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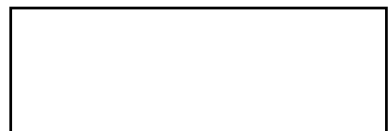
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Non-medical prescribing versus medical prescribing for acute and chronic disease management in primary and secondary care (Protocol)

Weeks G, George J, Maclure K, Stewart D

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[Intervention Protocol]

Non-medical prescribing versus medical prescribing for acute and chronic disease management in primary and secondary care

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To assess the clinical, economic and humanistic health outcomes of non-medical prescribing for managing acute and chronic health conditions in primary and secondary care settings compared with medical prescribing.

BACKGROUND

Description of the health care challenge

A range of health workforce strategies are needed to address issues of health service access and efficiency. In developed countries, the increasing demand for health services arises from an ageing population and the resultant increasing burden of chronic disease (Bhanbhro 2011; Duckett 2005; Phillips 2008; WHO 2012).

Increased health demands can be met in part by task substitution within the health workforce. One health workforce strategy for task substitution is to permit prescribing by healthcare providers other than medical staff (doctors or dentists). Non-medical prescribers may include nurses, pharmacists, allied health professionals and physician assistants. Extending a health provider's scope of

practice, including the right to prescribe, has been supported in a number of countries as a means of benefiting patient care by the effective use of health professionals' skills, improving patient access to timely care, improving patient choice and enhancing teamwork and better use of resources (Department of Health 1999; Ellis 2006; Hooker 2006; Stewart 2010).

The devolution of prescribing rights in developed countries has continued from a historical base in the United States of America (USA) in the 1970s through to more recent government led reforms in the United Kingdom (UK), Canada, the Netherlands, New Zealand and Australia. While the definition of prescribing may vary between countries for the purpose of our review prescribing is defined as "an iterative process involving the steps of information gathering, clinical decision making, communication, and evaluation that results in the initiation, continuation or cessation of a medicine" (Australian National Health Workforce 2010).

The term 'medical prescribing' is prescribing by medically qualified doctors. Prescribing by dentists is excluded from the definition of 'medical prescribing' and this review. The supply of non-prescription (over-the-counter) medicines by pharmacists or pharmacy assistants working in community pharmacies is excluded from our definition of prescribing. The term 'non-medical prescribing' originates from the UK, where it is defined as "prescribing by specially trained nurses, optometrists, pharmacists, physiotherapists, podiatrists and radiographers, working within their clinical competence as either independent or supplementary prescribers" (National Prescribing Centre 2012).

Supplementary prescribing which was introduced in 2003, is defined as "a voluntary partnership between an independent prescriber (a doctor or dentist) and a supplementary prescriber (e.g. nurse, optometrist, pharmacist, physiotherapist, chiropodist/podiatrist and radiographer) to implement an agreed patient-specific Clinical Management Plan with the patient's agreement" (Department of Health 2003). Non-medical prescribing rights were extended in 2006 with the introduction of independent prescribing. The UK Department of Health defines independent prescribing as "prescribing by a practitioner (e.g. doctor, dentist, nurse, pharmacist, and optometrist) responsible and accountable for the assessment of patients with undiagnosed or diagnosed conditions and for decisions about the clinical management required, including prescribing". Independent prescribing is one element of the clinical management of a patient and occurs in partnership with the patient. It requires an initial patient assessment, interpretation of that assessment, a decision on safe and appropriate therapy, and a process for ongoing monitoring. The independent prescriber is responsible and accountable for at least this element of a patient's care. (Department of Health 2006). Independent prescribing does not require a Clinical Management Plan. From 1 May 2006, nurse and pharmacist independent prescribers who completed the appropriate training could prescribe, with a few exceptions, any licensed medicine for any medical condition within their competence. In 2009, independent prescribing rights were extended to include unlicensed medicines. While prescribing of controlled drugs was restricted, this limitation was removed through legislative change in April 2012 (Home Office 2012).

