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Micropollutant fluxes in urban environment – a catchment perspective

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Abstract

This study provided a holistic understanding of the sources, fate and behaviour of 142 compounds of emerging concern (CECs) throughout a river catchment impacted by 5 major urban areas. Of the incoming 169.3 kg d^{-1} of CECs entering the WwTWs, 167.9 kg d^{-1} were present in the liquid phase of influent and 1.4 kg d^{-1} were present in the solid phase (solid particulate matter, SPM). Analysis of SPM was important to determine accurate loads of incoming antidepressants and antifungal compounds, which are primarily found in the solid phase. Furthermore, these classes and the plasticiser, bisphenol A (BPA) were the highest contributors to CEC load in digested solids. Population normalised loads showed little variation across the catchment at 154 ± 12 mg d^{-1} $inhabitant^{-1}$ indicating that population size is the main driver of CECs in the studied catchment. Across the catchment 154.6 kg d^{-1} were removed from the liquid phase during treatment processes. CECs discharged into surface waters from individual WwTWs contributed between 0.19 kg d^{-1} at WwTW A to 7.3 kg d^{-1} at WwTW E, which correlated strongly with the respective contributing populations. Spatial and temporal variations of individual CECs and their respective classes were found in WwTW influent (both

solid ($influent_{SPM}$) and liquid phases ($influent_{AQ}$)) throughout the catchment, showing that different urban areas impact the catchment in different ways, with key variables being lifestyle, use of over-the-counter pharmaceuticals and industrial activity. Understanding of both spatial and temporal variation of CECs at the catchment level helped to identify possible instances of direct disposal, as in the case of carbamazepine. Analysis of surface waters throughout the catchment showed increasing mass loads of CECs from upstream of WwTW A to downstream at WwTW D, showing clear individual contributions from WwTWs. Many CECs were ubiquitous throughout the river water in the catchment. Daily loads ranged from 0.005 g d^{-1} (ketamine, WwTW A) up to 1890.3 g d^{-1} (metformin, WwTW C) for the 84/138 CECs that were detected downstream of the WwTWs. For metformin this represents the equivalent of ~1,890 tablets (1,000 mg per tablet) dissolved in the river water downstream of WwTW C.

Key words: pharmaceuticals, pesticides, endocrine disruptors, river, wastewater, solids, personal care products, chemicals of emerging concern

1. Introduction

Anthropogenic substances, such as pharmaceuticals, pesticides, plasticizers, UV filters, industrial chemicals etc., have been widely recognised to be entering the environment from a variety of sources. Many of these substances, particularly pharmaceuticals and personal care products ingredients, enter primarily via point sources such as wastewater treatment works (WwTWs), or for other classes such as veterinary pharmaceuticals and pesticides, as diffuse sources such as agriculture.

There are many studies that detail the presence of a range of compounds in a variety of matrices, however the majority of this existing work has been focused on one or two classes at a time, or a small number of compounds of emerging concern (CECs), primarily in aqueous matrices (Boogaerts et al., 2019; Loos et al., 2009; Mole and Brooks, 2019; Musolff et al., 2009; Petrie

et al., 2014a). There is a broad range of existing data from a variety of studies (Geissen et al., 2015; Petrie et al., 2014a; Sousa et al., 2018) but due to the large number of potential substances, matrices, methods, and multiple lines of investigation that can be pursued, comparisons between the studies are limited due to the different methods utilised, as they have different quantification parameters. Even the sampling process can have a huge effect on how the results are interpreted, methodological details are often lacking (Ort et al. , 2010a; Ort et al., 2010b).

There are fewer studies investigating larger numbers of CECs in solid matrices such as solid particulate matter (SPM), activated and digested sludge, sediments and soils, this may be due to the difficulty of analysing CECs with a variety of different physicochemical parameters in such complicated matrices leading to issues with recoveries and matrix effects with a single extraction method (Petrie et al., 2014a; Proctor et al., 2019). Analysis of solid matrices alongside liquid matrices is critical for a better understanding of the fate and impact of many compounds (Langdon et al., 2012; Petrie et al., 2014a). Some CECs, such as antidepressants, are excreted in or adsorb to SPM before they reach the WwTWs, as well as being released during treatment (Baker and Kasprzyk-Hordern, 2011). The solids produced during WwTW processes, are treated to remove excess water and dangerous pathogens by a variety of processes. This digested sludge, usually termed 'biosolids' is often applied directly to soil as it is rich in nutrients suitable for crops (Kinney et al., 2006; Langdon et al., 2012), but these biosolids have been widely found to be a concentrated source of contaminants. Despite this the CEC content is not widely monitored on a national level nor are the levels of any of CECs entering the environment in this manner controlled by any legislation, although steps are being put in place to review the current chemicals lists of interest in biosolids in a number of countries (Stutt et al., 2019)..

Despite the limitations of studies discussed above, they clearly show that a single wastewater or environmental sample can or has the potential to contain many different CECs from different

classes. Furthermore, many studies have shown the products of metabolism, degradation and transformation of many of these CECs are/have the potential to also be present. Overall this leads to a very complex issue in understanding true exposure levels in the environment and the potential risk they may pose.

Identification of mixtures of co-occurring, high risk CECs, or priority mixtures, is one of the challenges in water quality monitoring (Altenburger et al., 2015). To gain further understanding of these mixtures, their consistency/fluxes within the environment will allow a better understanding of the environmental risk posed by these CECs. Understanding the fluxes of these mixtures will allow the potential changes in risks to be anticipated, potentially leading to optimised treatment and mitigation of risk to the environment. Currently, further work is required to investigate the composition of the mixture in samples from a range of matrices. This will not only require analysis of the mixtures present, but it will provide insight into spatial and temporal trends, between matrices and across a catchment.

The aim of the paper is to investigate the changes in micropollutant load throughout a river catchment system in the South-West of the UK, to gain further information on their sources, fate and behaviour. This was achieved by undertaking a comprehensive investigation of 142 CECs, previously prioritised and analytical method validated (Proctor et al., 2019), at five strategic WwTWs representing >75% of the catchment population. At each WwTW, influent (both liquid and solid phases) and effluent wastewater, digested solids, and upstream and downstream river water were monitored for 7 consecutive days. Five aspects were considered: 1) spatial and temporal variations in the influent, 2) partitioning between aqueous ($influent_{AQ}$) and solid phases ($influent_{SPM}$) in the influent, 3) percentage removal of CECs from the liquid phase, 4) mixture profiles of CECs in all matrices, and 5) spatial trends in river water composition throughout the catchment. This provides a high resolution and more holistic view of the distribution of these CECs throughout the catchment.

2. Materials and methods

2.1. Materials

All materials used in the investigation are detailed in the Supporting information (SI), Section S1. The analytical standards were of the highest purity of ≥97 %, with the exception of azithromycin with 94.2 % and benzophenone-2 with 95.0 % and purchased from Sigma Aldrich, LGC standards or Toronto Research Chemicals (TRC). The solvents used were of HPLC grade. All glassware was silonised to prevent losses of analytes to the untreated glassware. The classes covered by this study are shown in Table 1. Due to the wide range of CECs and complex matrices, not all CECs could be validated for every matrix. Table 1 shows the CECs which are present in each class (green box) and which are validated for each matrix in a previous paper (Proctor et al., 2019).

2.2. Sampling methods and location

Samples were collected at each of the five WwTWs (A-E) for 7 consecutive days between June and October 2015. The five WwTWs utilise a range of treatment technology and receive wastewater from different sized populations (Table 2). Sampling was carried out using volume proportional sampling for influent wastewater, time-proportional for effluent and grab sampling for river water upstream and downstream of the effluent discharge point (sample point distance from discharge point is in Table 2). Digested sludge was collected, via grab sampling, on three consecutive days from WwTW B and WwTW E. Further detail and discussion on the methods and location used can be found in the SI: Section S1, 2.1 and 2.2.

2.3. Sample preparation and analysis

Liquid samples were spiked with internal standards and analytes extracted by solid phase extraction (SPE) using OASIS HLB cartridges before analysis with ultra-performance liquid chromatography coupled with tandem mass spectrometry (UPLC-MS/MS) (Waters). The solid

samples were frozen, freeze-dried, homogenised, weighed and spiked with internal standard before undergoing microwave assisted extraction (MAE) followed by SPE with OASIS MCX cartridges. Further detail and discussion on the methods used can be found in the SI, Section S1, 2.3, or in the previously published paper on the validation of the method (Proctor et al., 2019)

2.4. Quality control

To ensure the quality of generated data, spiked quality control samples were analysed for both liquid and solid matrices. All samples were spiked with internal standards to compensate for matrix suppression effects, as well as any losses of analyte during sample preparation. All sample analysis was performed in duplicate.

A further element of quality control was considered with regards to river water sampling. To ensure downstream river waters were completely mixed with effluent, mass balances were estimated for carbamazepine (e.g. Equation 1). Carbamazepine was selected due to its resistance to biological degradation and photodegradation, which is expected to be negligible over the short distances between sampling points (Heberer, 2002). Further discussion of this can be found in the SI, Section S1, 2.2.1 and Section S2 and results can be found in Table 2.

3. Results and discussion

The discussion of results in this paper is primarily in loads, i.e. g d^{-1}, as it allows direct comparison between different matrices and sites. Number of CECs per class (c) and number of samples with measurable concentration in each matrix (n) are discussed for some CECs within the text and can be found for all classes in Table 1. General chemical information and physicochemical parameters of the CECs of interest is gathered in Table S8. Further information is available in the SI.

3.1. Solid-liquid phase distribution of CECs within communal discharges

149 Overall, 112 of the 138 CECs quantifiable in influent$_{AQ}$ were detected at least once during the
150 study entering the five WwTWs. The majority of micropollutants were found at quantifiable
151 levels in influentSPM (74 of the 96). Many of these chemicals (39) were found in all influent$_{AQ}$
152 and influent$_{SPM}$ samples their classes ranging from antidepressants, analgesics and their
153 metabolites to illicit stimulants e.g. cocaine and industrial chemicals such as parabens, the
154 plasticiser BPA and the UV filter, benzophenone-1.

155 The chemical content of each phase of influent is distinctly different (Figure 1 and 2). With
156 lifestyle chemicals, such as caffeine, nicotine and their metabolites, NSAIDs (and
157 acetaminophen) and antidiabetics, predominantly found in the aqueous phase (99.4 %, 99.8 %
158 and 96.2 % of the total load of each chemical present in the aqueous phase, on average across
159 the catchment) and making up the majority of the incoming wastewater. Whilst influent$_{SPM}$, is
160 primarily made up of the plasticiser, BPA (69.6 %), antidepressants (12.9 %) and antifungals
161 (4.1 %). The latter two of which in particular show high levels of sorption to the solid phase
162 over the aqueous, 36.3 % (including metabolites) and 55.4 % respectively.

163 Much of the differences between the influent$_{AQ}$ and influent$_{SPM}$, is of course likely due to the
164 physicochemical characteristics of these compounds such as their log K_{ow}, and water solubility.
165 For example, the NSAIDs: ibuprofen, naproxen and acetaminophen have log K_{ow} values of
166 3.79, 3.10 and 0.29 respectively and water solubility of 41.1, 145, and 30400 mg L^{-1} and all are
167 primarily found in influent$_{AQ}$ (0.3%, 0.3% and 0.01% of the total load of each compound).
168 These levels of partitioning are far lower than previously reported by Samaras et al. (Samaras
169 et al., 2013), however similar phase distribution was shown by Petrie et al. for crude wastewater
170 (Petrie et al., 2014b). This may be due to differences between WwTWs sewer retention time,
171 as well as physicochemical properties of the matrix (e.g. pH). Despite these low levels of
172 partitioning, ibuprofen, naproxen and acetaminophen are in the top 20 CEC contributors (16,
173 12, 11 respectively) to total influent$_{SPM}$ load in this study with daily loads of 8.6, 10.1, 11.8 g

d^{-1} (or 6.0 – 9.1 mg d^{-1} 1000 inh^{-1} (ibuprofen), 5.7 – 12.8 mg d^{-1} 1000 inh^{-1} (naproxen) and 4.6 – 13.2 mg d^{-1} 1000 inh^{-1} (acetaminophen) if considering population normalised loads). Within $influent_{SPM}$ these three painkillers show similar loads, however with the $influent_{AQ}$ phase, acetaminophen has a much higher normalised load; 44.8 – 77.0 g d^{-1} 1000 inh^{-1} (18.0 % daily variation across the catchment). Whilst, loads for naproxen and ibuprofen were much lower with 3.1 ± 0.6 g d^{-1} 1,000 inh^{-1} and 2.7 ± 0.7 g d^{-1} 1,000 inh^{-1} respectively. These pharmaceuticals are commonly found in the $influent_{AQ}$ of many WwTWs across the globe, due to their high usage and availability without a prescription (Sousa et al., 2018). This is despite low excretion rates due to the extensive metabolism of these NSAIDs (Luo et al., 2014). These results are similar to those found by Mendoza et al., where ibuprofen, naproxen and acetaminophen were found to be the most abundant pharmaceuticals of the study (Mendoza et al., 2015; Paíga et al., 2019). Diclofenac and ketoprofen, which are not so readily available over the counter in the UK, present much lower loads (131.2 ± 37.9 mg d^{-1} 1,000 inh^{-1} (n = 35) and 8.7 ± 17.5 mg d^{-1} 1,000 inh^{-1}, (n = 7) respectively) in $influent_{AQ}$ and less frequently in the case of ketoprofen, which only appears at WwTW E. Despite their worldwide use and abundance, their presence in $influent_{SPM}$ is often overlooked.

As previously mentioned, antidepressants and antifungals are two classes for which a high proportion of the total incoming load can be found within $influent_{SPM}$ (36.3% and 55.4 % respectively). Antidepressants (no. of analytes = 13) contribute 12.9 % to the total $influent_{SPM}$ load and antifungals (no. of analytes = 2) contribute 4.1 % (Figure 2). All antidepressants and metabolites in this study, apart from paroxetine (3.95 log K_{ow}, 35.3 mg L^{-1} water solubility) and duloxetine (4.68 log K_{ow}, 13.0 mg L^{-1}) can be found in $influent_{SPM}$. With log K_{ow} of the parent compound ranging from 3.28 (venlafaxine) to 5.29 (sertraline), the percentage of the total load of each compound found in $influent_{SPM}$ is between 2.9 % (venlafaxine) to 67.0 % (sertraline). These results are not unusual and similar data has been obtained from wastewater

199 samples collected in a week long study in the Czech Republic (CR) and over a yearlong study
200 in the UK by Baker et al., (Baker et al., 2012; Baker and Kasprzyk-Hordern, 2013). The
201 presence of antifungals, on the other hand, is primarily due to ketoconazole (log K_{ow} 4.45).
202 This CEC is primarily found in the influent$_{SPM}$, with 55.8 % of the load in this phase. This
203 result is comparable to a study by Peng et al. (Peng et al., 2012), who also found ketoconazole
204 primarily in influent$_{SPM}$. In that study, other azoles were also analysed, such as fluconazole,
205 clotrimazole, miconazole, and econazole, all of which were found in influent$_{SPM}$ only and not
206 influent$_{AQ}$, showing that this may be a key matrix to investigate for this class and a wider range
207 of antifungals should be considered in future.

208 Overall lifestyle chemicals, have the highest contribution to this catchment with 38.6% of the
209 load, furthermore the daily variation of this load, normalised by population for these
210 compounds, over the seven days of sampling at each of the five sites (n = 35), shows caffeine
211 has one of the lowest daily load variations (23.1 %) of most compounds in this study. The other
212 lifestyle chemicals show more variation; 1,7-dimethylxanthine (26.5 %), nicotine (42.5 %) and
213 its metabolite cotinine (26.2 %) and creatinine (52.1 %). This can provide some insight into the
214 patterns of people's lifestyle habits across a catchment. As an example, wastewater-based
215 epidemiology was applied to caffeine and its metabolite 1,7-dimethylxanthine (methodological
216 details can be found in the SI, Section S3, 1.2.1) to understand usage patterns across the
217 catchment. Overall it was found the loads present suggest an intake of 26 – 57 mg of caffeine
218 per person per day, which is in line with a cup of coffee of a few cups or black tea per day (de
219 Mejia and Ramirez-Mares, 2014; Wishart et al., 2018).

220 The loads calculated in influent$_{SPM}$ represent a large proportion of antidepressants and
221 antifungals but also for other individual compounds; the anti-cancer drug imatinib (39.9 %
222 partitioning to influent$_{SPM}$) and the anti-psychotic risperidone (87.7 % partitioning to
223 influent$_{SPM}$). For some CECs, such as verapamil, thiamethoxam, oxadiazon, methiocarb and

donepezil, influent$_{SPM}$ represents all of the total load for these compounds and is therefore the primary route of entry of these CECs to the environment, which may have gone undetected in studies which focus only on the influent$_{AQ}$. SPM matrix is therefore key to understanding the fate of these classes and CECs.

Various factors are considered important in the consideration of partitioning between liquid and solid phases, these include, water solubility, log K_{ow}, partition coefficient (K_d), log D_{ow}, as well as a compounds polarity and structure. It has been reported before, the likelihood of a compound to sorb to the solid phase increases with log K_{ow} (Hyland et al., 2012). In this study, when considering the classes individually, there is some correlation between these factors, however, considering the full range of CECs the simplistic model of 'the higher the log K_{ow}, the more partitioning to solids' cannot be easily applied. Further work is needed to understand this behaviour.

