Investigating entry pathways for pharmaceuticals into wastewater

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Disclaimer

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Contents

1. Executive Summary

The continuing presence of pharmaceutical compounds in wastewater and the environment is a major environmental and public health concern. Pharmaceuticals in wastewater and the environment can damage ecosystems and cause human health impacts. This issue is expected to worsen in the coming years due to an ageing population, improved access to healthcare and climate change impacts.

Metro Vancouver's Source Control Program is responsible for developing actions to reduce the entry of potentially harmful substances into wastewater. Pharmaceuticals can enter wastewater through numerous pathways, including consumption and excretion, pharmaceutical manufacturing and incorrect disposal. To understand this issue further Metro Vancouver has commissioned this report as part of the Sustainability Scholars Program at UBC. This report was designed to be an exploratory scoping project investigating the pathways of pharmaceutical compounds into Metro Vancouver wastewater. The research and findings generated through this project contributes to and supports Metro Vancouver's objectives to:

1. Understand the entry pathways of pharmaceuticals into wastewater
2. Understand the prevalence and risks of pharmaceuticals in wastewater and identify areas of concern
3. Gather insights on the policies used to manage and monitor pharmaceutical pollution in other jurisdictions
4. Gather feedback from pharmacists about the operation of Vancouver's drug take back program
5. Identify opportunities for interventions to reduce pharmaceutical discharge entering Metro Vancouver wastewater through the Source Control Program

The research conducted included:

1. Literature reviews (jurisdictional scan and pharmaceuticals of concern)
2. Analysis of Metro Vancouver pharmaceutical concentration data
3. Interviews with Health Product Stewardship Association (HPSA)
4. Interviews with pharmacists in Metro Vancouver
5. Short statements from prescribers

The first part of the literature review considered the **multiple ways in which pharmaceuticals can enter wastewater**. The main pathways investigated were pharmaceutical consumption and excretion and the incorrect household disposal of pharmaceuticals. Factors affecting these pathways were investigated including drug metabolism, drug usage, prescription rates, adherence, and pharmaceutical consumption. Several pharmaceuticals of particular concern were explored as case studies to examine the contribution of these factors to these compounds entering wastewater. For each compound, their behavior in wastewater and environmental risks were also characterized. This literature review informed the recommendations by identifying potential intervention pathways, and strategies for monitoring and assessing the impact of interventions.

The second part of the literature review is a **jurisdictional scan**. The review analyzed three jurisdictions; Sweden, Switzerland, and King County, Washington, all of which have significant policies already in place for drug take back programs, pharmaceutical pollution monitoring and wastewater management. The drug-take back programs allow customers to return used and expired medications to pharmacies so they can be safely incinerated to prevent them entering wastewater through the environment or landfill. This review was undertaken to identify any successful policies used in other jurisdictions that could be applied to Metro Vancouver.

Metro Vancouver provided **concentration data of pharmaceuticals measured in the influent and effluent of two wastewater treatment plants and three maintenance stations.** The data was analyzed to make initial interferences about entry pathways, identify priority areas of concern and investigate the removal efficiencies of various pharmaceuticals. Removal efficiencies were varied, but mostly better with secondary treatment than primary. Effluent concentrations were comparable to the maximum WWTP effluent concentrations found in one study, which may warrant further investigation or study. In influent there were variety of drugs present for a number of different conditions. By concentration, the predominant drug categories were painkillers and anti-diabetics, but by number of drugs the predominant categories were heart disease and antibiotics. Key concerns include the multiple antibiotics entering wastewater, which can be a source of antibiotic resistance, and the potential for pharmaceuticals to mix within wastewater, which can increase their environmental toxicity.

Drug take back programs offer the safe collection of expired or unwanted medications and other health products through local pharmacies. In BC HPSA operate the B.C. Medications Return Program. The drug take back program is funded by pharmaceutical manufacturers to fulfil Extended Producer Responsibility (EPR) obligations as regulated by the Recycling Regulation under authority of the Environmental Management Act in BC (Government of British Columbia, 2021)(Government of British Columbia, 2021; Health Products Stewardship Association, 2021). An **interview with HPSA** was conducted to understand how the drug take back program operates in Metro Vancouver. HPSA stated that approximately 90% of BC pharmacies are part of the program and the collection volume is increasing yearly. However, due to the high workload required for audits they do not have information on the exact type of drugs returned, or how drug take back program performance varies between pharmacies.

Multiple interviews with pharmacists in Metro Vancouver were conducted to see how the drug take back program operated in practice. Many pharmacists reported that they did not actively promote the program nor display posters for the public. Rather, the program was only discussed directly with customers in limited circumstances. Pharmacists also raised issues with how the program operation relies on considerable unpaid labor in preparing drugs for correct disposal and that there were significant health and safety issues in the way medications were collected, treated and stored within pharmacies. Concerns raised included the HPSA provided storage box being an unsafe way to store chemicals, customers bringing illicit drugs for disposal which needed to be destroyed on site and sharps being mixed in with the disposal drugs.