In the USA, devolution of prescribing authority varies from State to State. Collaborative Practice Agreements in 46 States allow a pharmacist to partner with a physician to manage a number of health services, including drug therapy (Law 2013; Thomas 2006). Physician assistants and nurse practitioners were introduced in 1967 to support medical care. These practitioners undertake a range of clinical functions including prescribing (Hooker 2006). Within Canada, a pharmacist's scope of prescribing practice varies between the provinces from independently prescribing to adapting (modifying) or continuing prescriptions (Law 2012). A collaborative prescribing model has emerged as the preferred model of practice within New Zealand and Australia. Collaborative prescribing is undertaken within a multidisciplinary team and can

include the continuum of prescribing from transcription of orders (with or without medical signature), prescribing specified drugs and doses by protocol, prescribing by clinical management plan (allowing choice of drugs and doses) to independent prescribing where a prescribing consultation with a medical practitioner is not required (Weeks 2008; Wheeler 2012). Health Workforce Australia has recently developed a pathway for non-medical prescribing. Prescribing models emphasise team communication and are divided into autonomous prescribing, prescribing under supervision and prescribing via a structured prescribing arrangement (Health Workforce Australia 2013). As part of the reform process health agencies in Australia, Canada, New Zealand and the UK have developed prescribing competency frameworks for non-medical health professionals (National Prescribing Centre 2012; National Prescribing Service 2012; Pharmacy Council of New Zealand 2013; Yuksel 2008).

Description of the intervention

For the purpose of our review the term 'non-medical prescribing' will be used to cover the prescribing of medicines by a broad range of healthcare providers other than doctors and dentists, prescribing in primary or secondary care. No limitation is set on the type of non-medical health care provider undertaking prescribing nor the scope of their prescribing practice. Our review looks at prescribing, which as per our definition is much broader than issuing a prescription. Frequently, non-medical prescribing is done in collaboration or partnership with doctors, and within this practice there are different models of prescribing. Our review may cover degrees of substitution and supplementation.

The role of non-medical prescribers in the secondary care settings may involve supporting acute or chronic care by prescribing in a timely way medication on admission, discharge or where there is a specialist need e.g. total parenteral nutrition. Specialist outpatient clinics managed by non-medical health professionals may exist in either the primary or secondary care setting e.g. for the management of hypertension, lipids, diabetes and pain. In primary care settings, prescribing may be undertaken by nurses or other healthcare providers caring for patients in their homes or through involvement with general practice teams, community health centres, mental health teams or community pharmacies.

How the intervention might work

Non-medical prescribing has developed as an accepted health care policy in a number of countries to improve access to health care, to better use the skills of doctors who can focus on more acute patient needs, to better use the skills of pharmacists, nurses and other health providers, to potentially reduce costs for achieving the same or better health outcomes for consumers, and to retain health workers by increasing job satisfaction (Department

of Health 1999; Tonna 2007). While qualitative studies support non-medical prescribing from a patient and practitioner perspective, robust evidence is required of clinical, economic and humanistic outcomes. It is noted that where non-medical prescribers are practicing in collaborative teams it may be difficult to apportion the impact of the non-medical prescriber on the primary and secondary outcomes of this review. Wider adoption of non-medical prescribing practice in developed countries frequently faces local regulatory hurdles and opposition from the medical establishment which has raised concerns about professional autonomy, patient safety, the diagnostic competency of non-medical prescribers and costs (Cooper 2008). Evidence that patient outcomes arising from non-medical prescribing are equivalent or better than doctors will provide a basis for policy makers to support wider implementation of this practice outside of the UK.

Why it is important to do this review

It is important for health practitioners and policy makers to understand the evidence existing for non-medical prescribing to address access or health workforce needs. This information will also guide future decision making with regards to implementing or expanding non-medical prescribing.

Potential beneficiaries of the findings include:

- policy makers seeking to use workforce resources more efficiently;
- policy makers seeking to improve health systems in primary and secondary care;
- policy makers seeking to meet a clinical need;
- policy makers and consumers seeking evidence of safe and effective practice;
- consumers seeking greater choice and easier access to medicines;
- non-medical health professionals seeking to better utilise their skills and/or extend their scope of practice;
- medical staff seeking to focus on patients with the greatest medical need; and
- researchers interested in evaluating non-medical prescribing.

Despite gradual rolling out of reforms, the evidence for the potential benefits of non-medical prescribing from well controlled trials involving a wide range of health professionals requires identification, synthesis and evaluation. Several narrative reviews of the non-medical prescribing literature have been undertaken (Australian National Health Workforce 2010; Kay 2004; Tonna 2007), and the British government commissioned two evaluations covering supplementary and independent prescribing (Bissell 2008; Latter 2010).

