. I understand that the findings will be utilised for research purposes. Initials:_______
8. I understand that relevant data collected during the study may be looked at by responsible individuals from Robert Gordon University. I give permission to these individuals to have access to this data. Initials:_______
9. I understand that hard copies of documents are kept for 5 years in a locked drawer before shredding, in line with standard operating procedures of Robert Gordon University. Data is also secured in password protected documents in the computer for 5 years. Initials:_______
10. I hereby assign the copyright for my research contribution to Robert Gordon University. Initials:_______
11. I agree to participate in this study. Initials:_______

Name of participant: ___________________________________

Signature of participant: ________________________________

Date: ____________

Name of researcher: Alison Brincat

Signature of researcher: ______________________

Contact details of researcher
Email: a.brincat@rgu.ac.uk
Contact Number: 79933433

B. Maltese version

27 ta’ Frar 2018

Il-formola ta’ kunsens għall- persuna importanti fil-kura tal-pazjent

Titlu ta’ l-istudju: Studju prospettiv fuq medda ta’ żmien fuq l-esperjenza reali ta’ pazjenti li qed ibatu minn kanċer kolorettali u jirċievu trattament b’mediċina antineoplastika f’Malta

Wara li inti qrajt il-karta ta’ informazzjoni dwar dan l-istudju, inti mistenni li timmarka dawn is-sentenzi bl-inizjali tiegħek u tiffirma fl-aħħar tal-formola biex tagħti il-kunsens tiegħek biex tipparteċipa f’dan l-istudju.

1. Jiena nikkonferma li qrajt u fhimt il-karta ta’ informazzjoni dwar l-istudju msemmi hawn fuq bid-data 27 ta’ Frar 2018. Inizjali:_______
2. Jiena nikkonferma li kelli l-opportunita li nsaqsi mistoqsijiet dwar l-istudju u dawn ġew imwieġba b’mod sodifaċenti. Inizjali:_______
3. Jiena nifhem li il-parteċipazzjoni tiegħi hija waħda volontarja u li nista’ nieqaf nipparteċipa fl-istudju meta nixtieq mingħajr ma tiġi mittifsa il-kura medika u d-drittijiet legali tal-pazjent. L-informazzjoni anonima li tkun nġabret sat-tlestijja ta’ l-istudju tista’ tintuża għal għanijiet ta’ riċerka. Inizjali:_______
4. Jiena nifhem li ser niġi mistoqsi biex nipparteċipa f’intervista fit-tul li tiġi rrekordjata. Inizjali: _________
5. Jiena naqbel li l-intervista rrekordjata tiġi miżmuma fi spazju provdut mill-Universita’ ta’ Robert Gordon li hu protett minn kodiċi u tiġi meqruda wara li tiġi transkritta jew wara li nwaqqaf il-parteċipazzjoni tiegħi. Inizjali: ___________
6. Jiena naqbel li jkun hemm użu ta’ kwotazzjonijiet diretti f’rapporti u publikazzjonijiet sakemm jiena u l-pazjent ma niġux identifikati. Inizjali:_______
7. Jiena nifhem li r-riżultati tal-istudju se jintużaw ghal-għanijiet mediċi u xjentifiċi. Inizjali:_______
8. Jiena nifhem li d-data relevanti miġbura fl-istudju tista’ tiġi analizata b’mod responsabbli minn individwi oħra mill-Universita’ ta’ Robert Gordon. Jien nagħti kunses lil dawn l-individwi li jkollhom aċċess ghall-informazzjoni. Inizjali:_______
9. Jiena nifhem li kopji stampati tad-dokumenti ser jinżammu ġo kexxun msakkar għall-ħames snin qabel it-tqattigħ, f'konformità ma 'standard operating procedures’ tal-Universita’ ta’ Robert Gordon. L-informazzjoni ser tinżamm ukoll f’dokumenti protetti minn kodici sigrieti fil-kompjuter għal-hames snin. Inizjali:_______
10. Jiena nagħti id-dritt tal-copyright għal għanijiet ta riċerka lil Universita’ ta Robert Gordon. Inizjali:_______
11. Jiena naqbel li nippartecipa f’dan l-istudju. Inizjali:_______