3.2. Spatial and temporal CEC trends in WwTWs

3.2.1. Overall spatial and temporal trends of CEC loads

The spatial and temporal trends (Figure 1 and 2) of the overall load, in both influent$_{AQ}$ and influent$_{SPM,}$ shows that similar chemical speciation between these two matrices is observed across all WwTWs within this catchment, with the loads in influent$_{AQ}$ being primarily driven by population size (Table S3 and Figure 1). The five WwTWs ranged in size from 18,274 to 867,244 population equivalents. The incoming flow ratio of residential population to commercial/trade also varied from site to site, which is displayed as a percentage of the total population equivalents in Table 2. However, influent$_{SPM}$, (Table S4 and Figure 2) shows there is far more temporal and spatial variation than appears in the influent$_{AQ.}$

3.2.1.1. Industrial chemicals

Figure 1 shows a correlation can be seen between higher industrial contributions to wastewater seen at WwTW B (30.0%) and E (23.9%),the total weekly load of BPA, UV filters and parabens

and particularly the weekly influent$_{SPM}$ load e.g. 92.8 g week^{-1} (B) to 6522 g week^{-1} (E) (BPA), 2.9 g week^{-1} (B) to 10.3 g week^{-1} (E) (UV filters), and 14.8 g week^{-1} (B) to 218.5 g week^{-1} (E) (parabens) compared with 7.5 g week^{-1} (D) to 23.6 g week^{-1} (C), 0.1 g week^{-1} (D) to 0.6 g week^{-1} (C), 1.2 g week^{-1} (D) to 5.0 g week^{-1} (C) respectively at the other WwTWs. This can also be seen in the population normalised loads (Figure 1 and 2), although the correlation is far clearer in the influent$_{SPM}$, than the influent$_{AQ}$. BPA, in particular, contributes 45.4 % (WwTW B) to 72.8 % (WwTW E) to the total load of influent$_{SPM}$ throughout the campaign. This equates to total population equivalent normalised loads of 29.5 – 694.3 mg d^{-1} 1,000 inh^{-1} and 40.6 – 2827 mg d^{-1} 1,000 inh^{-1} for WwTWs B and E, respectively. When comparing these results to the 7.0 %, 10.8 % and 16.8 % (partitioning to influent$_{SPM}$) or 6.7 mg d^{-1} 1,000 inh^{-1} (minimum at C) to 307.2 mg d^{-1} 1,000 inh^{-1} (maximum at D), it is a considerable portion. Furthermore, clear temporal trends can also be seen for BPA in both phases (Figure S3), showing increasing levels throughout the working week, reducing to lower levels over the weekend. The presence of BPA in domestic wastewater has previously been linked to leaching from plastics, such as pipes or drinking bottles which would account for the low level loads commonly seen (Flint et al., 2012; Petrie et al., 2019; Rubin, 2011). The increase levels from industrial waste may be linked to the production of epoxy resins, polycarbonate plastics and thermoprinting paper, however it has not been linked to a specific trade within this catchment at this time. The presence and trends of this compound in this catchment is described in more detail by Petrie et al. and Lopardo et al. (Lopardo et al., 2019; Petrie et al., 2019).

The personal care product ingredient methylparaben, also shows specific industrial spatial and temporal trends. It is present at a constant level across the week at WwTWs A, C and D, with normalised loads in influent$_{AQ}$ ranging from 564.6 – 976.1 mg d^{-1} 1,000 inh^{-1}. It is often found in personal care products such as shampoos and shower gels. Therefore, for this CEC, a consistent level across the week is expected. However, at WwTWs with higher industrial input

e.g. WwTW B and E, the trends seen in influent$_{AQ}$ show significant increase of methylparaben on certain days of the week, which may be as a result of relevant industrial processes, such as toiletry manufacture, which is known to be present in the area. These trends can be seen in both influent$_{AQ}$ and influent$_{SPM}$ (FigureS3), as levels increase from across the working week and decrease over the weekend (up to 16,242 mg d^{-1} 1000 inh^{-1} on Thursday to 681.0 mg d^{-1} 1,000 inh^{-1} on Sunday in influent$_{AQ}$ and up to 48.2 mg d^{-1} 1,000 inh^{-1} on Thursday to 8.5 mg d^{-1} 1,000 inh^{-1} on Sunday in influent$_{SPM}$ at WwTW B, whereas for WwTW E the trends are strongest in the influent$_{SPM}$ with trends increasing up to 41.9 mg d^{-1} 1,000 inh^{-1} on Friday to 15.5 mg d^{-1} 1,000 inh^{-1} on Sunday). The influence of industrial activity on the highly variable loads of these chemicals, may have a significant environmental impact, if they are not effectively removed.

3.2.1.2. Illicit drugs

Spatial trends were also observed for some illicit stimulants, demonstrating variation in the usage behaviour throughout the catchment area. It was postulated that those areas with the greater population size and night life (WwTWs C and E) would see the greater loads of illicit stimulants (e.g. MDMA, cocaine, amphetamine and mephedrone) due to recreational usage. Cocaine, amphetamine and MDMA followed this trend. For example, at WwTWs C and E, total MDMA loads (sum of both influent$_{AQ}$ and influent$_{SPM}$) were found up to 120.8 and 157.1 mg d^{-1} 1,000 inh^{-1} respectively (Tables S3 and S4). At the remaining sites, maximum loads were found in the range 33.3 – 79.9 mg d^{-1} 1,000 inh^{-1}. Previous studies have found cocaine, amphetamine and MDMA use to be greater in large urban populations than in smaller more rural locations (Lai et al., 2016; Nefau et al., 2013). In contrast, mephedrone loads were highest at WwTW D which treats wastewater from the smallest population size (18,274 inhabitants). Total influent loads ranged between 13.1 and 38.9 mg d^{-1} 1,000 inh^{-1} in comparison to loads of 3.8 to 8.5 mg d^{-1} 1,000 inh^{-1} at WwTW C and 7.2 to 20.5 mg d^{-1} 1,000 inh^{-1} at WwTW E (Table S3 and S4). Mephedrone was not detected in wastewater at WwTWs A and B.

The weekly trends for stimulants are also very pronounced (Figure S2). There was an increasing weekend load of not only MDMA and cocaine but also their metabolites: MDA (MDMA), benzoylecgonine (cocaine) and cocaethylene (combination of cocaine and alcohol), but not anhydroecgonine methylester (metabolite from smoking crack cocaine). This shows increased usage of both MDMA and cocaine throughout the catchment during the weekend, though this is less pronounced in areas that are less populated, more rural and with less night life. These trends have previously been seen on numerous occasions across the world (US, (Gushgari et al., 2018), Czech Republic (Baker et al., 2012), England and Europe (Castrignanò et al., 2018b), China (Zhang et al., 2019). The trends, shown in Figure S3, can also been seen in influent$_{SPM}$ for both cocaine, benzoylecgonine and MDMA, despite there being proportionately less load present in influent$_{SPM}$, 1.4 %, 0.1 %, and 0.9 % respectively. Interestingly, a spike in load is observed on one day for influent$_{SPM,}$ rather than over the entire weekend for influent$_{AQ}$.

3.2.1.3. Pharmaceuticals linked to hospital effluent

Total population normalised loads of the analgesic morphine were greater at WwTWs C and E. With ranges between 377.5 to 607.6 mg d^{-1} 1,000 inh^{-1} at WwTW C and 372.2 to 443.1 mg d^{-1} 1,000 inh^{-1} at WwTW E, compared to the other sites which ranged between 184.5 mg d^{-1} 1,000 inh^{-1} at WwTW A to 284.9 mg d^{-1} 1,000 inh^{-1}, also at WwTW A (the ranges of the remaining two WwTWs are quite similar and fall within this range (Tables S3 and S4). Higher morphine loads at WwTWs C and E can be attributed to hospitals within their catchment areas, similar to a study conducted in Portugal, which found that 51 % of the total analgesic load in municipal wastewater was from hospitals (Santos et al., 2013). However, within this catchment a more detailed investigation is required to confirm the contribution of hospital wastewater. Furthermore, the anti-cancer drug ifosfamide was only detected in wastewater at WwTWs C and E (Table S3 and Table S4). Although ifosfamide is not directly linked to hospital

wastewater, as it can be excreted from the homes of patients receiving chemotherapy, it was not detected at WwTWs which did not receive hospital wastewater.

3.2.1.4. Lifestyle chemicals and pharmaceuticals

Many CECs, such as lifestyle chemicals and some NSAIDs, which are freely available without prescription and used widely, show little variation between sites across the catchment e.g. caffeine, with average loads of 23,826 ± 5,498 mg d^{-1} 1,000 inh^{-1}, showing 23.1% daily variation across the catchment, acetaminophen, with 58,374 ± 10,494 mg d^{-1} 1,000 inh^{-1} and 18.0%, and ibuprofen with 3,092 ± 629 mg d^{-1} 1,000 inh^{-1} and 20.4%.

This trend continues with many pharmaceuticals which are prescribed widely for chronic conditions e.g. the anti-diabetic, metformin, (daily variation across the catchment = 21.5 %, with average total influent load of 20,260 ± 4,357 mg d^{-1} 1,000 inh^{-1}), analgesic for moderate pain, tramadol, (17.4 %, 241.3 ± 42.1 mg d^{-1} 1,000 inh^{-1}), and the antidepressants, citalopram (14.5 %, 108.0 ± 15.6 mg d^{-1} 1,000 inh^{-1}) and amitriptyline (20.5 %, 53.9 ± 11.1 mg d^{-1} 1,000 inh^{-1}). Interestingly, compounds in the same class, which appear at much lower loads, show more spatial variation and minimal temporal variation e.g. the anti-diabetic, sitagliptin (35.7 %, 70.2 ± 25.0 mg d^{-1} 1,000 inh^{-1}), and the antidepressant, fluoxetine (41.0 %, 20.7 ± 8.5 mg d^{-1} 1,000 inh^{-1}). This may be a sign of variation in prescribing behaviour of healthcare professionals (Rowlingson et al., 2013), spatial variation in the prevalence of relevant conditions, or it may be due to differences in the stability of the pharmaceutical within the sewer and the difference in sewer residence time to the site. This has been found to be an issue with illicit drug monitoring and other pharmaceuticals have shown the potential to degrade within sewers (Gao et al., 2017; Jelic et al., 2015; McCall et al., 2016). Further investigation is required to provide a more detailed assessment.

347 Antibiotics and antibacterial compounds (c = 19), only contribute a small proportion, 1.1 %, to
348 the total influent$_{AQ}$ load, and influent$_{SPM}$ load, 1.0% (c =7). Several of these CECs, such as
349 sulfasalazine, clarithromycin, azithromycin, trimethoprim, sulfamethoxazole and triclosan
350 were found in all influent$_{AQ}$ samples at all WwTWs (with the exception of azithromycin, which
351 was missing from one sample at WwTW A), but showed highly variable population normalised
352 loads (Table S3). Within influent$_{SPM}$, only trimethoprim was found in all samples, ranging from
353 1.4 mg d^{-1} 1,000 inh^{-1} at WwTW B to 13.7 mg d^{-1} 1,000 inh^{-1} at WwTW C. Few other antibiotics
354 were found in SPM, only sulfadiazine was found with some regularity and only at WwTW B
355 (100% of samples at population normalised loads between 0.9 to 2.2 mg d^{-1} 1,000 inh^{-1}).
356 Unfortunately, this method was unable to quantify fluoroquinolones in this matrix, a class of
357 antibiotics known for their ability to partition to the solid phase (Castrignanò et al., 2018a;
358 Martín et al., 2015; Petrie et al., 2014b), therefore the antibiotic load of this matrix is likely to
359 be underestimated for these compounds. Despite this it is clear that these compounds are widely
360 used (from influent$_{AQ}$ results) and two, azithromycin and clarithromycin, have been placed on
361 the WFD Watch List as substances of potential environmental concern (Carvalho et al., 2015).

362 Ciprofloxacin and erythromycin are also present on this list and yet within this catchment they
363 are detected less frequently within the influent$_{AQ}$ (n = 7 and 21), though their loads, when
364 found, are significant (ciprofloxacin 15.8 ± 10.6 g d-1 at WwTW A only, and erythromycin is
365 found at levels between 9.0 ± 1.9 g d-1 at WwTW D to 189.6 ± 13.6 g d-1 at WwTW E). Other
366 antibiotics, such as metronidazole, sulfadiazine, cefalexin, ofloxacin, tetracycline,
367 danofloxacin, and chloramphenicol are found sporadically in the influent$_{AQ}$ throughout the
368 catchment, often at lower loads than the other antibiotics. Their sporadic presence may be due
369 to limited use. Further consideration of prescription levels will provide a clearer understanding,
370 but this is outside the scope of this paper.

371 Trends of the population normalised loads for antibiotic and antibacterial compounds show
372 some variation between WwTWs and between individual compounds. For example, WwTW
373 B shows the highest population normalised loads for sulfasalazine (93.1 ± 28.5 mg d^{-1} 1,000
374 inh^{-1} compared to 45.0 ± 15.1 mg d^{-1} 1,000 inh^{-1} at WwTW A which has the lowest),
375 azithromycin (135.7 ± 70.4 mg d^{-1} 1,000 inh^{-1} compared to 21.9 ± 15.5 mg d^{-1} 1,000 inh^{-1} at
376 the lowest at WwTW A), and triclosan (405.5 ± 181.1 mg d^{-1} 1,000 inh^{-1} compared to 154.1 ±
377 10.2 mg d^{-1} 1,000 inh^{-1} at the lowest at WwTW C). However, WwTW B also has the lowest
378 levels for other antibiotics such as clarithromycin (209.8 ± 49.4 mg d^{-1} 1,000 inh^{-1} compared
379 to 369 ± 86.6 mg d^{-1} 1,000 inh^{-1} at WwTW D), trimethoprim (99.0 ± 7.8 mg d^{-1} 1,000 inh^{-1}
380 compared to 247.1 ± 21.5 mg d^{-1} 1,000 inh^{-1} at WwTW C), and the second lowest for
381 sulfamethoxazole levels at 18.8 ± 6.7 mg d^{-1} 1,000 inh^{-1}, which is less than 20 % of the highest
382 levels (100.5 ± 6.6 mg d^{-1} 1,000 inh^{-1} WwTW E). This variation may be due to differences in
383 the prescription practices, which could be influenced by variable uptake of prescription advice
384 from the Government as part of the UK Five Year Antimicrobial Resistance Strategy
385 (Department of Health & and Department for Environment Food and Rural Affairs United
386 Kingdom, 2013).

387 Some CECs, particularly pharmaceuticals, that are regularly and widely used by the population,
388 show no temporal trends throughout the week. This is to be expected, as those pharmaceuticals
389 that are sporadically but widely used, such as NSAIDs and painkillers e.g. acetaminophen and
390 ibuprofen (Figure S2), will show only small variations in load. Other pharmaceuticals, such as
391 antibiotics, are used in treating specific conditions and often require courses of several days,
392 but may be prescribed less often, so are used less widely. Antibiotics, such as sulfamethoxazole
393 and trimethoprim which are often prescribed together (as co-trimoxazole) as a long
394 administration course (14 - 21 days), show a steady trend across the week. Other antibiotics,
395 with typically shorter courses, such as azithromycin, clarithromycin, metronidazole and

ciprofloxacin, show more variation across the week. To see trends of these compounds, longer term studies are required to cover time periods encompassing seasons or even years, such as those performed in CR, Greece, Spain, and New Zealand (Golovko et al., 2014; Kumar et al., 2019; Mastroianni et al., 2017; Papageorgiou et al., 2016). This would be particularly useful for antibiotics as it will indicate whether reducing prescription reduces the influent load and any seasonal trends may indicate incorrect prescribing practices (from prescriptions of antibiotics for flu during winter months for which it is not effective) (Coutu et al., 2013; Golovko et al., 2014).

3.2.1.5. Veterinary pharmaceuticals and pesticides

Surprisingly, the veterinary antibiotic, sulfapyridine, is present at population normalised loads, for total influent, ranging from 205.4 ± 23.8 mg d^{-1} inh^{-1} to 299.8 ± 25.8 mg d^{-1} inh^{-1} and shows little daily variation (17.8 %) across the sampling campaign. It has been found previously at low level in $influent_{AQ}$ and its presence has been linked to human use (Ebele et al., 2017; Golovko et al., 2014; Paíga et al., 2016; Wilkinson et al., 2017) as well as veterinary use (Sarmah et al., 2006). However, this antibiotic is no longer prescribed or advised for use by humans in the UK, as it is of critical importance for use with food producing animals, but it is also produced during the human metabolism of sulfasalazine (European Medicines Agency, 2019; Kasprzyk-Hordern et al., 2008; Peppercorn, 1984; Wishart et al., 2018). In this study, it is thought this metabolism of sulfasalazine may be the main source contributing to sulfapyridine's consistent presence across the catchment. This can also be seen in the similarity of their temporal and spatial trends. It is thought that if the main contributing factor was due to usage on livestock, its presence would not be consistent across the catchment, as large variances between rural areas (WwTW B) and highly urban areas (WwTW E) would be expected. Furthermore, the similarity in temporal and spatial trends with sulfasalazine would be very unlikely. Sarafloxacin and diazinon were the only other veterinary pharmaceuticals

found, with sarafloxacin only found at in one influent$_{AQ}$ sample at WwTW D at 5.7 mg d^{-1} 1000 inh^{-1} and diazinon found across the catchment in 80% of the influent$_{AQ}$ samples and 22.9% of the influent$_{SPM}$ samples at total influent loads ranging from 0.6 mg d^{-1}1000 inh^{-1} (WwTW C) to 85.5 mg d^{-1} 1000 inh^{-1} (WwTW E). Interestingly, diazinon is primarily found in influent from the larger WwTWs serving the two major cities. This is it perhaps an indication of a larger numbers of pets relative to inhabitants in these areas compared to more rural areas, or a higher prevalence in the use of deworming medication for which it is primarily used. Overall, veterinary pharmaceuticals and pesticides represent a small proportion, < 0.5% of the total influent chemical load, of the CECs analysed.

3.2.1.6. Anticipated and accidental micropollutant fluxes

Considering the temporal and spatial distribution of CECs across the catchment allows a better understanding over the micropollutant mixtures and fluxes of load that are experienced by the WwTWs, allowing for pattern to emerge regarding human behaviour, degradation and seasonal changes in larger studies. This will allow the loads and fluxes to be anticipated allowing optimisation of treatment technologies for better removal of these contaminants. However, studying the trends in this work anomalies can be detected.

Figure 2 shows a significantly higher proportion of the total load of influent$_{SPM}$ is due to antifungals, specifically ketoconazole, as griseofulvin was not found at this site. Ketoconazole was found in all influent$_{SPM}$ samples at all sites, showing its frequent and widespread use. At WwTW C however, the normalised loads were on average 79.2 ± 35.7 mg d^{-1} 1,000 inh^{-1} compared to the 27.5 to 50.2 mg d^{-1} 1,000 inh^{-1} at the other sites. The high standard deviation seen at WwTW C compared to the other sites may be more indicative of incorrect usage, incidental release or direct disposal rather than difference in prescription.

445 A similar situation is seen at WwTW A, as anti-epileptics represent a far higher proportion of
446 influent$_{SPM}$ (25.4 %, Figure 2). This is entirely due to the presence of the parent compound as
447 the metabolite 10,11-dihydro-10-hydroxycarbamazepine was not detected in influent$_{SPM}$ and
448 the other metabolite, carbamazepine-10,11-epoxide could not be analysed in influent$_{SPM}$. The
449 normalised loads of carbamazepine at WwTWs B-E were in the range of <MQL (1 sample at
450 WwTW D) to 5.3 ± 8.0 mg d^{-1} 1,000 inh^{-1}, whilst at WwTW A they were 119.3 ± 287.4 mg d^{-1}
451 1,000 inh^{-1}. This standard deviation indicates a very skewed distribution of carbamazepine
452 load at WwTW A, which is not consistent for a pharmaceutical used solely to treat chronic
453 conditions. This is likely a further example of incorrect usage or direct disposal of unused
454 carbamazepine. To gain further understanding of this distribution, the temporal trends were
455 considered.