A Cochrane systematic review on substitution of doctors by nurses in primary care cautiously found substitution of doctors in primary care with suitably trained nurses can produce as high a quality of care and as good health outcomes with no appreciable difference

between doctors and nurses in resource utilisation outcomes associated with prescribing (Laurant 2004). The review was limited to nurses in the primary care setting as first contact or ongoing care for undifferentiated patients.

A further Cochrane review “found that the question of whether pharmacists can manage drug therapy as well as physicians remains unanswered due to a shortage of studies” (Benney 2000). The review found a single randomised controlled trial (RCT) of pharmacist managed drug therapy including prescribing drugs (Hawkins 1979), which demonstrated some improvement in process outcomes but there was no big difference in patient outcomes.

Against this background, we seek to systematically identify, review and update the evidence from controlled studies and uncontrolled studies (e.g. interrupted time series (ITS) studies) on the clinical, humanistic and economic outcomes of non-medical prescribing in primary and secondary care settings. This review will also consider any adverse effects of non-medical prescribing which may be clinical (e.g. deterioration in care or incidence of adverse drug reactions), economic (e.g. increased treatment costs) or humanistic (e.g. decreased patient satisfaction).

The proposed review will cover a wider range of healthcare providers undertaking non-medical prescribing; span primary and secondary care settings and consider acute and chronic prescribing situations.

OBJECTIVES

To assess the clinical, economic and humanistic health outcomes of non-medical prescribing for managing acute and chronic health conditions in primary and secondary care settings compared with medical prescribing.

METHODS

Criteria for considering studies for this review

Types of studies

We will include studies of patients or health professionals or healthcare settings using the definitions of designs outlined in the Cochrane Effective Practice and Organisation of Care (EPOC) Group checklist (Cochrane EPOC Group 2002). We will include RCTs and cluster-randomised trials, non-RCTs where investigators have allocated participants to the different groups that are being compared using a method that is not random but where at least two groups with interventions are followed, controlled before-after (CBA) studies with at least two intervention sites and two control sites, and ITS studies, with at least three observations

before and after the intervention. We will include qualitative studies that are linked to quantitative studies and where qualitative analysis methods have been applied. We will exclude qualitative studies alone as the primary focus is on clinical outcomes.

Types of participants

Healthcare providers who are not medical doctors or dentists, undertaking prescribing including, nurses, optometrists, pharmacists, physician assistants and other allied health professionals or categories not specifically mentioned whose roles meet our definition of non-medical prescribing.

Setting

We will include studies based in any primary care or hospital setting where non-medical prescribing occurs.

Types of interventions

We will include studies involving the health providers other than doctors undertaking prescribing according to our definition of prescribing. We will exclude studies involving the supply function alone of pharmacists including over-the-counter products. We will exclude studies only involving subjective outcomes not linked to quantitative measures.

We will include the following six comparisons for non-medical prescribing in acute and chronic care:

1. non-medical prescribing versus medical prescribing in acute care;
2. non-medical prescribing versus medical prescribing in chronic care;
3. non-medical prescribing versus medical prescribing in secondary care;
4. non-medical prescribing versus medical prescribing in primary care;
5. comparisons between different non-medical prescriber groups;
6. non-medical healthcare providers with formal prescribing training versus those without formal prescribing training.

Types of outcome measures

We anticipate the studies included in the review would report a wide variety of outcome measures. We will only include studies with objective measures of patient outcomes. Non-inferiority will be regarded as a positive outcome where a non-medical prescribing outcome is at least as good as the comparator. We will exclude studies reporting only economic or humanistic outcomes without clinical outcomes.

Primary outcomes

Clinical outcomes

Patient outcomes

We will use standard outcome measures covering health and well-being including physiological measures of treatment such as blood pressure, lipid control into dichotomous and continuous outcomes e.g. dichotomous outcomes will include the proportion of patients with improved disease management or markers of disease.

We will also consider the following outcomes:

- proportion of prescribers, medical and non-medical, appropriately adhering to practice guidelines;
- proportion of patients demonstrating treatment adherence;
- proportion of patients and items appropriately prescribed or deprescribed;
- patient satisfaction where measured by a validated tool and part of an effectiveness study;
- non-medical prescriber versus medical prescriber waiting time to care;
- non-medical prescribers adversely affecting the health outcomes of patients through medication errors, prescribing errors, adverse effects, wrong diagnoses or treatment, increased hospitalisations or representations for medical care.