Key Recommendations

The main recommendation from this investigation is that the focus should be on interventions that can reduce or prevent the entry of pharmaceuticals into wastewater influent (source control). This is due to the risk that various compounds pose in wastewater and the high potential for meaningful prevention in certain prevention pathways. Meaningful interventions can also be made without necessarily understanding the exact contributions each pathway makes towards influent. Accessing prescription and sales data could improve Metro Vancouver's ability to monitor the prevalence of pharmaceuticals in wastewater and assess the impact of interventions to reduce pharmaceuticals entering wastewater. The creation of a database containing pharmaceutical usage (prescription and sales data and adherence), environmental occurrence, metabolism and risk is recommended to support the design of interventions and to assess their effectiveness. Ensuring that this database incorporates multiple risk metrics will allow for a more contextual understanding of chemical risk and risk reduction strategies, including acknowledging that danger that some compounds may pose at low concentrations.

The drug-take back program provides multiple potential opportunities to intervene. The pharmacist interviews demonstrated that pharmacy outreach needs to be undertaken to convince pharmacists of the importance of the drug take back program, although this may be insufficient unless funds are allocated to compensate pharmacists for their current unpaid labor in supporting the program. The health and safety concerns with the program operation need to be urgently addressed, as these are also preventing pharmacists from engaging in the program. There are additional opportunities to improve access, by considering drug take back events and mail back service (as demonstrated in King Country). There are also opportunities for wider promotion by strategically building promotional and social media partnerships with organizations who also have an interest in improving the drug take back program. These could include elderly homes, pharmacy colleges, chain pharmacies, environmental organizations and patient groups. The jurisdictional scan suggests that specific environmental and social messaging could be effective to persuade people to return their medications, as could targeting messaging to different demographics.

2. Characterizing Pathways Literature Review

This literature review contributes to the first two objectives of this report:

1. Understand the entry pathways of pharmaceuticals into wastewater
2. Understand the prevalence and risks of pharmaceuticals in wastewater and identify areas of concern.

2.1. Sources, Occurrence and Risk

Firstly, it is important to establish the potential sources of pharmaceuticals into wastewater. This review will focus on understanding how pharmaceuticals are prescribed, purchased, and used. Occurrence refers to the volume and variety of pharmaceuticals entering wastewater and the environment and their level of persistence in the receiving environment. This section also collates the ways in which the risk of chemicals in the environment are understood.

2.1.1. Sources

Entry Pathways

There are multiple pathways for pharmaceuticals to enter wastewater. This report mostly focuses on two pathways of entry. The first is pharmaceuticals entering wastewater through the consumption and usage of drugs. Pharmaceuticals are used and excreted, which is one entry pathway described below. The second pathway, termed incorrect disposal is pharmaceuticals entering wastewater from people incorrectly disposing of their expired and unused medications down toilet/sinks or in garbage.

There are multiple pathways of pharmaceuticals into wastewater (Illustrated in Figure 1 (OECD, 2019)). Five key pathways have been identified:

Pathway 1: Medications consumed (or incorrectly disposed of) by patients in households. This pathway is further defined by specific sources (1a – c):

a) A proportion of the medication will be metabolized, but some will be excreted unchanged and enter wastewater.
b) Pharmaceuticals can enter wastewater directly if they are incorrectly disposed of in toilets or sinks.
c) If pharmaceuticals are incorrectly disposed of in garbage receptacles, they can enter wastewater indirectly through leaching from landfill. The same goes for pharmaceutical packaging, as residues transferred to packaging can enter wastewater through this pathway.

Pathway 2: Pharmaceuticals entering the wastewater through manufacturing or industry usage. Whilst identified, this pathway is considered beyond the scope of this project since preliminary information indicates a lack of a significant pharmaceuticals manufacturing industry within the Metro Vancouver region. Further investigations into this potential pathway are recommended if more information becomes available on potentially significant industrial sources.

Pathway 3: Pharmaceuticals consumed in health care facilities and hospitals. This source is touched on in this project but are not the main focus. This is because Metro Vancouver has the hospital pollution prevention policy in place to address this pathway of entry.

Pathway 4: Veterinary consumption. Whilst identified, this pathway is considered beyond the scope of this project due to limited contributions of agricultural runoff to Metro Vancouver's wastewater system. Further investigations into contributions from household animals is recommended.

Pathway 5: Biosolids/residuals pathway. Biosolids originate from wastewater treatment processes, and as pharmaceuticals are present in wastewater, they can later be a component of biosolids that are applied to land. This is beyond the scope of this report but does warrant further investigation elsewhere.