Isem il-parteċipant: ________________________________

Firma tal-parteċipant: _____________________________

Data: ___________

Isem ir-riċerkatur: Alison Brincat

Firma tar-riċerkatur: ______________________

Dettalji biex taghmel kuntatt mar-riċerkatur:
Emajl: a.brincat@rgu.ac.uk
Telefon: 79933433

Appendix 6.1: Personal experience of conducting interviews and data analyses in non-English language (Maltese) for longitudinal qualitative studies

The undertaking of longitudinal qualitative research as a student was a daunting experience filled with moments of excitement and uncertainty. During my research journey, I was privileged to witness many real stories of patients living with colorectal cancer and receiving antineoplastic medicines. The stories provided by patients and their significant others detailed the moment of receiving the news of diagnosis and treatment, their perception and actual experience of the treatment journey as well as their adaptation to live with the effects of treatment.

Reflexivity helped me to examine my own beliefs and practices in the research process and how these influenced the research itself. This extract from my reflexive account focuses particularly on the challenges posed using non-English language for data collection. This is therefore written in the first person. I learnt that transparency of the research process is fundamental to achieve rigour and improve its credibility.

Qualitative data is commonly collected in the national language. The longitudinal qualitative studies (Phase II and III) were conducted in Malta, where English and Maltese are both official languages. Despite this, the majority of its citizens speak Maltese in preference to English. Maltese is a unique Semitic language, with influences from Arabic, Italian and English. The strategic location of Malta at the crossroads between East and West led to the development of rich and complex linguistic situation. The Maltese language has a relatively small number of speakers (fewer than a million speakers including individuals living abroad) (Fabri 2010, Vella 2013). Despite this, English is a dominant language in research and publications. Hence this poses challenges related to language differences for data collection, analysis and reporting.

Language is more than just a medium for communication; but rather considered as a “cultural resource” that reflects the social world. In fact the interview process is an “active production of meaning by interviewer and interviewee” where participants “bring about” their context and meaning in their interviews, not just “bring along” their preexisting understandings (Welch and Piekkari 2006 p. 419). The use of a common language between the interviewer and the participant allowed for rapport-building and construction of shared understanding. In comparison to the first interview, participants spoke more openly about their experience and voiced their opinion about cancer care in the subsequent interviews. In fact, interviews were taking longer time with richer and detailed narrative.

Discussions were held within the research team to identify the ideal point to carry out the translations from Maltese to English language. An option was to recruit an interpreter to carry out simultaneous translation during the interviews (real time translation) but the impact of an interpreter on the research process raised concerns such as confidentiality, interruption of the flow of conversation and distraction between myself as the interviewer and the participant. Another option was to recruit only participants fluent in English to avoid the issue with interpretation, translation and miscommunication. This was immediately refused due to risk of bias. For instance, the issue of patients who speak solely Maltese language would not have raised their concern about the need of a translator when cared for by healthcare professionals fluent solely in English. Therefore the initially agreed plan by the research team was to transcribe verbatim all audio-recorded interviews and then translate each transcript from Maltese to English prior to perform data analysis.

Interview guides were developed both in English and Maltese. This allowed patients and significant others to freely choose whichever language (Maltese or English) they preferred. The expert panel who was fluent in both languages provided feedback on the structure of interviews and ensured that the questions were suitable for the target population. All interviews were conducted in Maltese except for 2 participants (a patient and his significant other) who were European citizens living in Malta. The interviews of the latter were conducted in English.

Transcription was carried out verbatim in the language used by each participant whilst listening to the audio recorded interviews. This captured a comprehensive description of each participant’s experience of receiving treatment with antineoplastic medicines. Quality and accuracy of transcripts were ensured by an independent fluent researcher in both Maltese and English who assessed a sample of 10% of transcripts against the original audio-recordings.

The transcription of all 81 interviews by myself was already a daunting and time-consuming task, therefore I could not imagine how I would be able to translate all these transcripts! After re-discussing this concern with my research team, other options were evaluated such as hiring an official translator to translate the transcripts or carrying out data analysis in Maltese. Due to lack of financial resources and time restriction, the employment of an official translator did not seem adequate. Taking into consideration the expertise of the research team, whom there were three fluent bilingual speakers (Maltese and English), the most feasible option was to carry out data analysis in Maltese language followed by doing the write-up in English and then translate the selected quotations.