Secondary outcomes

Economic outcomes

Resource use

- Medical time saved by non-medical prescribers
- Non-medical prescriber versus medical prescriber prescription volume and cost, patient out of pocket expenses, service costs, deprescribing rate and cost
- Differential effects across advantaged and disadvantaged populations based on place of residence or socio-economic status
- Increased resource use

Humanistic outcomes

We will include patient reported outcomes of knowledge requirements, daily functioning and validated measures of quality of life. We will include non-medical prescriber outcomes of job satisfaction, skills utilisation, education needs and workload effects.

Search methods for identification of studies

Electronic searches

We will search the following databases:

- the Cochrane Central Register of Controlled Trials (CENTRAL) (EBM Reviews, OvidSP);
- Health Technology Assessment (HTA) (EBM Reviews, OvidSP);
- NHS Economic Evaluation Database (EED) (EBM Reviews, Ovid SP);
- MEDLINE (1946-, In-Process and other non-indexed citations) (OvidSP);
- EMBASE (1980-)- (OvidSP);
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) (1980-) (EBSCOhost);
- International Pharmaceutical abstracts (IPA);
- PubMed Central (<http://www.ncbi.nlm.nih.gov/pmc/>);
- ProQuest Dissertations & Theses Full Text;
- Science Citation Index Expanded (SCI-EXPANDED) (1900-present) (Web of Science);
- Social Sciences Citation Index (SSCI) (1900-present) (Web of Science);
- Conference Proceedings Citation Index-Science (CPCI-S) (1990-present) (Web of Science);
- Conference Proceedings Citation Index-Social Science & Humanities (CPCI-SSH) (1990-present) (Web of Science).

The MEDLINE search strategy as illustrated in [Appendix 1](#) was developed by the Cochrane Effective Practice and Organisation of Care (EPOC) Group Trials Search Co-ordinator in consultation with the authors. We will translate it for other databases using appropriate syntax and vocabulary for those databases. We will employ the Cochrane Highly Sensitive Search Strategy (sensitivity- and precision-maximizing version, 2008 revision) to identify randomised trials, and the Cochrane EPOC Group methodology filter to identify non-randomised studies. We will manage search results using reference management softwares and remove duplicates before screening is undertaken. We will also search the Cochrane Database of Systematic Reviews (CDSR) and the Database of Abstracts of Reviews of Effects (DARE) for related systematic reviews.

Searching other resources

Grey literature

We will conduct a grey literature search to identify studies not indexed in the databases listed above. We will use the following sources:

- OpenGrey (<http://www.opengrey.eu/>);
- Grey Literature Report by the New York Academy of Medicine (<http://www.greylit.org/>);

- Agency for Healthcare Research and Quality (AHRQ) (<http://www.ahrq.gov/>).

We will report any additional sites searched in the full review.

Trial registries

We will search one or both of the following registries:

- the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal (<http://apps.who.int/trialsearch/>);
- ClinicalTrials.gov (<http://clinicaltrials.gov/>).

We will report the corresponding search terms and numbers of results in the full review.

Other resources

- Screen individual journals and conference proceedings (e.g. handsearching)
- Review reference lists of all included studies, relevant systematic reviews; reference lists of other publications will be undertaken if required
- Contact authors of relevant studies or reviews when necessary to clarify reported published information or to seek unpublished results or data
- Contact researchers with expertise relevant to the review topic/EPOC interventions
- Conduct cited reference searches for all included studies in citations indexes

We will document additional sources, if any, in the final review.

Data collection and analysis

Selection of studies

We will merge the search results through the use of a reference management software and remove duplicate records. Two review authors (GW, JG) will then independently assess the titles and abstracts of the search results to evaluate their potential eligibility, and discuss articles that are clearly irrelevant to the topic. The two review authors will not be responsible for the selection of studies they were involved in or associated with. Neutral members of the review team will be in-charge of assessing the eligibility of each study for inclusion in the review. We will retrieve full text of all remaining relevant papers and the two review authors will assess these full-text articles independently based on the review's inclusion criteria. We will include a 'Characteristics of excluded studies' table in the review. This table will include studies that appear to meet inclusion criteria but were eventually excluded and we will report the reasons for exclusion e.g. not an RCT, insufficient observations for an ITS study, only one intervention and or control

site for a CBA study, a multifaceted intervention. If there is uncertainty or disagreement, consensus will be reached by discussion with other review authors. We will correspond with authors of included studies if necessary to obtain further information in order to assess compliance with eligibility and confirm data. Within the review we will map the flow of information of identified, included and excluded studies by depicting them in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Data extraction and management