456 For ketoconazole, with a normalised load of 79.2 ± 35.7 mg d^{-1} 1,000 inh^{-1} at WwTW C, it
457 shows high daily variation through the week (45.0%) with high loads seen on Monday-
458 Wednesday and lower throughout the rest of the week. A similar trend is also seen at WwTW
459 B with the highest loads on Tuesday and Wednesday and a daily variation of 44.1 %, the other
460 sites have daily variation of 21.5 – 29.7 %. From further research, this is likely due to the
461 primary mode of administration of this pharmaceutical in the form of a medicated shampoo
462 (based on prescription data from this catchment), which is applied one to two times a week for
463 the prevention or treatment of seborrheic dermatitis and dandruff (20 mg g^{-1}) and is available
464 both over the counter and with a prescription (National Health Service Business Services
465 Authority, 2019; Wishart et al., 2018).

466 Carbamazepine shows a significant increase in influent$_{SPM}$ load on Sunday at WwTW A, which
467 is not seen in the metabolites. In influent$_{AQ}$, the carbamazepine load increases by >300 %, from
468 the average load of 4.3 g d^{-1} to 12.7 g d^{-1}. Carbamazepine has previously shown no measurable
469 degradation under typical sewer conditions (O'Brien et al., 2017), therefore the levels seen are

likely unchanged from entering the sewer. Within the catchment of this WwTW, this pharmaceutical is mainly administered in tablet form as 100, 200, or 400 mg (National Health Service Business Services Authority, 2019; Wishart et al., 2018). Therefore, this peak represents disposal of between 21 × 400 mg tablets or 84 × 100 mg tablets. In $influent_{SPM}$, the same trend can be seen, however it occurs to a greater magnitude (from the mean of the rest of the week: 0.2 g d^{-1} to 30.2 g d^{-1} on Sunday). When $influent_{SPM}$ is combined with influent to calculate a total load, the increase is from 4.5 g d^{-1} to 42.9 g d^{-1}, which suggests disposal between 96 × 400 mg tablets or 384 × 100 mg tablets. The percentage partitioning for this day was drastically altered from the 3.6 % average for the remainder of the week to the high value to 70 % on the day. This is perhaps indicative of the disposal of a highly concentrated solid load.

Fluoxetine disposal has been previously observed within this catchment, which was attributed to ~915 pills, as described by Petrie et al. (Petrie et al., 2016), adding to evidence which suggests direct disposal of pharmaceuticals is more common than previously thought. Within that study Petrie et al. proposed a framework to differentiate between normal, daily usage of these CECs and direct disposal of them in influent. It is likely that the use of 24-hour composites with a short period between subsample collection allowed these events to be captured. Currently, the effects of these unexpected spikes of CECs are unknown. The biological treatments at WwTWs will largely adapt to the everyday fluxes of CEC load, however, the sudden increase in CECs such as carbamazepine, ketoconazole or fluoxetine could potentially cause changes in the microbiology that reduce treatment efficiency. Furthermore, these events will likely lead to an increase in load and concentration leaving the works, which may cause a similar phenomenon with the environmental flora and fauna, as it is exposed to an acute impact of CEC load.

3.2.2. CEC removal from the liquid phase during WwTW treatment

The catchment-scale study enabled the performance of five WwTWs for the removal of micropollutants to be assessed under similar weather conditions (Table S9). Percentage removal (% removal) was calculated as described in Section S2, SI. To summarise, it is the percentage reduction in load of a CEC between liquid phases of influent ($influent_{AQ}$) and effluent. The process types monitored include two activated sludge treatments, conventional activated sludge (CAS) (WwTWs A and E), and sequencing batch reactors (SBRs) (WwTW E). Trickling (rotating biological) filters (TF) configured with different bed media were used at the remaining WwTWs (WwTW B, C and D). CAS is generally considered to achieve greater micropollutant removals than TFs from collated full-scale data (Baker and Kasprzyk-Hordern, 2013; Kasprzyk-Hordern et al., 2009). This is considered to be as a result of longer hydraulic retention times (HRT) associated with CAS, enabling greater contact time for biodegradation. HRTs for this catchment can be found in Table 2. However, this study found this is not the case for all classes of CECs. Figure S1 shows average percentage removals ± relative standard deviation per site and overall removal in bar charts, the data for which can be found in Table S7. Figure 6 shows the removal data of selected classes of CECs across all WwTWs in the form of box plots.

The removal of lifestyle chemicals and creatinine were high, with creatinine removed at 99.6 ± 0.9 %, caffeine at 97.8 ± 1.8 %, nicotine at 96.6 ± 3.1 %, 1,7-dimethylxanthine at 95.6 ± 3.6 % and cotinine at 93.2 ± 5.7 %. The CAS and SBR WwTWs (WwTWs A, E) show better removals for caffeine and nicotine and significantly better removals for their metabolites. This is in line with removals seen at other sites in the UK with TFs and CAS in a study by Baker et al (Baker and Kasprzyk-Hordern, 2013).

This trend can be seen in the NSAIDs, where this pattern continues with acetaminophen (only slight improvement at WwTWs A, E due to such high removal 99.4 ± 0.7 %), ibuprofen (94.4 ± 5.3 %), and naproxen (83.0 ± 12.9 %). In contrast, diclofenac shows the best removal at sites

520 with TFs (WwTWs B-D, removal range 29.0 – 64.5 %), and worst at WwTW E (-3.0 ± 10.7
521 %). Ketoprofen showed 11.4 ± 9.9 % removal at WwTW E but was not detected at the other
522 sites and therefore removal cannot be determined. The trend seen for the other NSAIDs is
523 consistent with those found by Martín et al. and Kasprzyk-Hordern et al., (Kasprzyk-Hordern
524 et al., 2009; Martín et al., 2012).

525 The plasticiser, BPA (93.0 ± 3.6 %), and other industrial and personal care product ingredients,
526 generally show high removal across the catchment with little variation between sites, such as
527 the UV filters (benzophenone-1 with 96.6 ± 3.1 %, benzophenone-2 with 99.6 ± 0.8 %,
528 benzophenone-3 with 91.7 ± 2.0 %, not benzophenone-4 with 32.6 ± 32.3 % removal however),
529 and all parabens (methylparaben with 99.5 ± 0.3 %, ethylparaben with 99.8 ± 0.4 %,
530 propylparaben with 99.2 ± 0.7 % and butylparaben with 100.0 ± 0.0 % removal). This is
531 consistent with removals obtained for these CECs at sites with TFs and CAS treatment in Wales
532 (Kasprzyk-Hordern et al., 2009).

533 Several antidepressants show low-medium level removal with little variation between TF
534 WwTWs B-D, i.e. citalopram (average removals are between 17.3 to 20.5 %), amitriptyline
535 (50.9 to 57.6 %) and sertraline (53.1 to 58.2 %), but show the medium to high levels of removal
536 at CAS WwTW A (51.5 ± 19.4 %, 87.6 ± 10.2 %, and 54.4 ± 24.1 % for citalopram,
537 amitriptyline and sertraline respectively). Kasprzyk-Hordern et al., found similar levels of
538 removal for amitriptyline at both TFs and CAS sites (Kasprzyk-Hordern et al., 2009).
539 Mirtazapine shows similar levels of removal for WwTWs A-C (22.0 ± 6.3 %) and had the
540 highest levels of removal at WwTW D (39.8 ± 11.4 %). Venlafaxine saw negative removals at
541 WwTWs A-C (-28.8 ± 14.5 %) and, similarly to mirtazapine, showed the highest levels of
542 removal at WwTW D, 28.4 ± 23.6 %. Fluoxetine also shows negative removal at WwTW A-B
543 (-53.8 to -27.4 %), WwTW C showed high highest levels of removal 32.7 ± 8.9 %, no overall
544 removal at WwTW D. Both venlafaxine and fluoxetine have previously shown greater removal

levels at both TF and CAS sites (Baker and Kasprzyk-Hordern, 2013; Verlicchi et al., 2012). WwTW E showed the worst removals for all antidepressants, ranging from -81.3 % for fluoxetine to 35.7 % for sertraline (except venlafaxine, which showed negligible removal at this site), this may be due to the short hydraulic residence time (HRT = 10.9 h) in the main treatment stream (90 % sequencing batch rectors) at this site. The antidepressant metabolites were either completely removed (norfluoxetine, norsertraline), similar to results found by Baker et al., and Comber et al., (Baker and Kasprzyk-Hordern, 2013; Comber et al., 2019), were removed similarly to the parent drug (desmethylcitalopram), or increased in load between influent$_{AQ}$ and effluent, likely due to degradation of the parent drug into the metabolite (nortriptyline, desmethylvenlafaxine), similar to what was found by Baker et al. and Paiga et al., (concentration based calculation of removal, rather than load) (Baker and Kasprzyk-Hordern, 2013; Paíga et al., 2019).

Carbamazepine and its metabolites, carbamazepine-10,11-epoxide and 10,11-dihydro-10-hydroxycarbamazepine, show increased levels between influent$_{AQ}$ and effluent at the CAS WwTW A. 10,11-dihydro-10-hydroxycarbamazepine forms O-glucuronides during human metabolism, which can be cleaved by β-glucuronidase, from faecal bacteria, leading to this increase (Ta et al., 1999). Carbamazepine and carbamazepine-10,11-epoxide, on the other hand, form N-glucuronides during human metabolism, which have shown they cannot be degraded by this enzyme but still show increased loads in effluent (Bahlmann et al., 2014).

The lack of degradation for tramadol in this study contrasts with the results found by Baker et al., for both TFs and CAS, however, it is comparable to removal levels found by Kasprzyk-Hordern et al., and Archer et al., (Archer et al., 2017; Baker and Kasprzyk-Hordern, 2013; Kasprzyk-Hordern et al., 2009). The O-desmethyltramadol metabolite can be further metabolised to form O-glucuronides (Wishart et al., 2018), which as previously discussed, are cleaved during biological treatment.

570 The high removal of the lifestyle chemicals, NSAIDs, parabens and plasticisers has led to a
571 very different profile for treated wastewater compared to raw wastewater. This is observed in
572 analgesics and metabolites, which represent a quarter of the total load after treatment. Anti-
573 diabetics also show an increased proportion of the total load, due to relatively low removal at
574 the WwTWs. Overall, antibiotics are poorly removed, < 50 %, although WwTWs A and E have
575 higher levels of removal for sulfasalazine (73.7 ± 9.2 % WwTW A and 71.8 ± 3.2 % at WwTW
576 E) and clarithromycin (83.0 ± 9.8 % WwTW A and 64.3 ± 7.3 % WwTW E). WwTW E
577 removed 74.2 ± 7.3 % and 68.7 ± 6.1 % of azithromycin and sulfamethoxazole respectively,
578 but A has very poor removal for these compounds. WwTWs using biological activated sludge
579 have previously shown reasonable removal for these compounds, similar to what was seen at
580 WwTW E in this study (Golovko et al., 2014). Furthermore, it shows that long term seasonal
581 changes may have further effects on removal that are not seen in this study, but which should
582 be taken into account for the wider picture.

583 In summary, although, previously CAS was considered a better micropollutant removal process
584 than TFs, this considered a smaller range of compounds (Baker and Kasprzyk-Hordern, 2013;
585 Kasprzyk-Hordern et al., 2009). The larger range of compounds considered in this study shows
586 this is not so clear cut and there is great variation between classes, as well as CECs within the
587 classes. In the next section overall mass balance is taken into consideration and may provide a
588 clearer result.

589 ### 3.2.3. CEC mass balance in studied WwTWs

590 The estimated total mass of 119 of the 138 CECs in this work entering (quantifiable in total
591 influent) the WwTW of this catchment is 1,185 kg per week (wk^{-1}) (or 1,847 kg wk^{-1} with
592 creatinine). $Influent_{SPM}$ contributes only 0.8 % (9.6 kg wk^{-1}) of the total load, but as seen in
593 Figures 1 and 2, it has a very different chemical profile. This results in total mass loads of 135
594 to 167 g d^{-1} 1,000 inh^{-1} in influent, these are far higher than the 2.1 g d^{-1} 1,000 inh^{-1} mass loads

595 calculated from the work by Castiglioni et al., in Italy (based on the sum of the influent$_{AQ}$ loads
596 of five main classes, 5,049 g d^{-1}, divided by the estimated population (2,400,000) of the
597 contributing WwTWs)(Castiglioni et al., 2018). Though both studies cover a large range of
598 pharmaceuticals, industrial chemicals and personal care products ingredients, Castiglioni's
599 study only has 82 CECs, compared to 138 in this study, though both contain many similar high
600 usage CECs. Furthermore, there are likely to be large differences in prescriptions and industrial
601 contribution between Italy and the UK.
602 1,082 kg (1,696 kg, including creatinine) is removed from the influent$_{AQ}$ over the course of the
603 study, leaving 72 kg (73 kg including creatinine) in effluent and entering the environment. 51
604 kg of this is from WwTW E which discharges directly into the estuary, which could not be
605 sampled as part of this study. For the remaining WwTWs the highest contributor, by mass, was
606 WwTW C with 11.6 kg discharged and leads to clear increases in daily river loads both
607 downstream at WwTW C and upstream at WwTW D. The mass discharged by each WwTW
608 generally increases by population equivalents contributing to the WwTWs i.e. WwTW B <
609 WwTW C < WwTW E, however WwTW D, despite having around half the population of
610 WwTW A, shows much higher mass discharge. Normalising the daily load discharge by each
611 WwTW shows the highest population normalised loads are at WwTW D. WwTW A (5 g d^{-1}
612 1,000 inh^{-1}) < WwTW E (9 g d^{-1} 1,000 inh^{-1}) < WwTW B (12 g d^{-1} 1,000 inh^{-1}) < WwTW C
613 (15 g d^{-1} 1,000 inh^{-1}) < WwTW D (16 g d^{-1} 1,000 inh^{-1} (21 g d^{-1} 1,000 inh^{-1} with creatinine)).
614 Despite this, WwTW D removed the highest mass load per person, 151 g d^{-1} 1,000 inh^{-1}, which
615 is close to WwTW E's removal at 146 g d^{-1} 1,000 inh^{-1}. Based on this TF and SBR show similar
616 removal per person, however, as a proportion of the incoming load WwTW E removed 94.5
617 %, whereas WwTW D removed 90.4 %. Overall, WwTWs with TF appear to have a lower
618 capacity for removal of CECs than SBR, (WwTWs B and C removed 78.1 % and 88.7 %
619 respectively) whereas WwTW A appears to be the worst with 69.8 % total CEC mass removed.

620 Although, WwTW A showed the lowest contribution with only 0.2 kg over the course of the
621 study difference between upstream and downstream or 0.7 g d^{-1} 1,000 inh^{-1}. The small
622 discharge into a large river at WwTW D, shows only a small difference between upstream and
623 downstream of 0.4 kg over the course of the study or 3 g d^{-1} 1,000 inh^{-1} in the river. WwTW B
624 and C had the highest increase in mass between upstream and downstream at 6.5 kg and 10.2
625 kg, or 14 and 13 g d^{-1} 1,000 inh^{-1}, respectively. Overall, the river upstream of WwTW A
626 contained total mass loads of 1.8 kg, or 287 g d^{-1}, which increased to 25.2 kg, or 3.6 kg d^{-1}
627 downstream of WwTW D (distance between A and D, is approximately 60 km). Throughout
628 the catchment, 10.4 kg d^{-1} was discharged into the environment from the studied WwTWs.

629 **3.3. Impact of effluent discharge to receiving river water**

630 The river upstream of the WwTW A had 50/138 CECs above MQL ranging from 0.02 g d^{-1}
631 (cocaine) to 47.8 g d^{-1} (caffeine), which is due to other smaller WwTWs present upstream,
632 leaching from landfills sites, and possible infiltration from septic tanks, which are often used
633 in more rural areas in the UK. Other classes such as plasticisers, veterinary pharmaceuticals,
634 pesticides, fungicides and herbicides may possibly be present as well, due to surface runoff.
635 Samples from the river downstream of the sites show higher loads overall, but also a different
636 distribution of classes, with anti-diabetics, namely metformin, present at a larger proportion
637 (from first being undetectable upstream of WwTW A, to representing 1,309.6 ± 135.5 g d^{-1}
638 downstream of WwTW D). Daily loads ranged from 0.005 g d^{-1} (ketamine, WwTW A) to
639 1,890.3 g d^{-1} (metformin, WwTW C, equivalent to ~1,890 tablets (DrugBank, 2015)) for the
640 84/138 CECs that were detected downstream of the WwTWs. This trend of increasing load
641 down the river is both expected, although perhaps not to this degree, and concerning.

642 Figure 4 (and Figure S5-6) show spatial trends of daily cumulative load and shows a steady
643 increase down the river. Similar trends have been seen in Italy with samples which were
644 collected in the River Lambro basin either side of Milan (Castiglioni et al., 2018). WwTW C

is clearly the highest contributor to river load, which is not surprising as it has the highest population out of WwTWs A-D. The key classes of importance in river water are anti-diabetics, human indicators, NSAIDs, antihistamines, antibiotics, UV filters and analgesics and metabolites which contribute large portions to the total load with the river. This is interesting to compare with the distribution of classes within effluent, as analgesics and metabolites appear to contribute far more highly to effluent (21.0 %), however downstream from the discharge point they contribute far less, only 7.3 %. This indicates that once in the environment, they are far less persistent in the aqueous phase than other classes. A similar trend can also be seen for anti-depressants. Whether these compounds are truly degraded or have partitioned to solid phases (e.g. soils and sediments) within this river will need further investigation. However, a spatio-temporal study in the Llobregat showed that psychiatric drugs, among many other pharmaceuticals, were at levels ranging from 4.41 - 18.02 ng g^{-1} in sediment between the two sampling campaigns and locations. This may be indicative of portioning to solid phases within the river of this catchment. Sertraline in particular showed high concentration levels in Llobregat with 12.08 ng g^{-1} in one sampling campaign (Osorio et al., 2016). Furthermore, antibiotics, such as tetracyclines, will pose further concern as they have been shown to preferentially partition to sediment over surface waters (Kim and Carlson, 2007).