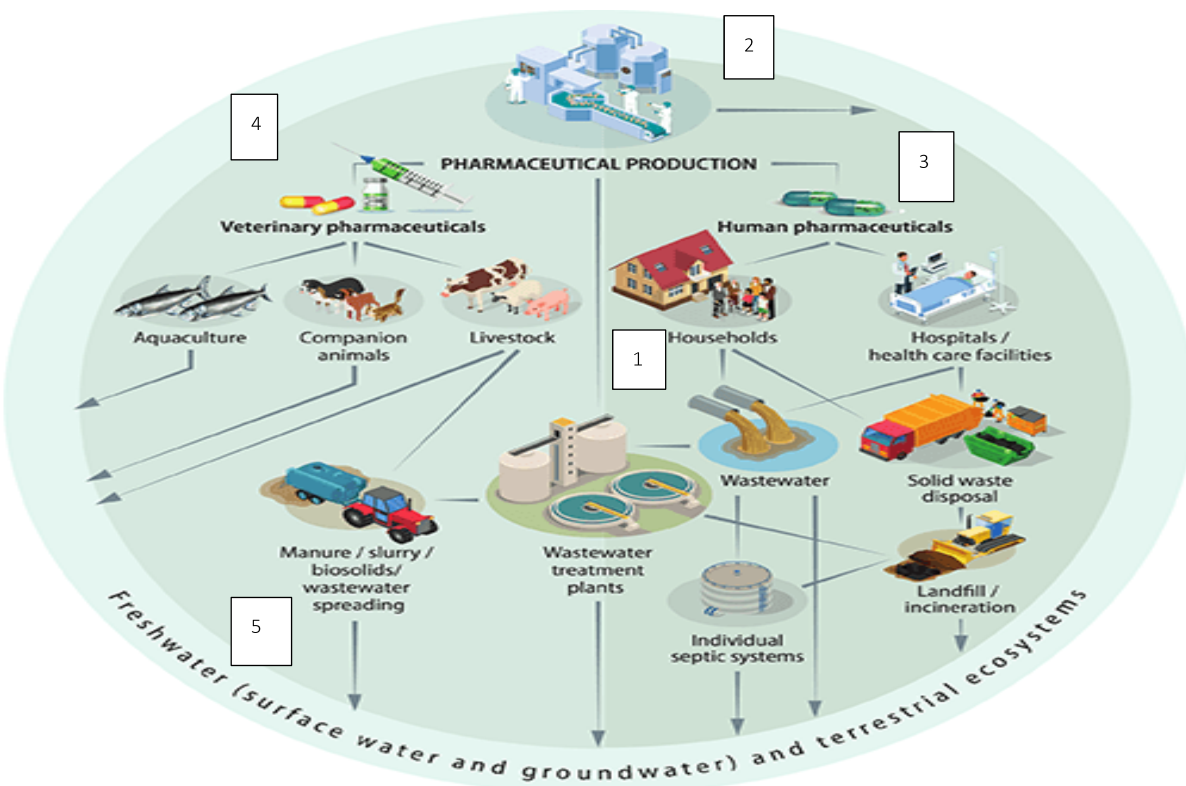


Figure 1 Pathways of pharmaceutical entry into wastewater, OECD 2019

Although Pathways 2-5 warrant further investigation, Pathway 1 was prioritized for several reasons. Firstly, it is estimated that about 70% of the pharmaceuticals in the wastewater originates from household, 20% comes from livestock farming, 5% is from hospital effluent, and the remaining 5% comes from runoff of non-particular sources (Das et al., 2017). In Switzerland, it is estimated that patient use (88%) is the main entry pathway for pharmaceutical residues to water, followed by inappropriate disposal (10%) and production (2%) (OECD, 2018). Although the proportion of contributions will vary in different locations, these two studies do indicate that household use is the major contribution to wastewater influent. Secondly, Pathway 1 has multiple opportunities for easy interventions, such as improving drug take back programs. Drug take back programs circumvent the pathways of drugs into wastewater by bringing them straight to incineration.

Medication Usage in BC and Canada

Stats Canada investigated prescription drug use in BC from 2007-2011. An estimated 41% of 6- to 79-year-olds who lived in private households reported taking at least one prescription medication in the past two days. Generally, prescription drug use was higher among females and among people in poorer health and increased with age. Approximately 11% of 45- to 64-year-olds and 30% of seniors aged 65 to 79 took at least five prescription medications concurrently. This is important to acknowledge as taking multiple medications is associated with lower adherence to prescribed use.

For adults aged 25 to 79, the leading prescription medication classes were lipid-lowering agents, ACE-inhibitors, peptic-ulcer and acid-reducers, beta-blockers (men), other analgesics and anti-pyretics (men), anti-depressants (women) and thyroid medication (women). Among children and young adults aged 6 to 24, the leading prescription medications were for attention deficit and hyperactivity disorder (males), depression, and hormonal contraception (females) (Statistics Canada, 2015). As for future trends in Canada, (Leung et al., 2019) predict that prescriptions for psychiatric disorders will increase in Alberta. It can be inferred that this trend will also present in BC.

BC Pharmanet is a database that tracks every prescription dispensed from community pharmacies and long-term care facilities, regardless of patient age or insurance status; however, it excludes prescription drugs used within acute care hospitals. It has therefore been used by multiple researchers to investigate prescription drug usage and trends.

Morgan et al. (2010) found regional variations in the cost, type and volume of prescriptions given across BC. Although these can be due to differences in age and health status, other significant variables include ethnic composition, physician supply and socio-economic factors. They also identified that the most significant factor contributing to regional variation in the cost and volume of prescription medicines used is variation in the likelihood that individuals will fill one or more prescriptions. Certain drug categories, including statins and anti-depressants tended to have people being more likely to have multiple prescriptions.