We will use a standard data extraction form based on the Cochrane EPOC Group's data collection checklist (Cochrane EPOC Group 2002). We will design and assess the form to suitably extract data on the characteristics of each study including study design, study participants, the interventions and comparators, outcomes and follow-up periods, funding source and interest declarations. Two authors (GW, JG) will extract independently study characteristics and outcome data outlined above. We will check the data against each other. If there is uncertainty or disagreement, we will reach consensus by discussion or in the presence of an adjudicating third author, if necessary. We will contact study authors to obtain any missing information. If studies are reported in more than one publication, we will extract the data from all publications into separate data collection forms and combine these.

Assessment of risk of bias in included studies

Two review authors (GW, JG) will independently assess the risk of bias of included studies with any disagreements resolved by consensus with a third review author (KMac). We will use the Cochrane EPOC Group nine-point criteria for RCTs, non-RCTs, and CBA studies (Cochrane EPOC Group 2013b):

1. sequence generation;
2. allocation concealment;
3. blinding, baseline characteristics;
4. baseline outcome measurement;
5. incomplete data outcome;
6. selective outcome reporting;
7. protection against contamination;
8. other reporting bias.

We will assess ITS studies using the seven standard Cochrane EPOC Group criteria (Cochrane EPOC Group 2013b):

1. intervention independent of other changes;
2. pre-specified effect shape;
3. intervention unlikely to affect data collection;
4. blinding;
5. incomplete outcome data;
6. selective outcome reporting;
7. other bias.

We will rate each component and categorise it in a 'Risk of bias table' as "low risk", "unclear risk" or "high risk" as described in the

Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). We will document for each included study a summary assessment of the risk of bias.

Measures of treatment effect

We will record and report measures of effect in the same way investigators have reported them. We will perform all analyses using the Cochrane Collaboration's statistical software, *Review Manager 2014*, and record data in the form of a table included in the Cochrane EPOC Group's data extraction template (Cochrane EPOC Group 2013a). We will report absolute differences and relevant per cent differences between intervention and control groups and the differences in the pre-post intervention change between groups. For dichotomous outcomes after adjusting for baseline differences, we will report risk ratios (RRs). For continuous data we will report mean differences (MDs) between the intervention and comparison group. For ITS studies, we will report regression analysis with time trends before and after the intervention. If possible we will re-analyse data for ITS studies where there is inappropriate analysis or reporting of results using the methods described in *Ramsay 2003*.

Unit of analysis issues

We will assess whether an appropriate adjustment has been made for clustering in RCTs and CBA studies to avoid unit of analysis errors. If there is insufficient data for re-analysis, we will attempt to correct such errors by contacting authors to obtain additional data. Where this is not possible and sufficient data exists, we will perform an approximate analysis and the P value will be annotated 're-analysed'. We will re-analyse inappropriately designed ITS studies using time-series regression and report a statistical comparison of time trends with a minimum of three data points before and after the intervention.

Dealing with missing data

We will apply the risk of bias criteria to exclude studies with a high risk of missing data as they pose serious threats to validity (Higgins 2011). Where appropriate we will contact study authors for further information. If this is not possible we will report the data as missing. We will follow the principles of intention to treat analyses as far as possible.

Assessment of heterogeneity

We may find that the range of healthcare settings, differing non-medical prescribers, differing clinical conditions being managed and variation in study designs will lead to clinical, methodological and statistical heterogeneity. Assessment of these differences will inform the analysis and determine whether results can be statistically combined in a meta analysis. The review team will make

this decision on a consensus basis. We will assess statistical heterogeneity by using the Chi^2 test to assess if differences in results are compatible with chance alone using a P value < 0.10 . Statistical heterogeneity will be quantified using the I^2 statistic as appropriate. We will determine that a high level of heterogeneity exists if I^2 is greater than 30%.

Assessment of reporting biases

We will assess the risk of publication bias based on the characteristics of included studies. If there are sufficient studies, consideration will be given to using funnel plots to assess risk of publication bias.