Anti-diabetics, metformin specifically, despite high level of removal (78.7 %), still represent a large proportion of effluent load (15.0 kg of 72.6 kg of the estimated total of the campaign, 20.7 % (Figure 3)). It shows that this removal level is insufficient in preventing anti-diabetics from entering the environment, as an increasing trend is observed through the catchment, as seen in Figure 7. A similar situation is seen for the lifestyle chemicals, which represents 38.6 % of the $influent_{AQ}$ load and despite their high removal rates they are at quantifiable levels in the environment and show an increasing trend through the catchment (Figure 7). This is less so for NSAIDs, which are similarly prevalent in $influent_{AQ}$, at 36.8 % of $influent_{AQ}$ load on

average, but show less of an increase through the catchment. Diclofenac shows clear decreases in loads between sites, whether this is degradation or partitioning to solids, is yet to be determined. However, it has been previously found to partition to river sediments downstream of discharge points, along with other NSAIDs, therefore this fate seems likely within this catchment (Duan et al., 2013).

Benzophenone-3, methylparaben and propylparaben are shown to increase between downstream at WwTW B and upstream at WwTW C. For many other CECs, there is a slight increase suggesting the presence of another source of these compounds in the catchment. The increase of these compounds, associated with personal care products, could be due to much smaller WwTWs contributing to tributaries in the area, however, a similar increase in other CECs would also be expected e.g. carbamazepine, which is not seen. These CECs are usually found in greywater, i.e. from showers and washing. It is currently allowed, although not advised, for greywater from boats to be disposed of directly into the river. It is a practice that may be common in areas outside of marinas where disposal points are few and storage of wastewater onboard is limited and reserved for sewage (Canal and River Trust, 2017). Therefore, the presence of a large number of moorings in this area may contribute to this increase in personal care product ingredients. However, further investigation is required as both locations were not sampled as the same time and the use of grab sampling adds a level of uncertainty.

The river trends of flufenacet and oxadiazon show some small contributions from WwTWs, however the increase between downstream at one site and upstream at the next (particularly between WwTW B and C) supports entry is not primarily via WwTWs but further investigation would be needed to determine the source. Entry of pesticides into environmental surface waters has previously been attributed to diffuse sources such as agricultural application, particularly in proximity to surface waters and further surface runoff during wet weather (Lefrancq et al.,

695 2017; Stuart et al., 2012). Due to the planning of the sampling campaign, rainfall and surface
696 water runoff were at a minimum though this still seems likely to be a source, especially
697 considering the level of agriculture and proximity of farming fields adjacent to the river
698 throughout most of the catchment.

699 **3.4. Presence of micropollutants in digested sludge for land application**

700 An alternative route of entry for anthropogenic micropollutants into the environment is the
701 application of digested sludge (biosolids) onto agricultural land. This area is often overlooked
702 due to the additional analytical requirements to extract micropollutants from solid matrices and
703 the lack of good analytical approaches available (Petrie et al., 2014b). Within the catchment,
704 two WwTW sites had facilities for anaerobic digestion of sludge. WwTWs B and E both receive
705 tankered and piped sludge (primary and secondary) from WwTWs within the catchment in
706 addition to the sludge produced on site.

707 Digested sludge collected from WwTWs B and E was found to contain 65/96 different CECs
708 (Table S5). This included NSAIDs (1.8 % of the total CEC concentration in digested solids
709 (Figure 5)), antidepressants (10.6 %) and analgesics (1.9 %) which were ubiquitous in all
710 samples studied. Ibuprofen, naproxen and diclofenac were all found in digested sludge, with
711 ibuprofen at the highest concentrations for the class with 200 ± 42 ng g^{-1} dry weight (dw) at
712 WwTW B. Although these concentrations are comparable to those previously reported (Guerra
713 et al., 2014; Martín et al., 2012; Radjenović et al., 2009; Sabourin et al., 2012). Of the 12
714 antidepressants and metabolites studied and quantifiable in sludge, all were detected, including
715 paroxetine and duloxetine which were found in no other samples throughout the catchment.
716 This is attributed to their tendency to sorb to organic matter in wastewater and during treatment,
717 as well as their recalcitrance in biologically mediated processes. Amitriptyline, sertraline and
718 citalopram were present at concentrations > 400 ng g^{-1}. Morphine was the analgesic found at

719 the highest levels with a mean concentration of 413 ± 43 ng g^{-1} at WwTW E. For such
720 compounds, there is limited published data on their occurrence.

721 Other CECs found at notable concentrations (>100 ng g^{-1}) were methylparaben, BPA,
722 chloramphenicol, ketoconazole, gemfibrozil, propranolol, carbamazepine and nicotine. Of
723 these micropollutants, BPA was found at the highest levels with mean concentrations of 4,366
724 ± 260 ng g^{-1} (WwTW B) and 37,025 ± 4,229 ng g^{-1} (WwTW E) (Table S5). These
725 concentrations are greater than has been observed in previous studies, which have found BPA
726 at concentrations of ~1,000 ng g^{-1} (Langdon et al., 2014; Samaras et al., 2013) to 14,400 ng g^{-1}
727 (carbon normalised concentrations) (Kinney et al., 2006). The levels reported here are
728 attributed to the relatively high concentrations observed in receiving wastewater from industrial
729 activities. In this study, BPA contributed 76.1 % to the total concentration in digested solids.

730 As described by Carballa et al., and Hyland et al., several factors including physicochemical
731 properties of both digested solid and the CECs, as well as the pH, temperature and water content
732 may influence sorption of CECs to the digested solids (Carballa et al., 2008; Hyland et al.,
733 2012). Crucially, the CECs present in digested solids, which have affinity with the aqueous
734 phase, e.g. ibuprofen and naproxen, may not stay partitioned to the solids upon application of
735 digested solids to the environment. These may enter landfill leachates or surface runoff from
736 agricultural applications and may enter the aqueous environment via this route. Other CECs
737 such as BPA show some recalcitrance in amended soils, possibly due to strong sorption and
738 lack of bioavailability, leading to a lack of degradation as found in a fraction of BPA by Zhang
739 et al., (Zhang et al., 2015).

740 **4. Conclusions**

741 This paper aimed to investigate the changes in micropollutants load throughout a river
742 catchment system in the South-West of the UK, to gain further information on their sources,

743 fate and behaviour. This was achieved by undertaking a comprehensive investigation of an
744 extended list of 142 CECs at five strategic WwTWs representing >75 % of the wastewater from
745 the catchment population. The main conclusions are as follows:

746 1. Lifestyle, availability of pharmaceuticals without prescription and industry have the
747 biggest effects on the content of influent. Population size and the extent of urbanisation
748 are key drivers of high variability across the catchment, and increased levels of CECs
749 in the environment down the catchment. This is confirmed by normalisation of CEC
750 loads for population, which results in a more even distribution of population normalised
751 CEC loads across the catchment(154 ± 12 mg d^{-1} inh^{-1}).
752 2. The analysis of $influent_{AQ}$ and $influent_{SPM}$ is key to determine true levels of CECs
753 entering the works. Furthermore, each phase has a distinct chemical composition and
754 some CECs may be found primarily in one phase or the other. Without analysis of both,
755 a holistic understanding of pollutant fluxes is not possible.
756 3. Investigating temporal trends can highlight potential instances of incorrect use,
757 incidental release or direct disposal. Although this is evident in both phases, it is
758 particularly clear in the solid phase in this study, e.g. carbamazepine and ketoconazole.
759 Furthermore, the current impact of these sudden, acute, events is currently unknown
760 but may have noticeable effects on wastewater treatment processes or pose an
761 environmental risk.
762 4. Despite WwTWs not being designed for the removal of CECs, the majority of the
763 studied CECs were removed from the works to the high extent (10.3 kg d^{-1} remaining
764 in effluent compared to 167.9 kg d^{-1} in influent). This markedly decreased the potential
765 environmental burden posed by the extent of urbanisation and size of the population
766 within this catchment.

5. Analysis of the river water upstream and downstream of the WwTW discharge point allowed the contribution of each WwTW to the environmental burden to be considered. It also highlights the potential for contribution to the environmental burden from other sources, which may include: septic tanks, sewer overflows, smaller WwTWs, surface runoff and greywater disposal. Furthermore, it showed that many CECs are ubiquitous throughout the catchment, with many increasing in load down the river due to the persistent addition of these compounds to the environment being higher than their degradation rate.
6. Analysis of digested solids has shown high levels of a wide range of CECs present (65/96). These concentrations are significant and considering the potential use of this 'treated' matrix in amended agricultural soils, further consideration should be given to the potential ecological risk of this matrix, which is currently barely understood. Furthermore, the removal trends/treatment efficiency require further study.

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Supplementary material:

Section S1 describes the material and methods used in this work in more detail.

Table S1 shows the instrumental and method performance data for the analytical method.

Section S2 describes the data processing that was used in this work

Section S3 add some additional information to the results in the main text for additional context or more indepth discussion

Table S2 shows the dilution factor of effluent in the river water at the discharge point at each site.

Table S3 provides the 7-day mean population normalised loads for $influent_{AQ}$.

Table S4 provides the 7-day mean population normalised loads for $influent_{SPM}$.

Table S5 presents the frequency of detection of each analyte, the minimum and maximum loads, the mean, standard deviation and variance across the 7 days in each matrix.

Table S6 shows the 7-day average percentage partitioning of CECs in influent for all sites.

Figure S1 presents the 7-day average percentage removal from $influent_{AQ}$ during WwTW treatment for each site and overall.

Table S7 shows the data of Figure S1, i.e. 7-day average percentage removal from $influent_{AQ}$ during WwTW treatment for each site and overall.

Table S8 shows the general and chemical information of all CECs analysed.

Figure S2 shows the temporal trends in influent for selected compounds.

Figure S3 shows the temporal trends in both $influent_{AQ}$ and $influent_{SPM}$ for selected compounds.

Figure S4 shows the spatial trends in river water through the catchment as cumulative load by class.

811 Figure S5 shows the spatial trends in river water through the catchment as cumulative load by
812 individual CEC.

813 Table S9 shows the metadata of the sampling campaign, i.e. daily temperature, rainfall and pH
814 of samples.

815 Section S4 shows the references for the SI.

816 Tables S10-32 shows the detailed daily loads (g d^{-1}) for each CEC at each site in each matrix.

References

Altenburger, R., Ait-Aissa, S., Antczak, P., Backhaus, T., Barceló, D., Seiler, T.-B., Brion, F., Busch, W., Chipman, K., de Alda, M.L., de Aragão Umbuzeiro, G., Escher, B.I., Falciani, F., Faust, M., Focks, A., Hilscherova, K., Hollender, J., Hollert, H., Jäger, F., Jahnke, A., Kortenkamp, A., Krauss, M., Lemkine, G.F., Munthe, J., Neumann, S., Schymanski, E.L., Scrimshaw, M., Segner, H., Slobodnik, J., Smedes, F., Kughathas, S., Teodorovic, I., Tindall, A.J., Tollefsen, K.E., Walz, K.-H., Williams, T.D., Van den Brink, P.J., van Gils, J., Vrana, B., Zhang, X., Brack, W., 2015. Future water quality monitoring — Adapting tools to deal with mixtures of pollutants in water resource management. Sci. Total Environ. 512–513, 540–551. https://doi.org/10.1016/j.scitotenv.2014.12.057

Archer, E., Petrie, B., Kasprzyk-Hordern, B., Wolfaardt, G.M., 2017. The fate of pharmaceuticals and personal care products (PPCPs), endocrine disrupting contaminants (EDCs), metabolites and illicit drugs in a WWTW and environmental waters. Chemosphere 174, 437–446. https://doi.org/10.1016/j.chemosphere.2017.01.101

Bahlmann, A., Brack, W., Schneider, R.J., Krauss, M., 2014. Carbamazepine and its metabolites in wastewater: Analytical pitfalls and occurrence in Germany and Portugal. Water Res. 57, 104–114. https://doi.org/10.1016/j.watres.2014.03.022

Baker, D.R., Kasprzyk-Hordern, B., 2013. Spatial and temporal occurrence of pharmaceuticals and illicit drugs in the aqueous environment and during wastewater treatment: New developments. Sci. Total Environ. 454–455, 442–456. https://doi.org/10.1016/j.scitotenv.2013.03.043

Baker, D.R., Kasprzyk-Hordern, B., 2011. Multi-residue determination of the sorption of illicit drugs and pharmaceuticals to wastewater suspended particulate matter using pressurised liquid extraction, solid phase extraction and liquid chromatography coupled with tandem mass spectrometry. J. Chromatogr. A 1218, 7901–13. https://doi.org/10.1016/j.chroma.2011.08.092

Baker, D.R., Očenášková, V., Kvicalova, M., Kasprzyk-Hordern, B., 2012. Drugs of abuse in wastewater and suspended particulate matter - Further developments in sewage epidemiology. Environ. Int. 48, 28–38. https://doi.org/10.1016/j.envint.2012.06.014

Boogaerts, T., Degreef, M., Covaci, A., van Nuijs, A.L.N., 2019. Development and validation of an analytical procedure to detect spatio-temporal differences in antidepressant use through a wastewater-based approach. Talanta 200, 340–349. https://doi.org/10.1016/j.talanta.2019.03.052

Canal and River Trust, 2017. A Canal Is Not A Bin [WWW Document]. URL https://canalrivertrust.org.uk/enjoy-the-waterways/boating/boating-blogs-and-features/boating-team/a-canal-is-not-a-bin (accessed 9.9.19).

Carballa, M., Fink, G., Omil, F., Lema, J.M., Ternes, T., 2008. Determination of the solid-water distribution coefficient (Kd) for pharmaceuticals, estrogens and musk fragrances in digested sludge. Water Res. 42, 287–295. https://doi.org/10.1016/j.watres.2007.07.012

Carvalho, R.N., Ceriani, L., Ippolito, A., 2015. Development of the first Watch List under the Environmental Quality Standards Directive water policy. https://doi.org/10.2788/101376

Castiglioni, S., Davoli, E., Riva, F., Palmiotto, M., Camporini, P., Manenti, A., Zuccato, E., 2018. Mass balance of emerging contaminants in the water cycle of a highly urbanized

and industrialized area of Italy. Water Res. 131, 287–298. https://doi.org/10.1016/j.watres.2017.12.047

Castrignanò, E., Kannan, A.M., Feil, E.J., Kasprzyk-Hordern, B., 2018a. Enantioselective fractionation of fluoroquinolones in the aqueous environment using chiral liquid chromatography coupled with tandem mass spectrometry. Chemosphere 206, 376–386. https://doi.org/10.1016/j.chemosphere.2018.05.005

Castrignanò, E., Yang, Z., Bade, R., Baz-Lomba, J.A., Castiglioni, S., Causanilles, A., Covaci, A., Gracia-Lor, E., Hernandez, F., Kinyua, J., McCall, A.K., van Nuijs, A.L.N., Ort, C., Plósz, B.G., Ramin, P., Rousis, N.I., Ryu, Y., Thomas, K. V., de Voogt, P., Zuccato, E., Kasprzyk-Hordern, B., 2018b. Enantiomeric profiling of chiral illicit drugs in a pan-European study. Water Res. 130, 151–160. https://doi.org/10.1016/j.watres.2017.11.051

Comber, S., Gardner, M., Sörme, P., Ellor, B., 2019. The removal of pharmaceuticals during wastewater treatment: Can it be predicted accurately? Sci. Total Environ. 676, 222–230. https://doi.org/10.1016/j.scitotenv.2019.04.113

Coutu, S., Wyrsch, V., Wynn, H.K., Rossi, L., Barry, D.A., 2013. Temporal dynamics of antibiotics in wastewater treatment plant influent. Sci. Total Environ. 458–460, 20–26. https://doi.org/10.1016/j.scitotenv.2013.04.017

de Mejia, E.G., Ramirez-Mares, M.V., 2014. Impact of caffeine and coffee on our health. Trends Endocrinol. Metab. 25, 489–492. https://doi.org/10.1016/j.tem.2014.07.003

Department of Health &, Department for Environment Food and Rural Affairs United Kingdom, 2013. UK Five Year Antimicrobial Resistance Strategy. Dep. Heal. Dep. Environ. Food Rural Aff. 43.

DrugBank, 2015. DrugBank v4.2 [WWW Document]. [Online]. URL http://www.drugbank.ca/ (accessed 5.1.15).

Duan, Y.P., Meng, X.Z., Wen, Z.H., Ke, R.H., Chen, L., 2013. Multi-phase partitioning, ecological risk and fate of acidic pharmaceuticals in a wastewater receiving river: The role of colloids. Sci. Total Environ. 447, 267–273. https://doi.org/10.1016/j.scitotenv.2013.01.017

Ebele, A.J., Abou-Elwafa Abdallah, M., Harrad, S., 2017. Pharmaceuticals and personal care products (PPCPs) in the freshwater aquatic environment. Emerg. Contam. 3, 1–16. https://doi.org/10.1016/j.emcon.2016.12.004

European Medicines Agency, 2019. European Medicines Agency (EMA). Committee for Medicinal Products for Veterinary use (CVMP) 44, 1–67.