Mamun et al. (2019) also used BC PharmaNet to investigate time series trends in antibiotics use across the province and found that that the average monthly prescription rate fell by 14.5%, from 54.3 to 46.4 per 1000 population between 2005 and 2014. This study was conducted to assess the effectiveness of the Do Bugs Need Drugs (DBND) educational program, which aims to reduce unnecessary antibiotic use because of antibiotic resistance concerns. Program components include freely accessible guidelines and continuing health education for prescribers, direct outreach through schools, day cares and community care facilities using a workforce of volunteer health sciences students and pharmacists, and public campaigns. This data could indicate that antibiotics will become less prevalent environmental pollutants in the future, but also that educational campaigns could be helpful in reducing unnecessary drug use. This will be discussed more in the recommendations section.

Medication Usage Worldwide

Data keeping on pharmaceutical consumption varies heavily between countries, as does consumption use. Patel et al. (2019) attempted to work out the proportion of pharmaceuticals consumed worldwide. This data was taken from the *Global Pharmaceutical Sales*, MIDAS database, 2013. From this data we can see the pharmaceuticals likely to have high prevalence in wastewater, including metformin and ibuprofen. It is worth noting that 30% of the pharmaceuticals consumed worldwide are at a rate less than 80 tons per year. This proportion will likely increase due to the rise of personalized medicine. Therefore, effective management may require the monitoring of compounds that are consumed at low doses as together these compounds will make a lager contribution to the pharmaceuticals entering wastewater.

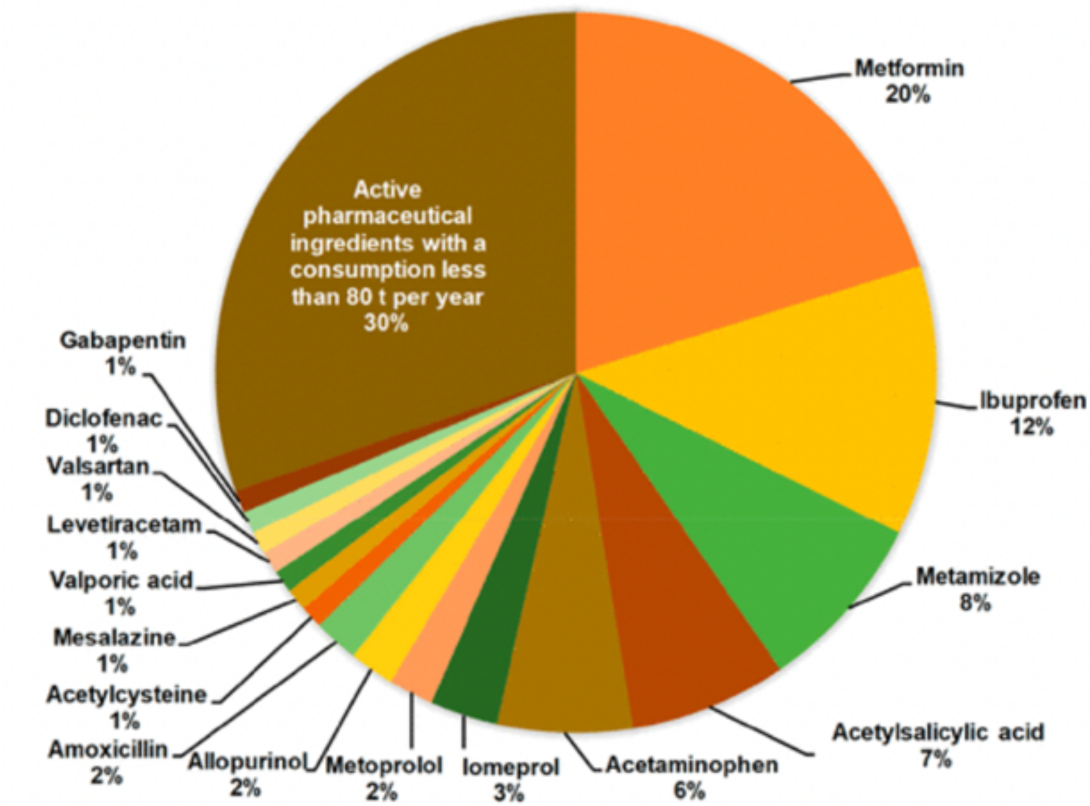


Figure 2 consumption patterns of different pharmaceuticals around the world, Patel et al., 2019

Broadly it is expected that the incidence of pharmaceuticals in the environment will increase because of a growing ageing population, longer life expectancies and improved access to healthcare. Because of the higher ageing population, we can reasonably assume that the incidence of certain diseases that tend to onset in this age group will increase. This includes conditions such as diabetes and heart disease.

Prescription drug use can be heavily affected by socio-economic conditions. For instance, during the economic crisis in Greece, prescription drug use for psychiatric disorders substantially increased (Patel et al., 2019). It is possible that various systematic factors such as rising living wage, unaffordable housing and the impacts of climate change could increase drug use in Canada.