Data synthesis

We will use a structured synthesis approach to analyses. We will use a random-effects model should a meta-analysis be possible. For any quantitative synthesis we will use [Review Manager 2014](#) for statistical analysis as appropriate. However, we anticipate the primary analyses will be quantitative anticipating explanatory factors such as the variation in the range of non-medical prescribers, their education, years of experience, location, practice setting and range of clinical conditions being treated, will make it difficult to combine intervention outcomes in a meta-analysis. We will include key data elements such as explanatory factors, results, effects and certainty of evidence in a table for each category of intervention. Where it is not applicable to use the average effect across studies of an intervention we will report interquartile ranges, range of effects or plain language summaries as appropriate.

Subgroup analysis and investigation of heterogeneity

We will undertake the following subgroup analyses if sufficient studies result in similar outcomes; however, it may not make sense to calculate an average effect of non-medical prescribing across these subgroups:

1. type of non-medical prescribers;
2. type of intervention;
3. type of setting (primary care, secondary care).

Explanatory factors e.g. level of education, location, patient condition being treated, adherence to therapy and practice guidelines,

type of prescribing within and across sub groups may explain differences in outcomes and limit the applicability of findings. Where appropriate we will use visual displays e.g. analyses of tables or bubble plots to explore the heterogeneity of results across studies. We will use multivariate statistical analyses to examine how the size of observed effects are related to the explanatory factors.

Sensitivity analysis

We will consider performing sensitivity analyses for missing data by imputing a plausible range of assumptions and discussing the implications of missing data. We will use sensitivity analyses to assess the robustness of results including the impact of notable assumptions and assess studies with a high or variable differing risk of bias. Should meta-analysis be possible for the specified outcomes, we will test the robustness of the overall results (and conclusions) by excluding each study individually to determine its effect. Where studies are combined with different scales we will ensure that higher scores for continuous outcomes have the same meaning. We will examine the impact of methodological decisions such as reanalysis of data or the inclusion/exclusion of studies on the stability of results.

Summary of findings

We will use a 'Summary of findings' table to record results, outcomes and outcome risks in our structured synthesis. In addition, we will use the five Grading of Recommendations Assessment, Development and Evaluation (GRADE) study considerations (study limitations, consistency of effort, imprecision, indirectness and publication bias) to assess the quality of the body of evidence and summarise our confidence in the effects of the interventions by outcome across studies.

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* Indicates the major publication for the study

APPENDICES

Appendix I. MEDLINE search strategy (1946 to 8 April 2014)

#	Searches	Results
1	((non-medical or non-medico) adj3 prescrib\$).ti,ab.	93
2	(prescribing adj3 autonomy).ti,ab.	17
3	((non-physician? or non-professional? or non-clinician) adj3 (prescribing or prescriber? or prescription? or "prescribed by")).ti,ab	7
4	((prescribing adj2 (independen\$ or collaborat\$)) or independent prescriber?).ti,ab	139
5	((delegat\$ adj10 prescribing) or (extend\$ adj3 prescrib\$ role?)).ti,ab	8
6	(task? adj2 (shift or shifting or substitution) adj10 (prescribing or prescriber?)).ti,ab	0
7	(prescrib\$ adj3 (autonomy or autonomous\$ or responsibilit\$ or authority or right?)).ti,ab	409
8	(prescription? adj3 (autonomy or autonomous\$ or responsibilit\$ or authority or right?)).ti,ab	188
9	((nurse or nurses or nursing staff or non-clinician or non-physician? or allied health) and pharmacotherapy).ti	8
10	((nurse or nurses) and prescrib\$).ti.	511
11	((role adj3 (change or substitut\$)) and (prescriber? or prescribing)).ti,ab	10
12	((task? adj2 (shift or shifting or substitution)) and (prescribing or prescriber?)).ti,ab	4
13	((allied health or ambulance or chiropractor? or counsel?or? or dental assistant? or emergency vehicle? or emergency worker? or health\$ worker? or midwife? or midwives or non-clinical or non-professional? or nurse or nurses or nursing staff or paramedic? or pharmacist? or physical therapist? or physician? assistant? or physician? extender? or physiotherapist? or podiatrist? or psychologist?) adj3 (prescribing or prescriber?)).ti,ab	1093

(Continued)