Flint, S., Markle, T., Thompson, S., Wallace, E., 2012. Bisphenol A exposure, effects, and policy: A wildlife perspective. J. Environ. Manage. 104, 19–34. https://doi.org/10.1016/j.jenvman.2012.03.021

Gao, J., Banks, A., Li, J., Jiang, G., Lai, F.Y., Mueller, J.F., Thai, P.K., 2017. Evaluation of in-sewer transformation of selected illicit drugs and pharmaceutical biomarkers. Sci. Total Environ. 609, 1172–1181. https://doi.org/10.1016/j.scitotenv.2017.07.231

Geissen, V., Mol, H., Klumpp, E., Umlauf, G., Nadal, M., van der Ploeg, M., van de Zee, S.E.A.T.M., Ritsema, C.J., 2015. Emerging pollutants in the environment: A challenge for water resource management. Int. Soil Water Conserv. Res. 3, 57–65. https://doi.org/10.1016/j.iswcr.2015.03.002

Golovko, O., Kumar, V., Fedorova, G., Randak, T., Grabic, R., 2014. Seasonal changes in antibiotics, antidepressants/psychiatric drugs, antihistamines and lipid regulators in a wastewater treatment plant. Chemosphere 111, 418–426. https://doi.org/10.1016/j.chemosphere.2014.03.132

Guerra, P., Kim, M., Shah, A., Alaee, M., Smyth, S.A., 2014. Occurrence and fate of antibiotic, analgesic/anti-inflammatory, and antifungal compounds in five wastewater treatment processes. Sci. Total Environ. 473–474, 235–243. https://doi.org/10.1016/j.scitotenv.2013.12.008

Gushgari, A.J., Driver, E.M., Steele, J.C., Halden, R.U., 2018. Tracking narcotics consumption at a Southwestern U.S. university campus by wastewater-based epidemiology. J. Hazard. Mater. 359, 437–444. https://doi.org/10.1016/j.jhazmat.2018.07.073

Heberer, T., 2002. Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: a review of recent research data. Toxicol. Lett. 131, 5–17. https://doi.org/10.1016/s0378-4274(02)00041-3

Hyland, K.C., Dickenson, E.R.V., Drewes, J.E., Higgins, C.P., 2012. Sorption of ionized and neutral emerging trace organic compounds onto activated sludge from different wastewater treatment configurations. Water Res. 46, 1958–1968. https://doi.org/10.1016/j.watres.2012.01.012

Jelic, A., Rodriguez-Mozaz, S., Barceló, D., Gutierrez, O., 2015. Impact of in-sewer transformation on 43 pharmaceuticals in a pressurized sewer under anaerobic conditions. Water Res. 68, 98–108. https://doi.org/10.1016/j.watres.2014.09.033

Kasprzyk-Hordern, B., Dinsdale, R.M., Guwy, A.J., 2009. The removal of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs during wastewater treatment and its impact on the quality of receiving waters. Water Res. 43, 363–380. https://doi.org/10.1016/j.watres.2008.10.047

Kasprzyk-Hordern, B., Dinsdale, R.M., Guwy, A.J., 2008. The occurrence of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs in surface water in South Wales, UK. Water Res. 42, 3498–518. https://doi.org/10.1016/j.watres.2008.04.026

Kim, S.C., Carlson, K., 2007. Temporal and spatial trends in the occurrence of human and veterinary antibiotics in aqueous and river sediment matrices. Environ. Sci. Technol. 41, 50–57. https://doi.org/10.1021/es060737+

Kinney, C.A., Furlong, E.T., Zaugg, S.D., Burkhardt, M.R., Werner, S.L., Cahill, J.D., Jorgensen, G.R., 2006. Survey of organic wastewater contaminants in biosolids destined for land application. Environ. Sci. Technol. 40, 7207–7215. https://doi.org/10.1021/es0603406

Kumar, R., Sarmah, A.K., Padhye, L.P., 2019. Fate of pharmaceuticals and personal care products in a wastewater treatment plant with parallel secondary wastewater treatment train. J. Environ. Manage. 233, 649–659. https://doi.org/10.1016/j.jenvman.2018.12.062

Lai, F.Y., O'Brien, J., Bruno, R., Hall, W., Prichard, J., Kirkbride, P., Gartner, C., Thai, P., Carter, S., Lloyd, B., Burns, L., Mueller, J., 2016. Spatial variations in the consumption of illicit stimulant drugs across Australia: A nationwide application of wastewater-based epidemiology. Sci. Total Environ. 568, 810–818. https://doi.org/10.1016/j.scitotenv.2016.05.207

951 Langdon, K.A., Warne, M.S.J., Smernik, R.J., Shareef, A., Kookana, R.S., 2012. Field
952 dissipation of 4-nonylphenol, 4-t-octylphenol, triclosan and bisphenol A following land
953 application of biosolids. Chemosphere 86, 1050–1058.
954 https://doi.org/10.1016/j.chemosphere.2011.11.057

955 Langdon, K.A., Warne, M.S.T.J., Smernik, R.J., Shareef, A., Kookana, R.S., 2014.
956 Persistence of estrogenic activity in soils following land application of biosolids.
957 Environ. Toxicol. Chem. 33, 26–28. https://doi.org/10.1002/etc.2395

958 Lefrancq, M., Jadas-hécart, A., La, I., Landry, D., Payraudeau, S., 2017. Science of the Total
959 Environment High frequency monitoring of pesticides in runoff water to improve
960 understanding of their transport and environmental impacts. Sci. Total Environ. 587–
961 588, 75–86. https://doi.org/10.1016/j.scitotenv.2017.02.022

962 Loos, R., Gawlik, B.M., Locoro, G., Rimaviciute, E., Contini, S., Bidoglio, G., 2009. EU-
963 wide survey of polar organic persistent pollutants in European river waters. Environ.
964 Pollut. 157, 561–568. https://doi.org/10.1016/j.envpol.2008.09.020

965 Lopardo, L., Petrie, B., Proctor, K., Youdan, J., Barden, R., Kasprzyk-Hordern, B., 2019.
966 Estimation of community-wide exposure to bisphenol A via water fingerprinting.
967 Environ. Int. 125, 1–8. https://doi.org/10.1016/j.envint.2018.12.048

968 Luo, Y., Guo, W., Ngo, H.H., Nghiem, L.D., Hai, F.I., Zhang, J., Liang, S., Wang, X.C.,
969 2014. A review on the occurrence of micropollutants in the aquatic environment and
970 their fate and removal during wastewater treatment. Sci. Total Environ.
971 https://doi.org/10.1016/j.scitotenv.2013.12.065

972 Martín, J., Camacho-Muñoz, D., Santos, J.L., Aparicio, I., Alonso, E., 2012. Occurrence of
973 pharmaceutical compounds in wastewater and sludge from wastewater treatment plants:
974 Removal and ecotoxicological impact of wastewater discharges and sludge disposal. J.
975 Hazard. Mater. 239–240, 40–47. https://doi.org/10.1016/j.jhazmat.2012.04.068

976 Martín, J., Santos, J.L., Aparicio, I., Alonso, E., 2015. Pharmaceutically active compounds in
977 sludge stabilization treatments: Anaerobic and aerobic digestion, wastewater
978 stabilization ponds and composting. Sci. Total Environ. 503–504, 97–104.
979 https://doi.org/10.1016/j.scitotenv.2014.05.089

980 Mastroianni, N., López-García, E., Postigo, C., Barceló, D., López de Alda, M., 2017. Five-
981 year monitoring of 19 illicit and legal substances of abuse at the inlet of a wastewater
982 treatment plant in Barcelona (NE Spain) and estimation of drug consumption patterns
983 and trends. Sci. Total Environ. 609, 916–926.
984 https://doi.org/10.1016/j.scitotenv.2017.07.126

985 McCall, A.K., Bade, R., Kinyua, J., Lai, F.Y., Thai, P.K., Covaci, A., Bijlsma, L., van Nuijs,
986 A.L.N., Ort, C., 2016. Critical review on the stability of illicit drugs in sewers and
987 wastewater samples. Water Res. 88, 933–947.
988 https://doi.org/10.1016/j.watres.2015.10.040

989 Mendoza, A., Aceña, J., Pérez, S., López de Alda, M., Barceló, D., Gil, A., Valcárcel, Y.,
990 2015. Pharmaceuticals and iodinated contrast media in a hospital wastewater: A case
991 study to analyse their presence and characterise their environmental risk and hazard.
992 Environ. Res. 140, 225–241. https://doi.org/10.1016/j.envres.2015.04.003

993 Mole, R.A., Brooks, B.W., 2019. Global scanning of selective serotonin reuptake inhibitors:
994 occurrence, wastewater treatment and hazards in aquatic systems. Environ. Pollut. 250,
995 1019–1031. https://doi.org/10.1016/j.envpol.2019.04.118

Musolff, A., Leschik, S., Möder, M., Strauch, G., Reinstorf, F., Schirmer, M., 2009. Temporal and spatial patterns of micropollutants in urban receiving waters. Environ. Pollut. 157, 3069–3077. https://doi.org/10.1016/j.envpol.2009.05.037

National Health Service Business Services Authority, 2019. NHSBSA Practice prescribing dispensing data [WWW Document]. NHSBSA Copyr. URL https://www.nhsbsa.nhs.uk/prescription-data/dispensing-data/dispensing-contractors-data (accessed 5.21.19).

Nefau, T., Karolak, S., Castillo, L., Boireau, V., Levi, Y., 2013. Presence of illicit drugs and metabolites in influents and effluents of 25 sewage water treatment plants and map of drug consumption in France. Sci. Total Environ. 461–462, 712–722. https://doi.org/10.1016/j.scitotenv.2013.05.038

O'Brien, J.W., Banks, A.P.W., Novic, A.J., Mueller, J.F., Jiang, G., Ort, C., Eaglesham, G., Yuan, Z., Thai, P., 2017. Impact of in-sewer degradation of pharmaceutical and personal care products (PPCPs) population markers on a population model. Environ. Sci. Technol. acs.est.6b02755. https://doi.org/10.1021/acs.est.6b02755

Ort, C., Lawrence, M. G., Rieckermann, J., and Joss, a., 2010. Sampling for Pharmaceuticals and Personal Care Products (PPCPs) and Illicit Drugs in Wastewater Systems : Are Your Conclusions Valid ? A Critical Review Sampling for PPCPs in Wastewater Systems : Comparison of Different Sampling Modes and Optimization S. Environ. Sci. Technol. 44, 6024–6035. https://doi.org/10.1021/es100779n

Ort, C., Lawrence, M.G., Reungoat, J., Mueller, J.F., 2010. Sampling for PPCPs in Wastewater Systems: Comparison of Different Sampling Modes and Optimization Strategies. Environ. Sci. Technol. 44, 6289–6296. https://doi.org/10.1021/es100778d

Osorio, V., Larrañaga, A., Aceña, J., Pérez, S., Barceló, D., 2016. Concentration and risk of pharmaceuticals in freshwater systems are related to the population density and the livestock units in Iberian Rivers. Sci. Total Environ. 540, 267–277. https://doi.org/10.1016/j.scitotenv.2015.06.143

Paíga, P., Correia, M., Fernandes, M.J., Silva, A., Carvalho, M., Vieira, J., Jorge, S., Silva, J.G., Freire, C., Delerue-Matos, C., 2019. Assessment of 83 pharmaceuticals in WWTP influent and effluent samples by UHPLC-MS/MS: Hourly variation. Sci. Total Environ. 648, 582–600. https://doi.org/10.1016/j.scitotenv.2018.08.129

Paíga, P., Santos, L.H.M.L.M., Ramos, S., Jorge, S., Gabriel, J., Delerue-matos, C., 2016. Science of the Total Environment Presence of pharmaceuticals in the Lis river (Portugal): Sources , fate and seasonal variation. Sci. Total Environ. 573, 164–177. https://doi.org/10.1016/j.scitotenv.2016.08.089

Papageorgiou, M., Kosma, C., Lambropoulou, D., 2016. Seasonal occurrence, removal, mass loading and environmental risk assessment of 55 pharmaceuticals and personal care products in a municipal wastewater treatment plant in Central Greece. Sci. Total Environ. 543, 547–569. https://doi.org/10.1016/j.scitotenv.2015.11.047

Peng, X., Huang, Q., Zhang, K., Yu, Y., Wang, Z., Wang, C., 2012. Distribution, behavior and fate of azole antifungals during mechanical, biological, and chemical treatments in sewage treatment plants in China. Sci. Total Environ. 426, 311–317. https://doi.org/10.1016/j.scitotenv.2012.03.067

Peppercorn, M.A., 1984. Sulfasalazine. Ann. Intern. Med. 101, 377. https://doi.org/10.7326/0003-4819-101-3-377

1041 Petrie, B., Barden, R., Kasprzyk-Hordern, B., 2014a. A review on emerging contaminants in
1042 wastewaters and the environment: Current knowledge, understudied areas and
1043 recommendations for future monitoring. Water Res. 72, 3–27.
1044 https://doi.org/10.1016/j.watres.2014.08.053

1045 Petrie, B., Lopardo, L., Proctor, K., Youdan, J., Barden, R., Kasprzyk-Hordern, B., 2019.
1046 Assessment of bisphenol-A in the urban water cycle. Sci. Total Environ. 650, 900–907.
1047 https://doi.org/10.1016/j.scitotenv.2018.09.011

1048 Petrie, B., McAdam, E.J., Lester, J.N., Cartmell, E., 2014b. Obtaining process mass balances
1049 of pharmaceuticals and triclosan to determine their fate during wastewater treatment.
1050 Sci. Total Environ. 497–498, 553–560. https://doi.org/10.1016/j.scitotenv.2014.08.003

1051 Petrie, B., Youdan, J., Barden, R., Kasprzyk-Hordern, B., 2016. New Framework To
1052 Diagnose the Direct Disposal of Prescribed Drugs in Wastewater - A Case Study of the
1053 Antidepressant Fluoxetine. Environ. Sci. Technol. 50, 3781–3789.
1054 https://doi.org/10.1021/acs.est.6b00291

1055 Proctor, K., Petrie, B., Barden, R., Arnot, T., Kasprzyk-Hordern, B., 2019. Multi-residue
1056 ultra-performance liquid chromatography coupled with tandem mass spectrometry
1057 method for comprehensive multi-class anthropogenic compounds of emerging concern
1058 analysis in a catchment-based exposure-driven study. Anal. Bioanal. Chem.
1059 https://doi.org/10.1007/s00216-019-02091-8

1060 Radjenović, J., Jelić, A., Petrović, M., Barceló, D., 2009. Determination of pharmaceuticals
1061 in sewage sludge by pressurized liquid extraction (PLE) coupled to liquid
1062 chromatography-tandem mass spectrometry (LC-MS/MS). Anal. Bioanal. Chem. 393,
1063 1685–1695. https://doi.org/10.1007/s00216-009-2604-4

1064 Rowlingson, B., Lawson, E., Taylor, B., Diggle, P.J., 2013. Mapping English GP prescribing
1065 data: A tool for monitoring health-service inequalities. BMJ Open 3.
1066 https://doi.org/10.1136/bmjopen-2012-001363

1067 Rubin, B.S., 2011. Bisphenol A: An endocrine disruptor with widespread exposure and
1068 multiple effects. J. Steroid Biochem. Mol. Biol. 127, 27–34.
1069 https://doi.org/10.1016/j.jsbmb.2011.05.002

1070 Sabourin, L., Duenk, P., Bonte-Gelok, S., Payne, M., Lapen, D.R., Topp, E., 2012. Uptake of
1071 pharmaceuticals, hormones and parabens into vegetables grown in soil fertilized with
1072 municipal biosolids. Sci. Total Environ. 431, 233–236.
1073 https://doi.org/10.1016/j.scitotenv.2012.05.017

1074 Samaras, V.G., Stasinakis, A.S., Mamais, D., Thomaidis, N.S., Lekkas, T.D., 2013. Fate of
1075 selected pharmaceuticals and synthetic endocrine disrupting compounds during
1076 wastewater treatment and sludge anaerobic digestion. J. Hazard. Mater. 244–245, 259–
1077 267. https://doi.org/10.1016/j.jhazmat.2012.11.039

1078 Santos, L.H.M.L.M., Gros, M., Rodriguez-Mozaz, S., Delerue-Matos, C., Pena, A., Barceló,
1079 D., Montenegro, M.C.B.S.M., 2013. Contribution of hospital effluents to the load of
1080 pharmaceuticals in urban wastewaters: Identification of ecologically relevant
1081 pharmaceuticals. Sci. Total Environ. 461–462, 302–316.
1082 https://doi.org/10.1016/j.scitotenv.2013.04.077

1083 Sarmah, A.K., Meyer, M.T., Boxall, A.B. a, 2006. A global perspective on the use, sales,
1084 exposure pathways, occurrence, fate and effects of veterinary antibiotics (VAs) in the
1085 environment. Chemosphere 65, 725–759.

https://doi.org/10.1016/j.chemosphere.2006.03.026

Sousa, J.C.G., Ribeiro, A.R., Barbosa, M.O., Pereira, M.F.R., Silva, A.M.T., 2018. A review on environmental monitoring of water organic pollutants identified by EU guidelines. J. Hazard. Mater. 344, 146–162. https://doi.org/10.1016/j.jhazmat.2017.09.058

Stuart, M., Lapworth, D., Crane, E., Hart, A., 2012. Review of risk from potential emerging contaminants in UK groundwater. Sci. Total Environ. 416, 1–21. https://doi.org/10.1016/j.scitotenv.2011.11.072

Stutt, E., Wilson, I., Merrington, G., 2019. The Assessment of Organic Contaminants in Materials Spread on Land: Final Report To SEPA From WAC.

Ta, T., M, Stumpf, J, M., K, H., Rd, W., M, Servos, 1999. Behaviour and occurrence of estrogens in municipal sewage treatment plants: I. Investig. Ger. Canada Brazil. Sci Total Env. 225, 81–90.

Verlicchi, P., Al Aukidy, M., Zambello, E., 2012. Occurrence of pharmaceutical compounds in urban wastewater: Removal, mass load and environmental risk after a secondary treatment—A review. Sci. Total Environ. 429, 123–155. https://doi.org/10.1016/j.scitotenv.2012.04.028

Wilkinson, J., Hooda, P.S., Barker, J., Barton, S., Swinden, J., 2017. Occurrence, fate and transformation of emerging contaminants in water: An overarching review of the field. Environ. Pollut. 231, 954–970. https://doi.org/10.1016/j.envpol.2017.08.032

Wishart, D.S., Feunang, Y.D., Guo, A.C., Lo, E.J., Marcu, A., Grant, J.R., Sajed, T., Johnson, D., Li, C., Sayeeda, Z., Assempour, N., Iynkkaran, I., Liu, Y., Maciejewski, A., Gale, N., Wilson, A., Chin, L., Cummings, R., Le, D., Pon, A., Knox, C., Wilson, M., 2018. DrugBank 5.0: a major update to the DrugBank database for 2018. Nucleic Acids Res. 46, D1074–D1082. https://doi.org/10.1093/nar/gkx1037

Zhang, X., Huang, R., Li, P., Ren, Y., Gao, J., Mueller, J.F., Thai, P.K., 2019. Temporal profile of illicit drug consumption in Guangzhou, China monitored by wastewater-based epidemiology. Environ. Sci. Pollut. Res. 23593–23602. https://doi.org/10.1007/s11356-019-05575-3

Zhang, Z., Le Velly, M., Rhind, S.M., Kyle, C.E., Hough, R.L., Duff, E.I., McKenzie, C., 2015. A study on temporal trends and estimates of fate of Bisphenol A in agricultural soils after sewage sludge amendment. Sci. Total Environ. 515–516, 1–11. https://doi.org/10.1016/j.scitotenv.2015.01.053