Medication Adherence

Adherence is used to describe a situation when patients take their medications as prescribed, including duration, dosage, correct usage with other medications and obeying any prescription instructions (e.g. take after eating, do not take with alcohol). Adherence is important in this context because understanding how people use certain types of drugs can be indicative of how they dispose of them. For example, if drugs tend to have low adherence, they may be more likely to be disposed of incorrectly, whilst if they are generally taken as prescribed, they will be more likely to enter wastewater after being metabolized by the body, meaning only a proportion will enter wastewater through excretion. Low adherence of antibiotics can also contribute to antibiotic resistance.

There are various reasons why patients do not take their medications as prescribed: difficult side effects, patient perceived improvement in condition, difficult administration (e.g. injection), aversion to the medication’s taste and smell (Worthington, 2007) and complex and nuanced issues to do with addiction, mental health issues and other health issues (including dementia). It can be reasonably assumed that drugs with lower rates of adherence are more likely to not be taken, remain in people’s houses and eventually be disposed of improperly. Therefore, the incorrect disposal pathway may be a more significant path of entry into wastewater for low adherence drugs compared to those that are generally taken as prescribed.

Data from Express Scripts Canada (2019) prescription drug report indicates as many as 70 percent of Canadian patients are not taking their medications as directed by their physicians. It is known that adherence can vary between drug class. The more severe and complex a patient's condition(s) the more likely patients are not to take their medications as directed by their doctor. This is particularly true for chronic diseases (Ruhoy & Daughton, 2008). Express Scripts Canada (2019) reported medium to high non-adherence with the following conditions:

- 70% with asthma/COPD;
- 47% with cancer;
- 45% with diabetes;

- 45% with inflammatory conditions such as rheumatoid arthritis, MS and lupus
-

Understanding which pharmaceuticals have low adherence can indicate which ones are more likely to be kept in households and potentially incorrectly disposed of. Patients with these prescriptions and associated conditions can therefore be subject to targeted drug take back campaigns.

2.1.2 Occurrence

The occurrence of a pharmaceutical in wastewater or the environment can depend on several factors; the initial amount entering wastewater can depend on how much is sold and used, in addition to the amount metabolized in the human body and the amount metabolized and transformed in wastewater processes. It is important to note that occurrence does not necessarily correlate with risk.

Metabolism

Metabolism is when a compound is altered through a biological process, for instance by enzymes in the human body or by bacteria in biological wastewater processes. Consumed drugs undergo a process of metabolism in the body. This means that only a proportion of the original drug will be excreted unchanged, which varies heavily between drugs. It is therefore important to be aware of what metabolites are also being excreted. If there are a lot of a drug metabolites in wastewater influent, it can be inferred that drug consumption and excretion is a significant entry pathway, because if a drug is improperly disposed of then it will not undergo metabolism. It is also important to note that metabolism can vary significantly between individuals and between demographics. There is limited research on drug metabolites. The metabolism pathways of certain drugs may not be well understood and even if certain metabolites have been identified, there may be no reliable method to sample them in wastewater. For some metabolites, their environmental and health risks may not have been thoroughly investigated even though some metabolites have been found to be more toxic than their parent compounds.

Wastewater

Drugs can be metabolized in the wastewater process by certain bacteria. Drugs can also form transformation products as a result of chemical reactions or conditions in the WWTP. Specific rate constants can be calculated to identify the rate of formation for these products, but this can vary based on conditions within the plant.

Predicting Environmental Occurrence

Oosterhuis et al. (2013) investigated whether sales data of pharmaceuticals could be used to predict their loading and concentration in surface waters. They note that because monitoring programs tend to only consider certain pharmaceuticals (both due to resource prioritization and the lack of methods to investigate a variety of compounds and metabolites), predicting pharmaceuticals for monitoring using prescription data could compensate for the limitations of more traditional monitoring programs.

The equation used:

$$consumption\ (location) = \frac{\frac{DDD}{yr} location * (\frac{g}{DDD})}{population}$$

Sales data reported as Defined Daily Doses per year DDD/yr, and consumption is recorded as g/person per day. Importantly, this assumes that the contribution from hospitals is negligible and that medications are taken as prescribed.

Load to the wastewater treatment plant is then calculated in g/day as:

$$load = \frac{\frac{DDD}{year} location * \left(\frac{g}{DDD}\right) * excretion}{365}$$

Excretion factor is the % of the compound that is excreted unmetabolized. This varies between compounds and can generally be found through a literature search. Measured influent concentrations were on average 78% with a range of 31–138% of predicted influent concentrations. It is specified that regional prescription data is more informative than national as regional prescription behaviors can deviate significantly from national ones. This can be due to a range of factors including demographic differences or socio-economic factors.

They noted that differences in predicted and measured concentrations were due to seasonal trends. Interestingly, it has also been proposed that differences between predicted and observed concentrations in wastewater influents can be attributed to incomplete use of prescribed and sold pharmaceuticals (Ruhoy & Daughton, 2008; Musson & Townsend, 2009). The relevance of this for Metro Vancouver is discussed in recommendations section.

2.1.3. Risk

Pharmaceuticals are usually problematic in the environment because they are designed to be both biologically active and persistent enough to not break down before they reach their target in the body. In the environment these behaviors mean that pharmaceuticals can cause adverse effects in organisms, which can disrupt ecosystems. Their high environmental persistence means that these pharmaceuticals tend to be present in the environment for significant amounts of time before they are broken down.