14	((allied health or ambulance or chiropractor? or counsel?or? or dental assistant? or emergency vehicle? or emergency worker? or health\$ worker? or midwife? or midwives or nurse or nurses or paramedic? or pharmacist? or physical therapist? or physician? assistant? or physiotherapist? or podiatrist? or psychologist?) adj3 prescription?).ti,ab	405
15	((allied health or ambulance or chiropractor? or counsel?or? or dental assistant? or emergency vehicle? or emergency worker? or health\$ worker? or midwife? or midwives or nurse or nurses or paramedic? or pharmacist? or physical therapist? or physician? assistant? or physiotherapist? or podiatrist? or psychologist?) adj3 ((adjust\$ or alter\$ or chang\$ or decision\$ or manage? or management or managing) adj2 (dosage? or dose))).ti,ab	20
16	Drug Prescriptions/nu [Nursing]	218
17	(Pharmacist? and pharmacotherapy).ti.	27
18	((nurse or nurses or nursing staff or pharmacist?) adj4 (pharmaceutical care or drug therapy)).ti,ab	393
19	supplementary prescribing.ti,ab.	64
20	(prescrib\$ adj2 team?).ti,ab.	26
21	or/1-20 [Keyword Set]	2703
22	allied health personnel/ or community health workers/ or emergency medical technicians/ or home health aides/ or exp nurses' aides/ or pharmacists' aides/ or physical therapists/ or exp physician assistants/ or infection control practitioners/ or exp nurses/ or exp nursing staff/ or pharmacists/	152862
23	*allied health personnel/ or *community health workers/ or *emergency * medical technicians/ or *home health aides/ or exp *nurses' aides/ or *pharmacists' aides/ or *physical therapists/ or exp *physician assistants/ or *infection control practitioners/ or exp *nurses/ or exp *nursing staff/ or *pharmacists/	112094
24	(chiropractor? or counsel?or? or dental assistant? or emergency vehicle? or emergency worker? or health\$ worker? or midwife? or midwives or nonphysician? or non-physician? or nurse or nurses or paramedic? or pharmacist? or physical therapist? or physician? assistant? or physiotherapist? or podiatrist? or psychologist?).ti	112243

(Continued)

25	((chiropractor? or counsel? or? or dental assistant? or emergency vehicle? or emergency worker? or health\$ worker? or midwife? or midwives or nonphysician? or non-physician? or nurse or nurses or paramedic? or pharmacist? or physical therapist? or physician? assistant? or physiotherapist? or podiatrist? or psychologist?) adj5 ((role? adj2 (chang\$ or new or newly)) or (responsibilit\$ adj3 (chang\$ or increas\$ or new or newly))))).ab	458
26	(pharmacist-led or pharma\$ initiated or ((driven or lead or led) adj2 pharmacist?)).ti	113
27	(prescribing adj3 (authority or right?)).ti,ab.	144
28	(taskshifting or task shifting).ti,ab.	268
29	(delegat\$ adj3 (authority or responsibility)).ti,ab.	408
30	((nurse or nurses or nursing staff or non-clinician or non-physician? or allied health or pharmacist?) adj4 pharmacotherapy).ti	14
31	or/22,24-30 [Allied Health Professionals--Broad]	217064
32	or/23-30 [Allied Health Professionals --Focussed]	182149
33	(prescribing or prescriber? or (prescription? adj3 (issue? or issuing or writing))).ti	9699
34	prescribing role?.ab.	40
35	(prescrib\$ adj3 (autonomy or autonomou\$ or responsibilit\$ or authority or right?)).ti,ab	409
36	Drug Prescriptions/	21831
37	*Prescriptions/	947
38	Prescriptions/ and (dt or tu or th).fs.	678
39	Electronic Prescribing/	503
40	Drug Dosage Calculations/	955
41	(pharmacist-led or pharma\$ initiated or ((driven or lead or led) adj2 pharmacist?)).ti	113
42	Medication Therapy Management/	653

(Continued)