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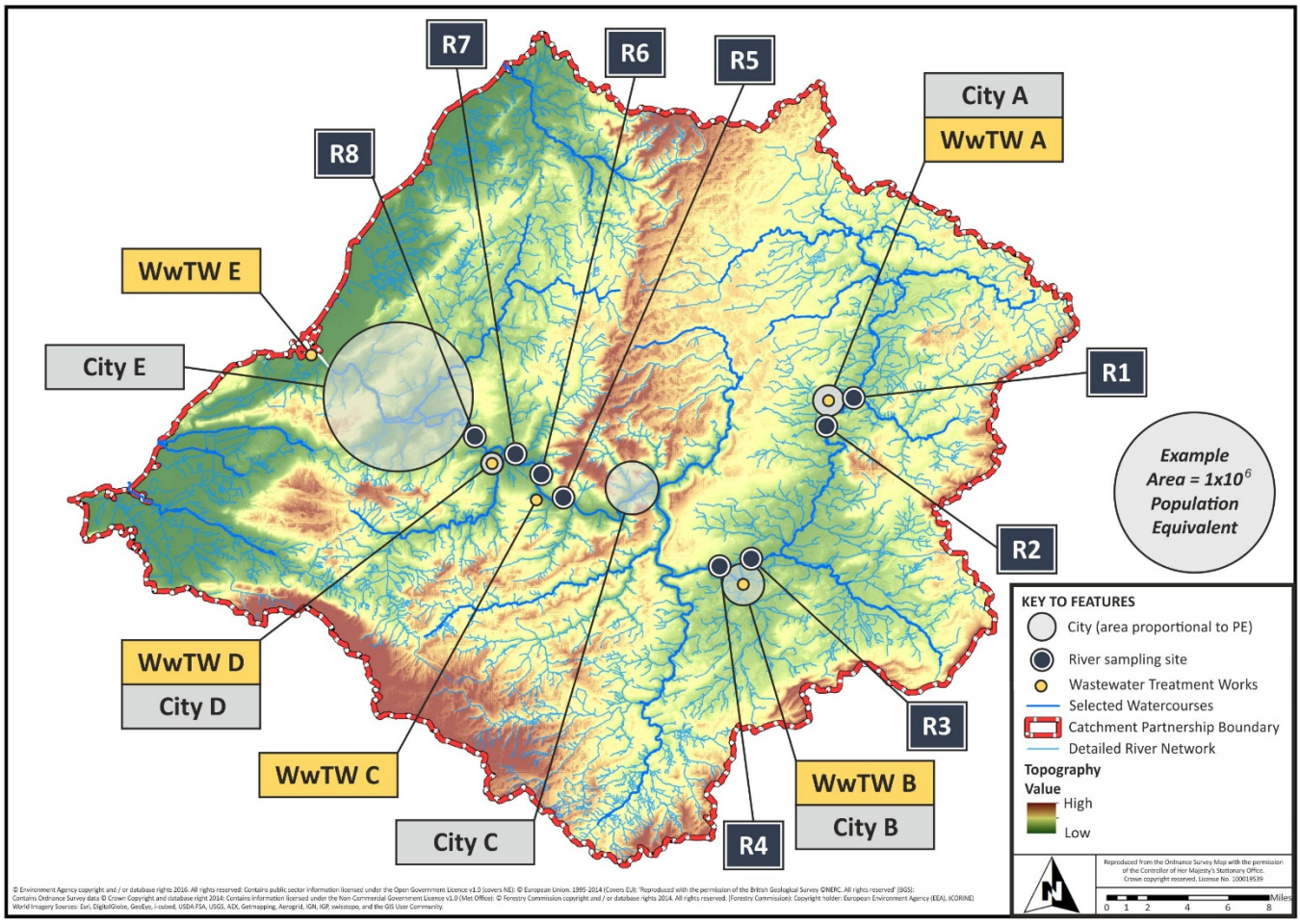
Main Paper Tables and Figures

Table 1 *Classes of CECs with names of analytes per matrix, total number of analytes in each matrix in first row.*

Class	Compound	River	Effluent	Influent	SPM	Dig. Solids
UV Filter	Benzophenone-1	4	4	4	3	3
	Benzophenone-2					
	Benzophenone-3					
	Benzophenone-4					
Parabens	Methylparaben	4	4	4	4	4
	Ethylparaben					
	Propylparaben					
	Butylparaben					
Plasticizer	Bisphenol-A	1	1	1	1	1
Steroid Estrogens	E1	3	3	3	2	2
	E2					
	EE2					
Antibiotics and Antibacterial	Sulfasalazine	19	20	19	7	7
	Clarithromycin					
	Azithromycin					
	Trimethoprim					
	Sulfamethoxazole					
	Triclosan					
	Amoxicillin					
	Metronidazole					
	Sulfadiazine					
	Cefalexin					
	Ofloxacin					
	Ciprofloxacin					
	Tetracycline					
	Danofloxacin					
	Oxytetracycline					
	Chloramphenicol					
	Penicillin G					
	Penicillin V					
	Erythromycin					
	Prulifloxacin					
	Norfloxacin					
Antifungal	Griseofulvin	2	2	2	2	2
	Ketoconazole					
Hypertension	Valsartan	3	3	3	1	1
	Irbesartan					
	Lisinopril					
NSAIDs	Ketoprofen	5	5	5	5	5
	Ibuprofen					
	Naproxen					
	Diclofenac					
	Acetaminophen					
Lipid regulator	Bezafibrate	2	2	2	1	1
	Atorvostatin					
Anti-hyperlipidemic	Gemfibrozil	1	1	1	0	1
Anti-hyperintensive	Candesartan Cilexetil	1	0	0	0	0
Antihistamine	Fexofenadine	2	2	2	0	0
	Cetirizine					
GUD/ED	Sildenafil	1	1	1	1	1
Antidiabetics	Metformin	3	3	3	1	1
	Gliclazide					
	Sitagliptin					
Cough suppressant	Pholcodine	1	1	1	1	1
Beta-blocker	Atenolol	4	4	4	4	4
	Metoprolol					
	Propranolol					
	Bisoprolol					
H2 receptor agonist	Ranitidine	2	2	2	1	1
	Cimetidine					
X-ray contrast media	Iopromide	1	1	1	1	1
Various	Buprenorphine	1	1	1	1	1
Drug precursor	Ephedrine/pseudoephedrine	2	2	2	2	2
	Norephedrine					
Anti-cancer	Azathioprine	7	7	7	5	5
	Methotrexate					
	Ifosfamide					
	Tamoxifen					
	Imatinib					
	Capecitabine					
	Bicalutamide					

Class	Compound	River	Effluent	Influent	SPM	Dig. Solids
Anaesthetic and metabolite	Ketamine	2	2	2	2	2
	Norketamine					
Anti-depressants	Venlafaxine	12	12	13	13	12
	Desvenlafaxine					
	Fluoxetine					
	Norfluoxetine					
	Sertraline					
	Mirtazapine					
	Citalopram					
	Desmethylcitalopram					
	Paroxetine					
	Duloxetine					
	Amitriptyline					
	Nortriptyline					
	Norsertraline					
Anti-epileptic	Carbamazepine	3	3	3	2	2
	Carbamazepine10,11-epoxide					
	10,11-Dihydro-10-hydroxycarbamazepine					
Calcium-channel blocker	Diltiazem	2	2	2	1	1
	Verapamil					
Hypnotic	Temazepam	3	3	3	2	2
	Oxazepam					
	Diazepam					
Anti-psychotic	Quetiapine	2	2	2	2	2
	Risperidone					
Dementia	Donepezil	2	2	2	2	2
	Memantine					
Creatinine	Creatinine	5	5	5	2	2
Lifestyle Chemicals	Nicotine					
	Caffeine					
	Cotinine					
	1,7 dimethylxantine					
Analgaesics and Metabolites	Morphine	11	11	11	10	10
	Dihydromorphine					
	Normorphine					
	Methadone					
	EDDP					
	Codeine					
	Norcodeine					
	Dihydrocodeine					
	Tramadol					
	N-desmethyltramadol					
	O-desmethyltramadol					
Stimulants and metabolites	Amphetamine	10	10	10	8	8
	Methamphetamine					
	MDMA					
	MDA					
	Cocaine					
	Benzoylecgonine					
	Anhydroecgonine methylester					
	Cocaethylene					
	Mephedrone					
	MDPV					
Opioid and metabolite	Heroin	2	2	2	1	1
	6-acetylmorphine					
Pesticides, fungicides and herbicides	Thiamethoxam	10	10	10	8	7
	Imidacloprid					
	Clothiniadin					
	Metazachlor					
	Terbuthylazine					
	Methiocarb					
	Dichlofluanid					
	Flufenacet					
	Oxadiazon					
	Chlorpyrifos					
	Triallate					
Veterinary Pharma	Tylosin	5	5	5	1	1
	Sulfapyridine					
	Sarafloxacin					
	Ceftiofur					
	Diazinon					

Table 2 *Site information of studied WwTWs and corresponding river locations*



Site	Sewer residence time[a] (h)	WwTW secondary process[b]	SRT (d)	HRT [a] (h)	Media type	Configuration	Population served (population equivalents)	Industrial contributions towards population equivalents	Mean flow (m^3 d^{-1})	River sampling, distance to discharge point (km)		Effluent-river mass balance[c] (%)
										Upstream	Downstream	
A	<0.5-4	AS	19	46.2	n/a	Carbonaceous & nitrifying	37,714	0.4 %	8,242 ± 3,085	0.5	n/a[d]	n/a[d]
B	<0.5-4	TF	n/a	24.5	Stone	Carbonaceous & nitrifying	68,453	30.0 %	11,202 ± 3,202	0.5	0.5	102
C	<0.5-9	TF	n/a	13.9	Stone – limestone	Carbonaceous & nitrifying	109,543	1.2 %	24,875 ± 2,167	2	2	111
D	<0.5-2	TF	n/a	17.6	Stone – blast furnace slag	Carbonaceous & nitrifying	18274	0.1 %	2,924 ± 199	1	1	97
E	<1-24	90 % SBR 10 % AS	4 8	10.9 25.8	n/a	Carbonaceous	867,244	23.9 %	153,061 ± 12,245	n/a[e]	n/a	n/a

Key: WwTW, wastewater treatment process; SRT, solids retention time; HRT, hydraulic retention time; p, 'pulses' or toilet flushes, AS, activated sludge; TF, trickling filter; SBR, sequencing batch reactor

[a] Under typical summer flows

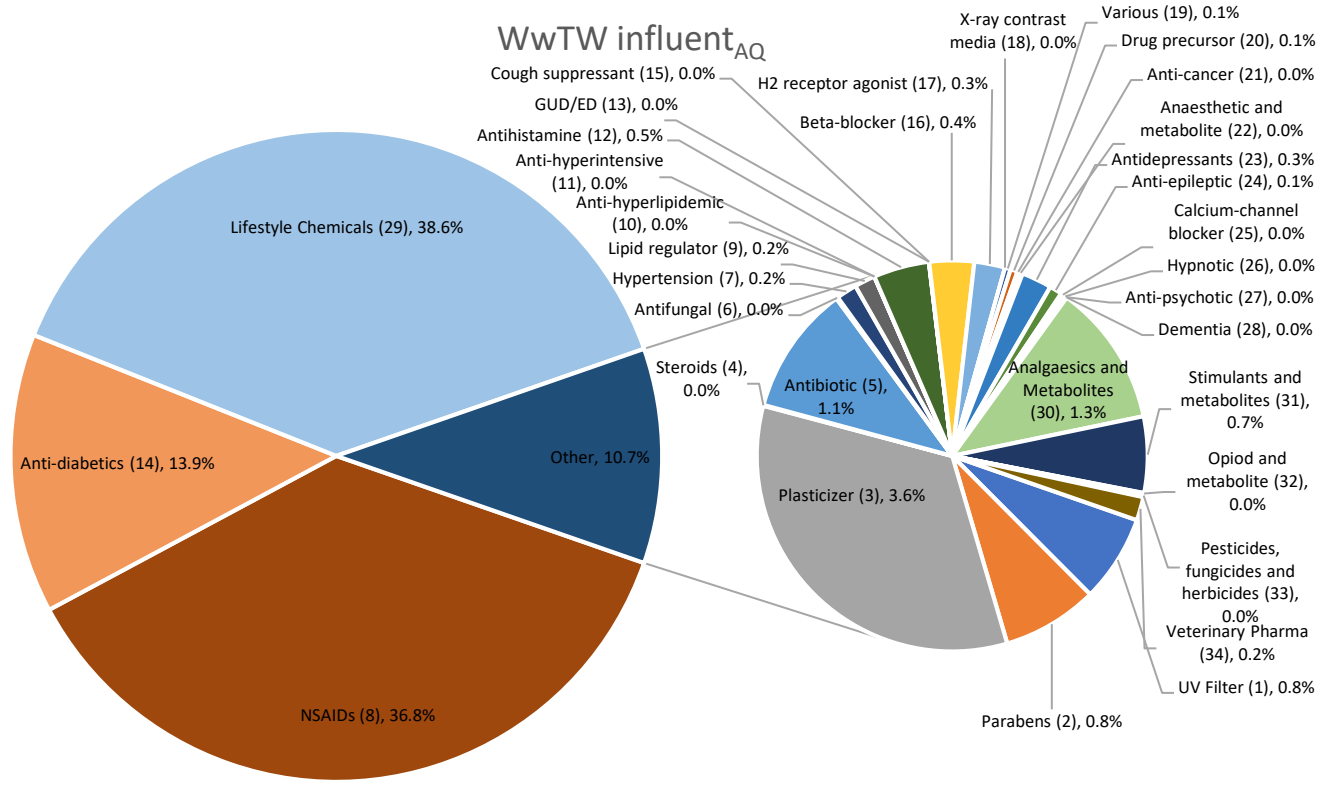
[b] All STWs utilised primary sedimentation dosed with ferric sulfate for phosphorus removal and all processes used conventional sedimentation following secondary treatment except SBRs which decanted following settling *in-situ*

[c] Mass balances were calculated according to: $Mass\ balance\ (\%) = \frac{Downstream}{Upstream + Effluent} \times 100$ where *Downstream* is the load of carbamazepine in river water downstream of the effluent discharge point (g d^{-1}), *Upstream* is the load of carbamazepine in river water upstream of the effluent discharge point (g d^{-1}) and *Effluent* is the load of carbamazepine in effluent (g d^{-1})

[d] Mass balance at site E was > 400 % demonstrating complete mixing of effluent and river water was not achieved at the sampling point due to restricted access to river. Therefore mass loads in river water downstream of the discharge point was calculated by adding effluent loads with river water loads upstream of the discharge point. This assumes complete mixing without any micropollutants losses. Micropollutant concentrations in downstream river water were then estimated using river flow data.

[e] Effluent discharged into estuary

Figure 1 *Weekly percentage of total loads in influent$_{AQ}$ of the entire catchment as a pie chart of classes, with chart showing spatial and temporal trends. Note: creatinine is not included.0.0% shows negligible to no contribution to the total. Numbers in brackets indicate numbers assigned for identification in small figures and table*



- UV Filter (1)
- Parabens (2)
- Plasticizer (3)
- Steroids (4)
- Antibiotic (5)
- Antifungal (6)
- Hypertension (7)
- NSAIDs (8)
- Lipid regulator (9)
- Anti-hyperlipidemic (10)
- Anti-hyperintensive (11)
- Antihistamine (12)
- GUD/ED (13)
- Anti-diabetics (14)
- Cough suppressant (15)
- Beta-blocker (16)
- H2 receptor agonist (17)
- X-ray contrast media (18)
- Various (19)
- Drug precursor (20)
- Anti-cancer (21)
- Anaesthetic and metabolite (22)
- Antidepressants (23)
- Anti-epileptic (24)
- Calcium-channel blocker (25)
- Hypnotic (26)
- Anti-psychotic (27)
- Dementia (28)
- Lifestyle Chemicals (29)
- Analgaesics and Metabolites (30)
- Stimulants and metabolites (31)
- Opiod and metabolite (32)
- Pesticides, fungicides and herbicides (33)
- Veterinary Pharma (34)

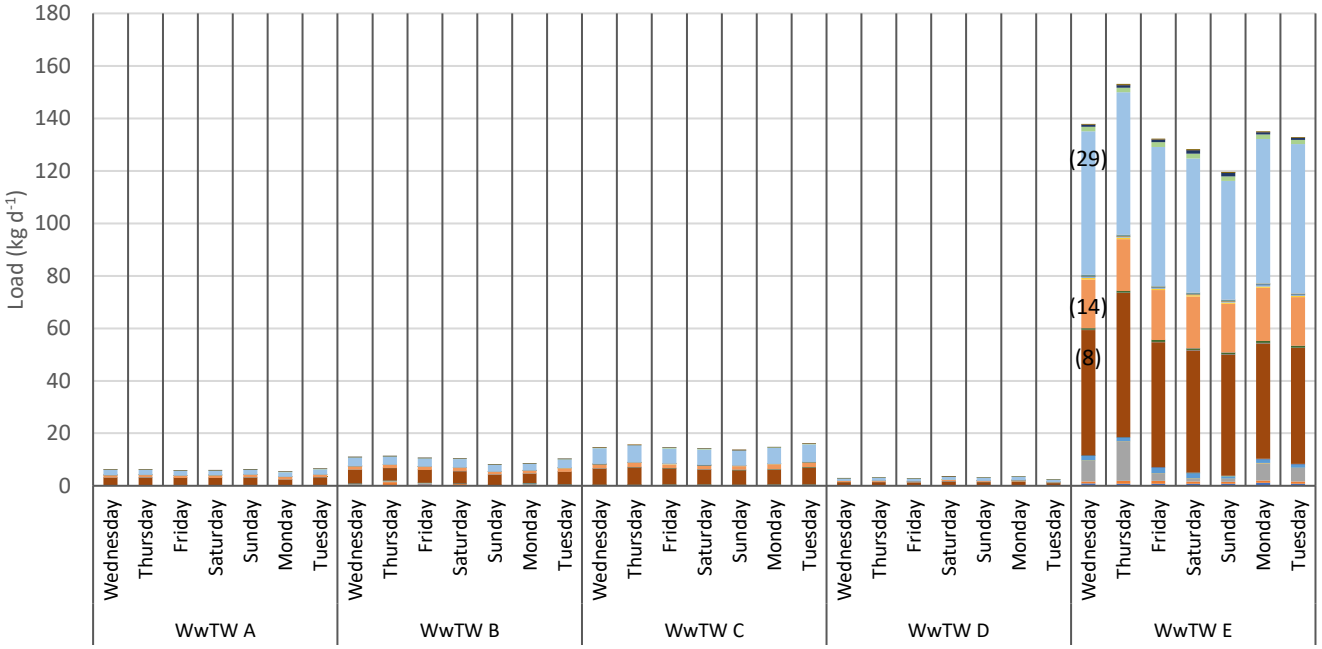
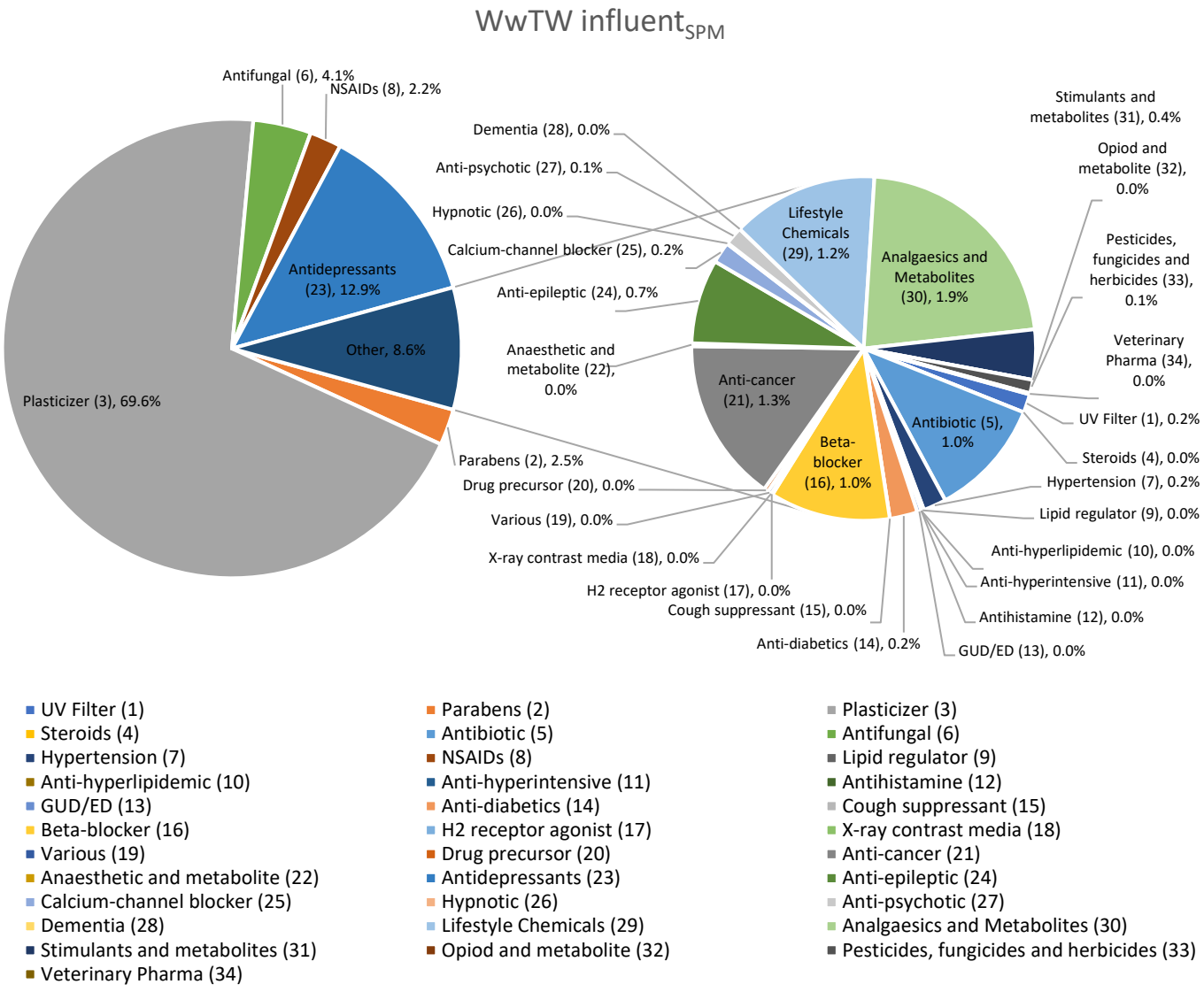