Assessing the risk that a chemical poses to the environment is a complex process. There are many metrics to assess chemical risk that come with their own strengths and limitations which will be discussed below. Therefore, there is not one comprehensive method or ideal metric that can be used to assess risk; a holistic and contextual approach must always be taken. For example, if a chemical is considered safe under one metric, that does not necessarily mean that it will not cause problems in an ecosystem. Risk metrics commonly included for characterizing the risks of chemical exposure include PEC and PNEC, concentration and comparison to minimum effective dose.

Risk Metrics for Chemicals in the Environment

Predicted Environmental Concentration (PEC) and Predicted No Effect Concentration (PNEC)

PEC is calculated through usage (prescription or sales data) combined with criteria that measure environmental persistence (ability to be degraded), transport (ability to accumulate inside organisms) and fate (the ability for organisms to metabolize and detoxify the pharmaceutical, nullifying any detrimental effects arising from the bioaccumulation of the pharmaceutical). This can be compared (or potentially substituted) by Measured Environmental Concentration (MEC), the actual concentration of the compound in the environment. Using this risk quotient approach, if the PEC/PNEC ratio is greater than one means that there needs to be further risk characterization or management of the pharmaceutical (Peake et al., 2016).

There are several limitations with using this approach. PEC can hard to calculate and varies heavily between area, and PNEC values are generally calculated using point exposure to a few model organisms. Therefore, determining a concentration that has no observable effect in one organism is not conclusive evidence to determine that the same concentration could not affect another organism. This approach also ignores long term exposure and associated affects with these and does not take into account that certain compounds display non-monotonic dose response curves. There is considerable debate among scientists about whether a safe exposure concentration exists, due to the complex biological mechanisms associated with carcinogenicity, latent exposure and endocrine disruption.

Concentration

In some cases, exposure to higher concentrations can lead to more severe health impacts, meaning that high concentrations are certainty concerning and an important measurement to evaluate risk. Concentration will generally be higher at a pollution source, so it can be used to indicate areas where there are either lots of sources or a specific high polluter. Concentration can also be a strong indicator of which pharmaceutical to wastewater pathways can be easily intervened in. It is worth noting however, that point concentration measurements can vary significantly by location, season, method used and even time of day. A long-term systematic monitoring program supported by pathway modelling is generally required to identify pollution sources from concentration data. In some cases, concentration can be proportional to the severity of an adverse effect or display some kind of upward correlation, known as a monotonic dose-response curve. Many risk assessment metrics assume a monotonic dose-response curve and use these curves to extrapolate no-effect concentrations from effects observed at higher concentrations. However, this is not always reliable, especially if the compound does not exhibit a monotonic dose response curve.

Long Term Exposure and Low Concentration Risk

Endocrine disruptors (EDs) are chemicals that act to mimic or block the action of the body's hormones to cause an adverse effect. Exposure to endocrine disruptors has been associated with a range of hormone meditated health conditions, including cancer, diabetes and thyroid disorders. Many EDs display non-monotonic dose response curves, meaning that at different doses they have many different effects, with lower concentrations potentially being more dangerous. Long term exposure at low concentrations is still considered very dangerous. This is similar for carcinogenicity. For chemicals with these effects, concentration is not a suitable sole risk metric. It must also be noted that many pharmaceuticals are endocrine disruptors because they are designed to be biologically active and, in some cases, target hormonal receptors. The effects and risk of EDs can be investigated by referring to epidemiological exposure studies, animal models and assays investigating whether a chemical targets a specific receptor.

Acceptable Daily Intake (ADI)

Defined as the maximum amount of a chemical that can be ingested daily over a lifetime with no appreciable health risk. This figure is usually derived from the No Observed Adverse Effect Level

(NOEL) determined from long term studies on sensitive test species. 100 or 10 is usually the default uncertainty factor to take into account differences between species and toxicokinetic factors.

ADI = Long-term NOAEL (lowest value)/100

It is important to note that ADI can vary both person to person and by demographic, and that it is disputes to whether there ever is a safe long term exposure concentration.

Comparison to minimum effective dose

The minimum effective dose is the concentration of a drug that produces a biological response. Although this is normally used to establish the therapeutic window for a drug and determine the most effective dose for treatment, it has also been considered as a risk metric. If the compound is present at a dose above the minimum effective dose in the environment that it could be a sign that the environmental concentrations are sufficient to cause a therapeutic impact, potentially a harmful one, in humans.

2.2. Specific Pharmaceuticals of Concern

Several pharmaceuticals of concern were selected as case studies to characterize their potential entry pathways into wastewater, and the risks they pose to the environment. This research further helps contextualize the Metro Vancouver data. The below drugs were selected because they meet one or more of the following criteria:

1. Highly prevalent in Metro Vancouver
2. Highly prevalent in other jurisdictions
3. Identified environmental risks
4. Have been flagged as concerning by other jurisdictions

It is recommended that this collated data is translated into an internal resource spreadsheet for Metro Vancouver, which will be discussed more in the recommendations section.