43	Drug Therapy/	27809
44	or/33-43 [Prescribing/Drug Therapy terms]	56707
45	(randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti	894174
46	exp animals/ not humans.sh.	3917953
47	45 not 46 [Cochrane RCT Filter 6.4.d Sens/Precision Maximizing]	825248
48	intervention?.ti. or (intervention? adj6 (clinician? or collaborat\$ or community or complex or DESIGN\$ or doctor? or educational or family doctor? or family physician? or family practitioner? or financial or GP or general practice? or hospital? or impact? or improv\$ or individuali?e? or individuali?ing or interdisciplin\$ or multicomponent or multi-component or multidisciplin\$ or multi-disciplin\$ or multifacet\$ or multi-facet\$ or multimodal\$ or multi-modal\$ or personali?e? or personali?ing or pharmacies or pharmacist? or pharmacy or physician? or practitioner? or prescrib\$ or prescription? or primary care or professional\$ or provider? or regulatory or regulatory or tailor\$ or target\$ or team\$ or usual care)).ab	159444
49	(pre-intervention? or preintervention? or “pre intervention?” or post-intervention? or postintervention? or “post intervention?”).ti,ab. [added 2.4]	10010
50	(hospital\$ or patient?).hw. and (study or studies or care or health\$ or practitioner? or provider? or physician? or nurse? or nursing or doctor?).ti,hw	711695
51	demonstration project?.ti,ab.	1941
52	(pre-post or “pre test\$” or pretest\$ or posttest\$ or “post test\$” or (pre adj5 post)).ti,ab	64885
53	(pre-workshop or post-workshop or (before adj3 workshop) or (after adj3 workshop)).ti,ab	606
54	trial.ti. or ((study adj3 aim?) or “our study”).ab.	621001
55	(before adj10 (after or during)).ti,ab.	354106

(Continued)

56	("quasi-experiment\$" or quasiexperiment\$ or "quasi random\$" or quasirandom\$ or "quasi control\$" or quasicontrol\$ or (quasi\$ or experimental) adj3 (method\$ or study or trial or design\$)).ti,ab,hw	100401
57	("time series" adj2 interrupt\$).ti,ab,hw.	1025
58	(time points adj3 (over or multiple or three or four or five or six or seven or eight or nine or ten or eleven or twelve or month\$ or hour? or day? or "more than")).ab	8951
59	pilot.ti.	39252
60	Pilot projects/	81205
61	(clinical trial or controlled clinical trial or multicenter study).pt	622190
62	(multicentre or multicenter or multi-centre or multi-center).ti	28689
63	random\$.ti,ab. or controlled.ti.	747170
64	(control adj3 (area or cohort? or compare? or condition or design or group? or intervention? or participant? or study)).ab. not (controlled clinical trial or randomized controlled trial).pt	405585
65	evaluation studies as topic/ or prospective studies/ or retrospective studies/ [Added Jan 2013]	942946
66	(utili?ation or programme or programmes).ti. [Added Jan 2013]	54298
67	(during adj5 period).ti,ab. [Added Jan 2013]	296950
68	((strategy or strategies) adj2 (improv\$ or education\$)).ti,ab. [Added Jan 2013]	18042
69	"comment on".cm. or review.pt. or (review not "peer review\$") .ti. or randomized controlled trial.pt. [Changed Jan 2013]	2887047
70	(rat or rats or cow or cows or chicken? or horse or horses or mice or mouse or bovine or animal?).ti	1333989
71	exp animals/ not humans.sh.	3917953
72	(or/48-68) not (or/69-71) [EPOC Methods Filter 2.5--added Evaluation Studies line forward--Jan 20130 Medline]	2792648

(Continued)

73	review.pt. and (systematic.ti,ab. or (medline or embase or cinahl or (search adj2 literature)).ab.)	83621
74	((systematic or literature) adj2 review) or (metaanalysis or meta-analysis).ti	80056
75	or/73-74 [REview filter]	133986
76	21 and 75 [REviews]	69
77	21 [Keyword Strategy]	2703
78	(and/31,44) not 21 [Non-physicians & prescribing terms]	2835
79	(and/32,44) not 21 [Non-physicians & prescribing terms-focused]	2080
80	(or/77-78) and 47 [RCT--export]	346
81	(and/72,77) not 80 [EPOC KW--export]	978
82	(and/72,79) not (or/80-81) [EPOC MeSH --export]	768

CONTRIBUTIONS OF AUTHORS

Johnson George (JG) and Greg Weeks (GW) devised the study and prepared the protocol which was reviewed by Derek Stewart (DS) and Katie MacLure (KMc).

DECLARATIONS OF INTEREST

The authors are researchers in the area of non-medical prescribing. While their studies may be referenced in the Review Background it is unlikely they will meet inclusion criteria for studies to be included in the Review.

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