Figure 2 *Weekly percentage of total loads in influent$_{SPM}$ of the entire catchment as a pie chart of classes, with chart showing spatial and temporal trends. Note: creatinine is not included. 0.0% shows negligible to no contribution to the total. Numbers in brackets indicate numbers assigned for identification in small figures and table*



- UV Filter (1)
- Parabens (2)
- Plasticizer (3)
- Steroids (4)
- Antibiotic (5)
- Antifungal (6)
- Hypertension (7)
- NSAIDs (8)
- Lipid regulator (9)
- Anti-hyperlipidemic (10)
- Anti-hyperintensive (11)
- Antihistamine (12)
- GUD/ED (13)
- Anti-diabetics (14)
- Cough suppressant (15)
- Beta-blocker (16)
- H2 receptor agonist (17)
- X-ray contrast media (18)
- Various (19)
- Drug precursor (20)
- Anti-cancer (21)
- Anaesthetic and metabolite (22)
- Antidepressants (23)
- Anti-epileptic (24)
- Calcium-channel blocker (25)
- Hypnotic (26)
- Anti-psychotic (27)
- Dementia (28)
- Lifestyle Chemicals (29)
- Analgaesics and Metabolites (30)
- Stimulants and metabolites (31)
- Opiod and metabolite (32)
- Pesticides, fungicides and herbicides (33)
- Veterinary Pharma (34)

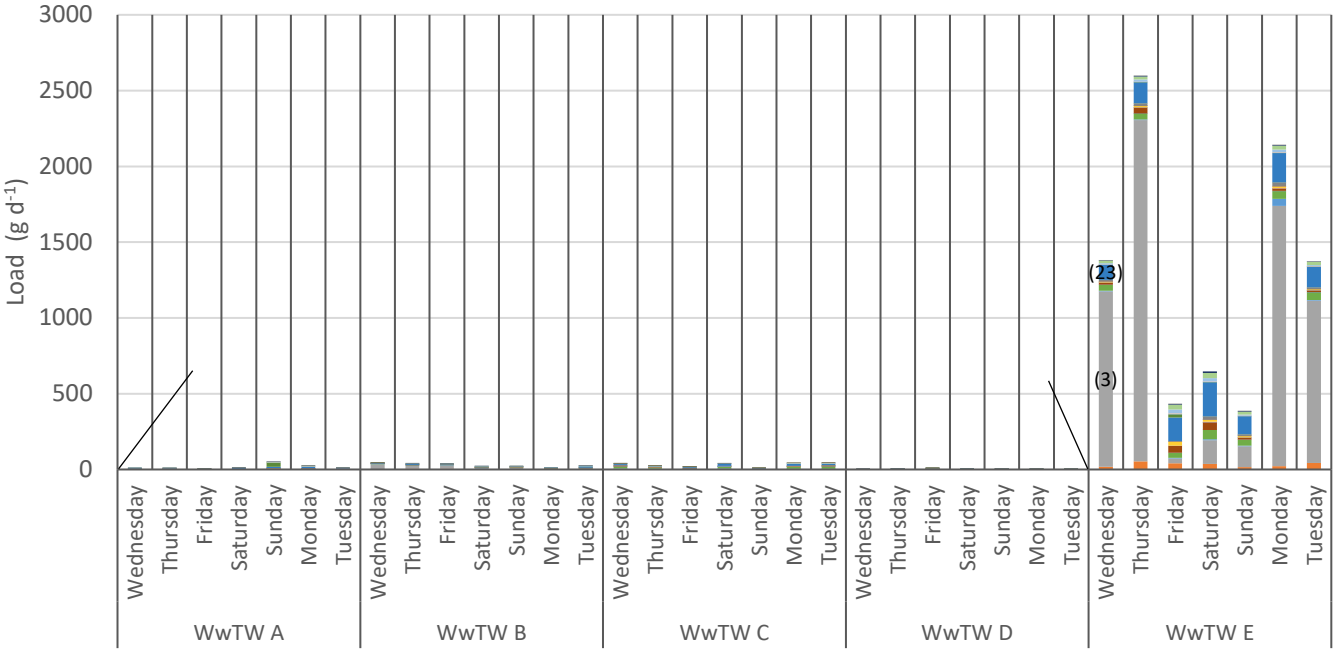
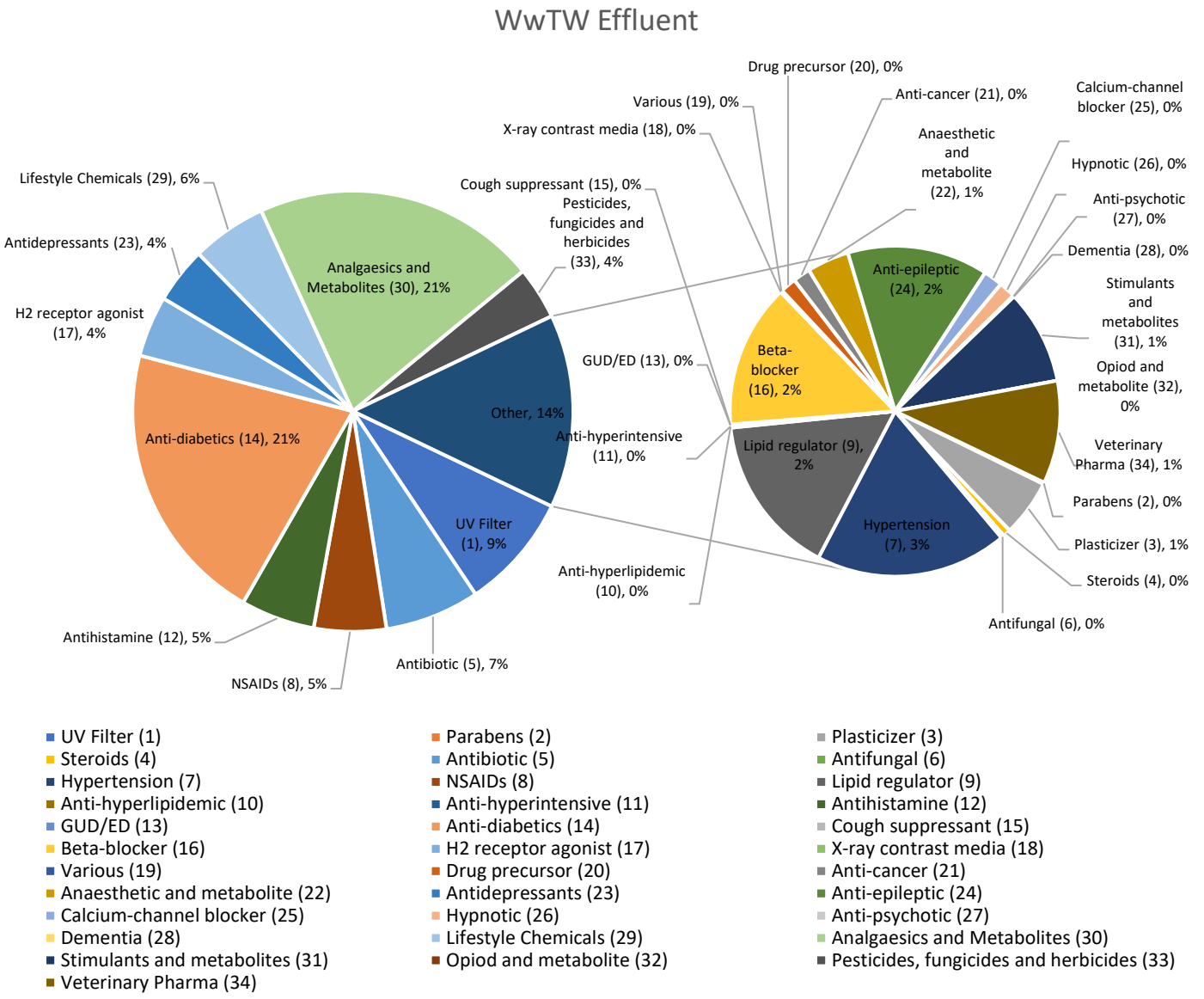


Figure 3 *Weekly percentage of total loads in effluent of the entire catchment as a pie chart of classes, with chart showing spatial and temporal trends. Note: creatinine is not included. 0.0% shows negligible to no contribution to the total. Numbers in brackets indicate numbers assigned for identification in small figures and table*



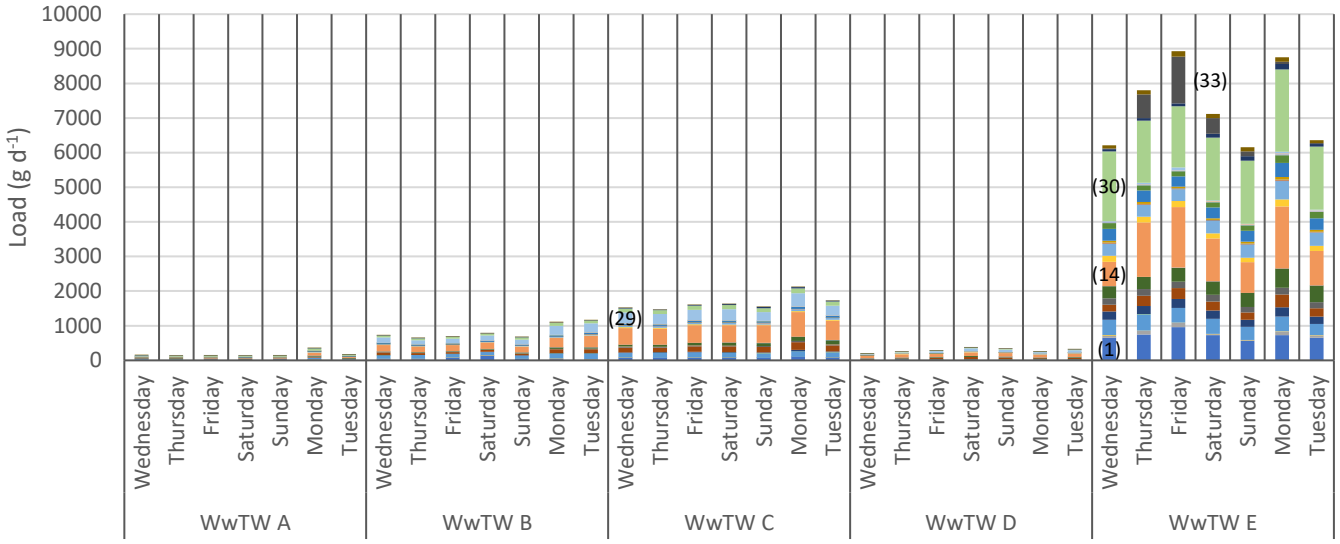
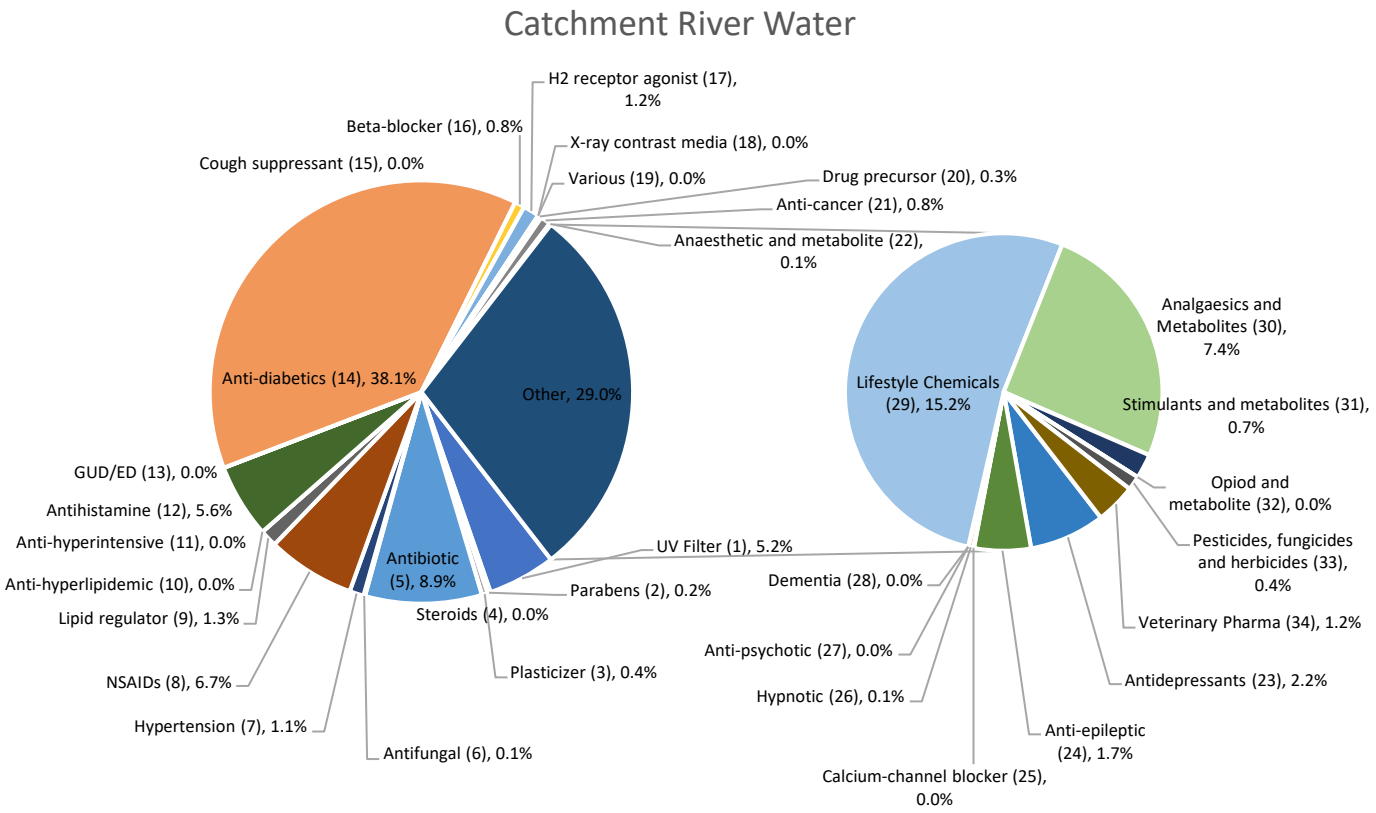


Figure 4 *Weekly percentage of total loads in river water of the entire catchment as a pie chart of classes, with chart showing spatial and temporal trends. Note: creatinine is not included. 0.0% shows negligible to no contribution to the total. Numbers in brackets indicate numbers assigned for identification in small figures and table*