2.2.1 Pharmaceutical Case Studies

Acetaminophen

Usage and Prescription

Acetaminophen is a common over-the-counter pain medicine, sold under the brand name Tylenol or paracetamol. It is not prescribed unless when recommended for administration by intravenous injection. Chong et al. (2017) evaluated consumers' usage patterns of acetaminophen and according to the results, majority of consumers use acetaminophen for a headache, fever, and common pain.

Metabolism and Excretion

Acetaminophen is metabolized by the liver by glucoronidation (60%), sulfation (30%), and a small amount (4- 7%) is excreted unchanged (Mcgill Critical Care Medicine, 2021).

Wastewater Sources and Fate

Removal rates vary for acetaminophen appear to vary very heavily between plants and on the wastewater treatment technologies in use. Al-Mashaqbeh et al. (2019) found that this varied from 99.9% in a secondary treatment plant in Jordan but were lower in other areas. Other literature has indicated that acetaminophen requires advanced treatment to remove and techniques investigated include photodegradation (Kurniawan et al., 2018), adsorptive removal (Natarajan et al., 2021) and electro oxidation (Mousset et al., 2019).

Environmental Occurrence and Risk

Żur et al. (2018) found that acetaminophen could at concentrations as low as 0.01 μ/L significantly inhibit acetylcholinesterase and selenium dependent glutathione peroxidase enzymes in *Daphnia magna*. At concentrations of 2.5 microgram/liter acetaminophen could disrupt hypothalamic-pituitary-gonadal axis, reduction of hemoglobin and hematocrit, increase in leukocytes and thrombocytes, reduction of testosterone and increase in estradiol levels, induction of oxidative stress, and hepatotoxicity in *Rhamdia quelen.*

Trends

There is evidence to suggest that acetaminophen usage and over-dosing increases during cold and flu season (Hider-Mlynarz et al., 2018; Shiffman et al., 2018). One study suggests that concomitant usage has increased over time (Kaufman et al., 2019).

Antibiotics

Prescription and Usage

Van Boeckel et al. (2014) estimate that antibiotic use will increase by 67% from 2010 levels by 2030. Antibiotics are used as treatment for both humans and animals, however the use of antimicrobials in animals is not regulated in many countries, leading to overuse. It is estimated that up to double the amount of antibiotics used in humans are used in animals (Al-Riyami et al., 2018). In Canada, the use of medically important antimicrobials must be limited to treatment and prevention of diseases, not growth promotion, and all medically important antimicrobials now require a veterinary prescription (Government of Canada, 2020a).

Metabolism

Most antibiotics are poorly absorbed by humans or animals and consequently 25 to 75% are excreted unaltered through urine and faeces (Chee-Sanford et al., 2001).

Treatment in Wastewater

The average concentrations for azithromycin, sulfamethoxazole and ciprofloxacin in the raw wastewater in the United State of America were 18.3, 1.11 and 1.44 µg/L, respectively, and 3.25, 1.23, and 0.59 µg/L, respectively in treated wastewater (Talaiekhozani et al., 2020). Antibiotics are not biodegradable, but they can be removed by technologies including electrocoagulation. osmotic membrane bioreactor, and chemical oxidation processes.

Antibiotic resistance in wastewater

WWTP processes provide ideal conditions for antibiotic resistant bacteria to proliferate. Especially if a membrane bioreactor is used in treatment, which uses both a filtration system and a biological process where microscopic bacteria consume waste products. When consuming organic waste the bacteria encounter antibiotics and start to express antibiotic resistance genes, which can rapidly spread to neighboring bacteria and to daughter cells (Zarei-Baygi et al., 2019).

The wastewater environment is an ideal environment for antibiotic resistance to spread because it brings together bacteria of environmental, human and animal origins and there is an abundance of nutrients, stable pH and temperature and particles for bacteria to absorb onto (Manaia et al., 2018). The activated sludge system of WWTPs is also the perfect setting for antibiotic resistance gene (ARG) transfer events. The mobilization of antibiotic resistant genes makes it very difficult to efficiently eliminate them once the transmission starts to spread (Alexander et al., 2020). Therefore, biological treatment processes may increase the abundance of antibiotic resistance genes (Zhu et al., 2021).

Wastewater treatment processes produce residual solids which are processed into biosolids. Depending on quality, biosolids are used as a fertilizer for agriculture and livestock feed crops, or, may need to be managed through landfilling (Zarei-Baygi et al., 2019). Studies have found that even low concentrations of just one antibiotic can lead to resistance in multiple classes of antibiotics. The products of wastewater have been found to contain trace amount of antibiotic resistance DNA, and small amounts of antibiotic resistant bacteria and free-floating DNA have been found to make it through filtrations membranes and be present in effluent (Zarei-Baygi et al., 2019).

Environmental Occurrence and Risk

Antibiotic-resistant bacteria and resistance genes found in environmental samples around WWTPs may pose a health risk to WWTP workers and nearby residents. Low and middle-income countries are likely to be the most affected, both in terms of impact on public health and economic burden (Fouz et al., 2020). Antibiotics discharged from effluent can lead to a selective pressure for the occurrence of antibiotic resistance in the environment (Barancheshme & Munir, 2018). Antibiotics have been found at high concentrations in the environment downstream of a WWTP with none detected upstream of the WWTP, suggesting that the effluent was a significant source of antibiotic entry into the environment (Rodriguez-Mozaz et al., 2015). As biomass from WWTPs can be applied on land this is another pathway for antibiotic resistance to spread. (Barancheshme & Munir, 2018).