Working with two languages in phenomenological research was not an easy task. When reading transcripts in Maltese, this leads to thinking in the Maltese language. Despite this, it was essential for me to maintain data accuracy and authenticity throughout the whole process. Translation is an interpretive act in its own right. By carrying out data analysis in our native language (Maltese), my research team and I familiarised ourselves with the original data and tried to understand the actual and implied meaning of words used by participants to describe their experience of receiving treatment with antineoplastic medicines. For example '*li terġa tigi lura għan-normal*' [S006-1] – '*to return to her normalcy'* [S006-1] or '*li tkun qerdet kollox* u *ma jaqbadhiex iżjed'* [S009-1] – '*to be totally eradicated and not to have any recurrence*' [S009-1] was a perception of treatment to *achieve cure*. In this way, it was ensured that the interpretation of meaning of the participants' speech was not missed.

Significant attention was paid to how the participants described their experience during the interviews. In fact, I noticed that at some point or another, the participants used metaphors to capture the richness of their experience. These metaphors are both language and culture specific providing depth and detail. For instance '*issa nħallu f'idejn il-Bambin u naraw minn hemm*' [P001-1] – '*leave it [the fate of the illness] in God's hands and then see from there'* [P001-1] is a common Maltese metaphor where the patient feel helpless and leaves everything in God's hand while following his path. Also featuring the strong religious aspect.

A key challenge in translation of quotations was the conceptual equivalence, particularly when specific culturally bound words were used by the participants. The term *'felul'* [P004-1] which directly translates as '*skin tags'*, was often used to refer to cancer. Another example is the word '*tbati minn din*' [S004-1] where in the local context refers to 'being diagnosed' but the literal translation is '*suffering'*. The latter has a negative connotation of pain. As both the participants and I spoke the same language, issues related to language differences were not identified during data gathering, transcription and initial coding. This is because we all remained close to the original Maltese data. During the translation process of the quotations from Maltese to English, I realised that some Maltese words had no linguistic equivalence in English or had more than one meaning across the two languages. For instance the term 'pantry' in English is a food storage cupboard whilst in Malta, this term refers to the space where patients can prepare tea whilst socialising. Therefore the use of the term 'tearoom' seemed to be more appropriate. This problem is unique in qualitative research, where the use of language is central throughout the research process from data gathering to analysis and reporting quotations. The identification of the correct English wording was essential to provide a good understanding of subtle meaning as expressed in the original transcript. For example '*kull parir li ttih il-konsulenta jobdi u anki jaċċetta kull mediċina li ttih'* [S002-1] translates to '*He blindly follows the advice being given by the* *consultant and accepts whatever medicine is recommended to him.'* [S002-1] - the use of the word *'blindly follows'* was more appropriate to portray the obedience followed by the patient with no discussion or questioning. Another example was the description of the challenges they encountered along the treatment journey. This was compared to *'climbing up a hill, reached the summit and will now be walking back down the slope.'* [P002-2]

In order to improve accuracy and validity, each quotation was reverse translated from English to Maltese by another member of the research team fluent in both languages. Discussions were also held with the research team to explore and identify the ideal English phrases that retained the original meaning in Maltese. This process proved valuable as it opened up a new avenue for achieving accuracy in translation. The use of additional words to express the original quotations was avoided as this risked altering the meaning of the participants thereby affecting the fundamental aim of qualitative research in giving a voice to participants.

From my own experience, I recommend keeping in contact with the original language for as long as possible to obtain an accurate meaning and interpretation of the data. Working in a team fluent in the original language increased rigour in the analysis and encouraged richer interpretation. Members who do not speak the original language will then ensure a correct understanding of the interpretations provided. I found it more beneficial to initially use fluid descriptions of meanings with various English terms rather than using one word translations. Also, keeping quotations in Maltese and English next to each other in the initial phases of the write-up assisted in the interpretations as it helped to go back to the preliminary findings in the original language.