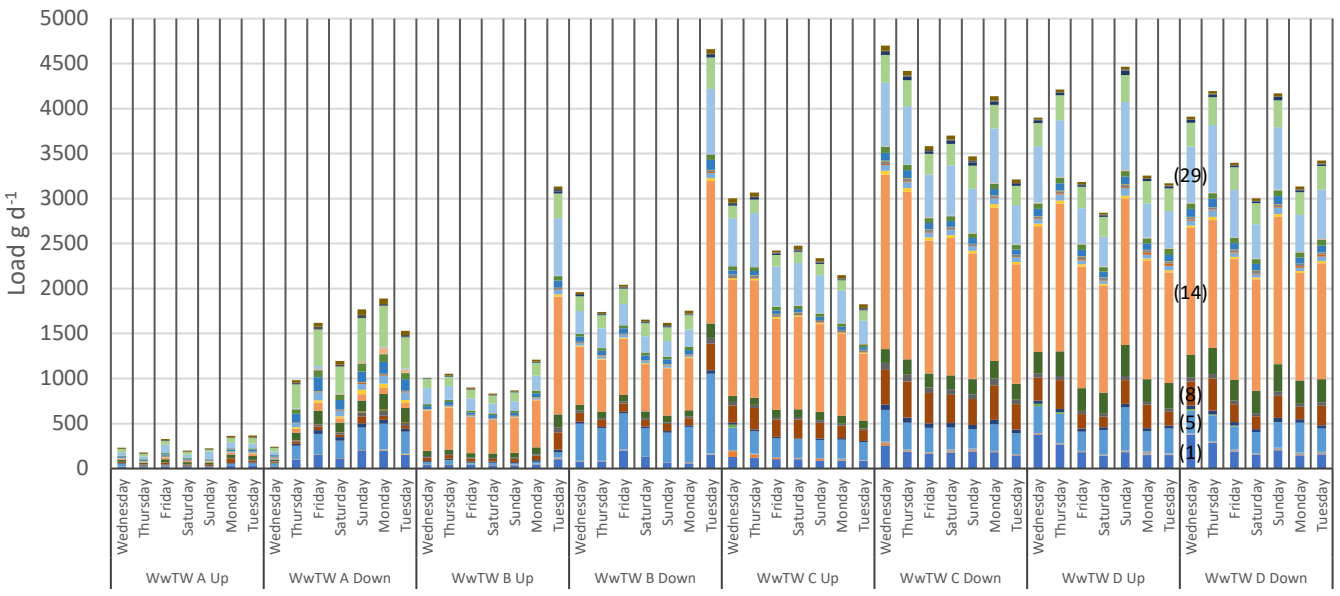
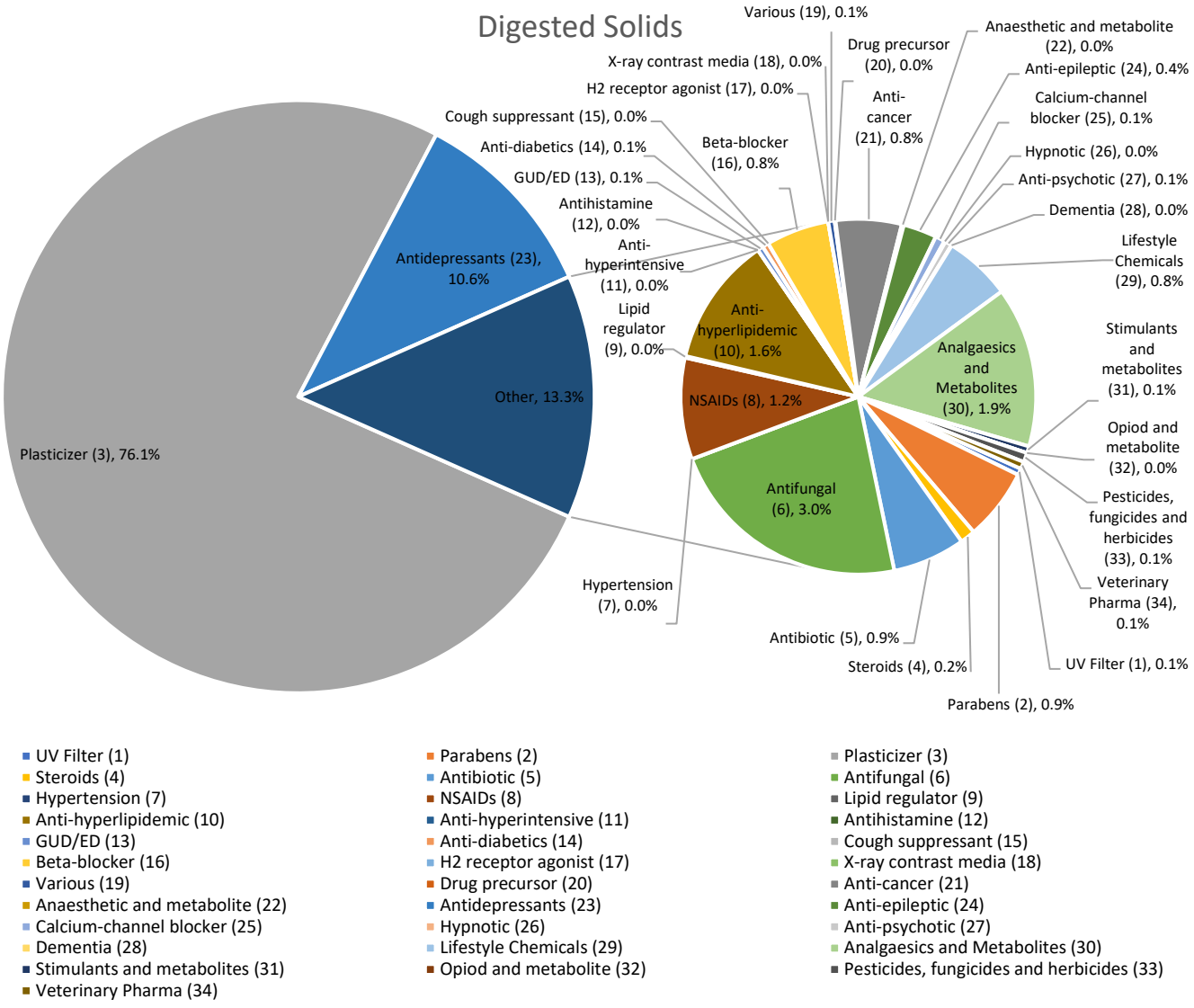
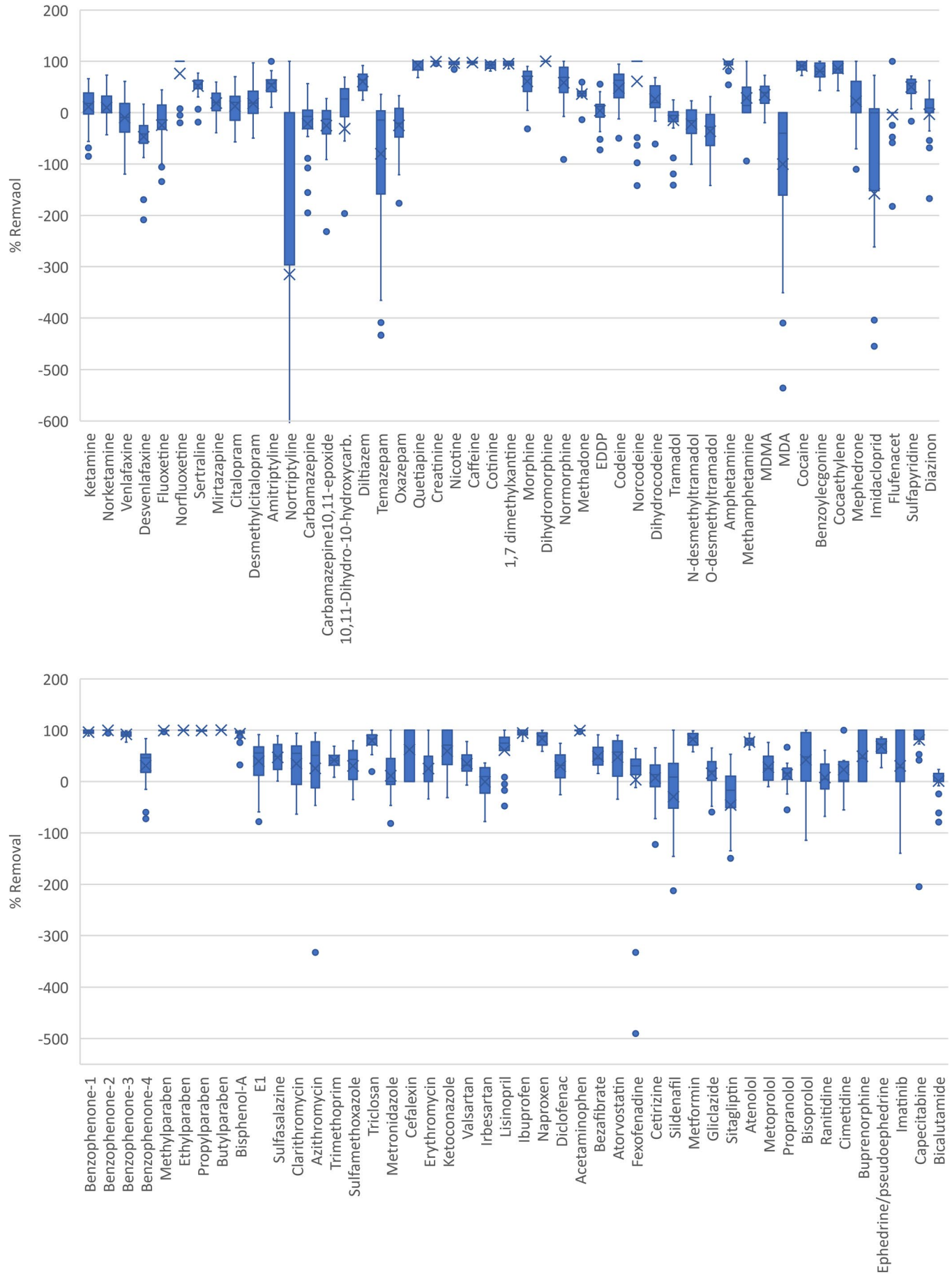


Figure 5 *Percentage of total concentration in digested solids of the entire catchment as a pie chart of classes, with individual pie charts for each site. Note: creatinine is not included. 0.0% shows negligible to no contribution to the total. Numbers in brackets indicate numbers assigned for identification in small figures and table*



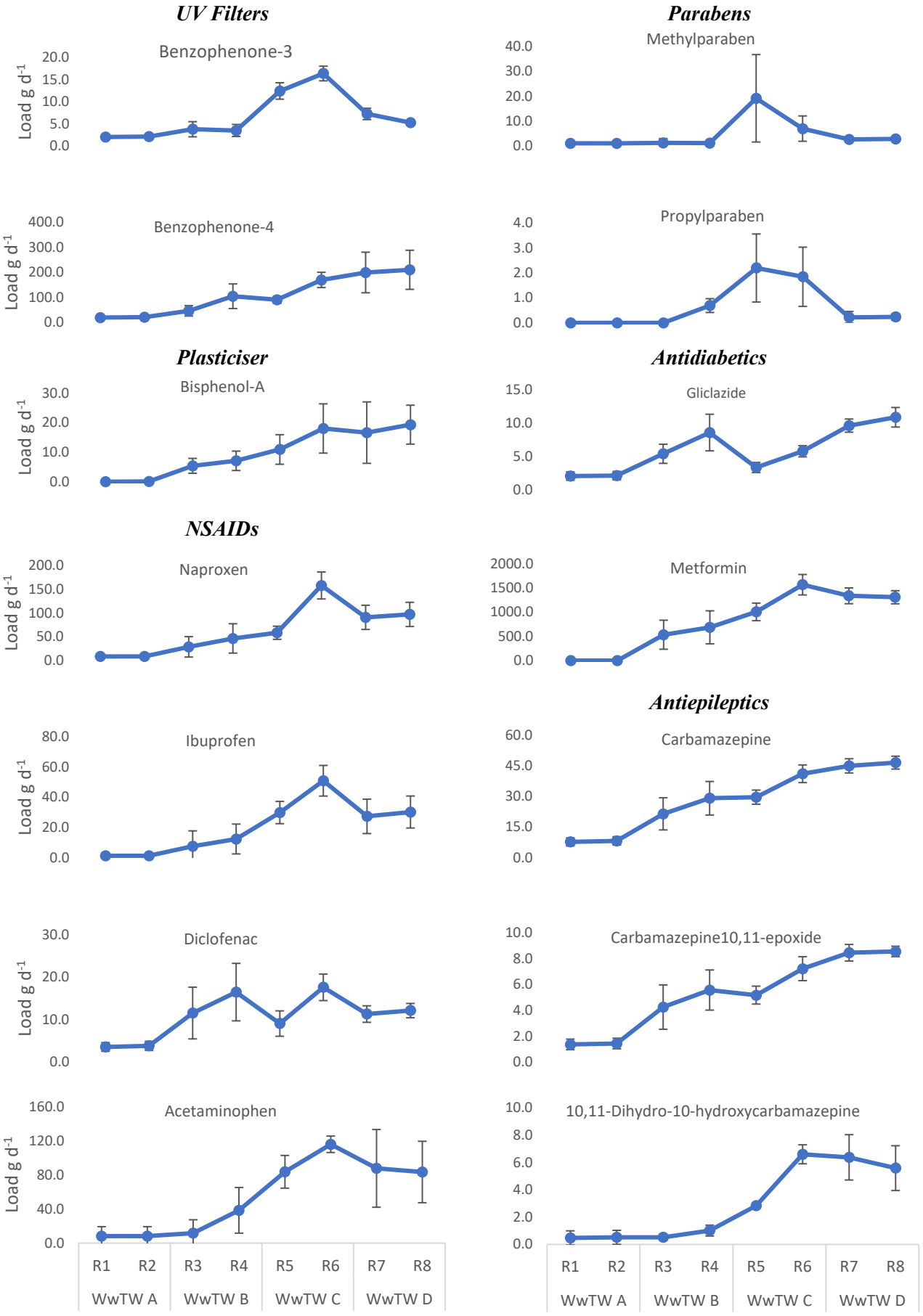
% of total	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34
WwTW B	3.9	0.1	0.4	0.0	2.1	0.2	1.3	4.7	1.5	0.0	0.0	5.5	0.0	43.8	0.0	0.7	1.3	0.0	0.0	0.2	0.6	0.1	3.1	2.1	0.0	0.1	0.0	0.0	16.7	10.2	0.7	0.0	0.6	0.0
WwTW E	5.8	0.1	0.5	0.0	8.4	0.2	1.0	6.1	1.1	0.0	0.0	7.6	0.0	39.2	0.0	0.7	1.5	0.0	0.0	0.4	0.7	0.1	2.1	1.7	0.0	0.2	0.0	0.0	14.2	7.2	0.8	0.0	0.3	0.0

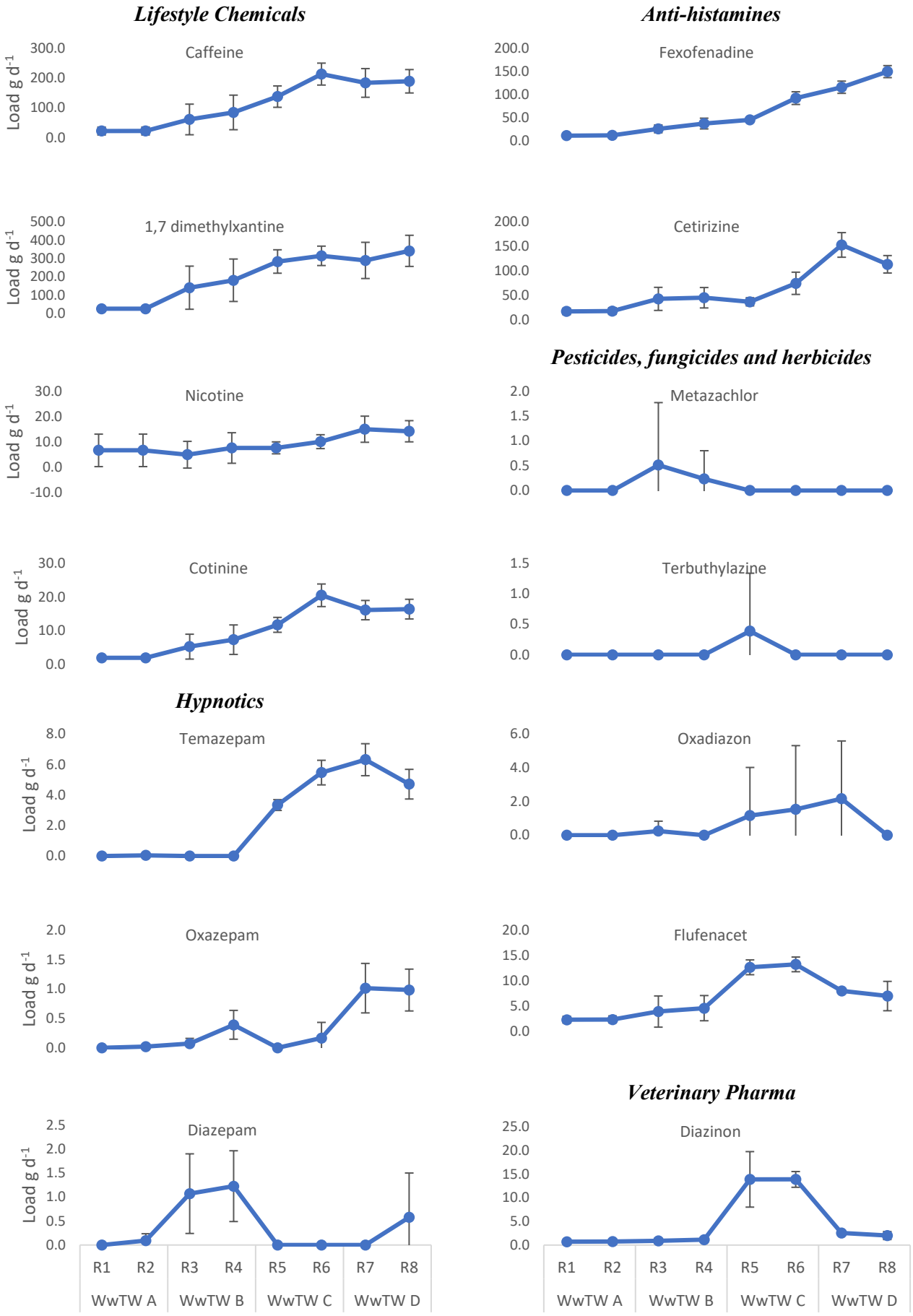
Figure 6 *Box plots showing removal of CECs from the liquid phase during WwTW treatment for each site and overall.*



*10,11-Dihydro-10-hydroxycarb. = 10,11-Dihydro-10-hydroxy-carbamazepine

Figure 7 *Weekly trends for selected compounds. Note: Error bars indicate weekly variation of the sampling site.*




Lifestyle Chemicals
Caffeine
Load g d-1
300.0
200.0
100.0
0.0
1,7 dimethylxantine
500.0
400.0
300.0
200.0
100.0
0.0
Nicotine
30.0
20.0
10.0
0.0
-10.0
Cotinine
Hypnotics
Temazepam
8.0
6.0
4.0
2.0
0.0
Oxazepam
1.5
1.0
0.5
Diazepam
2.5
R1
R2
R3
R4
R5
R6
R7
R8
WwTW A
WwTW B
WwTW C
WwTW D
Anti-histamines
Fexofenadine
200.0
150.0
50.0
Cetirizine
Pesticides, fungicides and herbicides
Metazachlor
2.0
Terbuthylazine
Oxadiazon
Flufenacet
20.0
15.0
Veterinary Pharma
Diazinon
25.0