Trends

Between 2014 and 2016, approximately one million people died due to untreatable of inefficient infections caused by antibiotic resistant bacteria (ARB). The situation is likely to worsen due to lack of new antibiotics and predictive models indicate a significant increase in ARB-related deaths over the next decades (Alexander et al., 2020). It is unclear whether there will be higher concentrations of antibioitcs entering wastewater, but this trend indicates that the contibued prescence of antibiotics in wastewater presents a major public health issue.

Caffeine

Metabolism and Excretion

After consumption, caffeine is extensively metabolized, with < 5% being excreted unchanged in urine. Paraxanthine (1,7-dimethylxanthine) is the main metabolite in humans, accounting for 80% of the total caffeine excretion in humans. Caffeine is a commonly used anthropogenic marker (Rodríguez-Gil et al., 2018).

Carbamazepine

Usage and Prescription

Carbamazepine is used to prevent and control seizures. This medication is an anticonvulsant or anti-epileptic drug and must always be prescribed. It is also used to relieve certain types of nerve pain, such as trigeminal neuralgia (Government of British Columbia, 2019a). The Government of British Columbia recommends:

"The dosage is based on your medical condition and response to treatment. In children, the dosage is also based their weight. To reduce your risk of side effects, your doctor may direct you to start this medication at a low dose and gradually increase your dose. Follow your doctor's instructions carefully." (Government of British Columbia, 2019a)

Metabolism and Excretion

Carbamazepine is almost completely metabolized in the liver with only around 5% of the drug excreted unchanged. The major metabolite is 10,11-epoxycarbamazepine, with minor metabolites being 2-hydroxycarbamazepine and 3-hydroxycarbamazepine (Thorn et al., 2011).

Wastewater Treatment

Miao et al. (2005) detected carbamazepine and five of its metabolites in in all wastewater samples collected from four different stages of treatment in Peterborough, Ontario. The results showed that 29% of the carbamazepine was removed from the aqueous phase during treatment in the WWTP, while the metabolites were not effectively removed. They mentioned that the calculated daily inputs into the WWTP were somewhat less than the inputs of 192 g estimated from Canadian annual sales data for carbamazepine. Y. Li et al. (2021) state that advanced oxidation processes, including ozonation, Fenton/Fenton like reaction, photocatalysis and sulfate radical based AOPs are considered to be the most effective technologies for CBZ elimination.

Environmental Occurrence and Risk

Oldenkamp et al. (2019) represented the flow of carbamazepine from excretion to the environment.

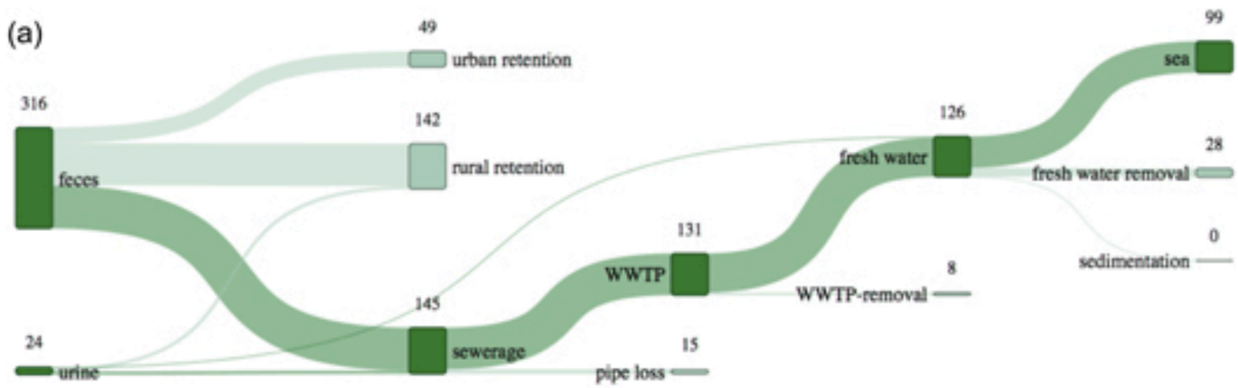


Figure 3 global flow of carbamazepine. Dark flows represent transport flows, light represents actual removal and retention. Thickness represents actual amount in tonnes/year (Oldenkamp et al., 2019).

Environmental concentration of carbamazepine accelerates fish embryonic development and disturbs larvae behavior (Qiang et al., 2016). Exposure to an environmentally relevant concentration (1 µg/L) of carbamazepine disturbed the expression pattern of neural-related genes of zebrafish embryos and larvae, which could influence fish population structure

Trends

Rehrl et al. (2020) found that carbamazepine displayed little annual fluctuation and Oldenkamp et al. (2019) attempted to record temporal trends of carbamazepine. Both studies showed an increase in the consumption of carbamazepine and increasing environmental concentrations.

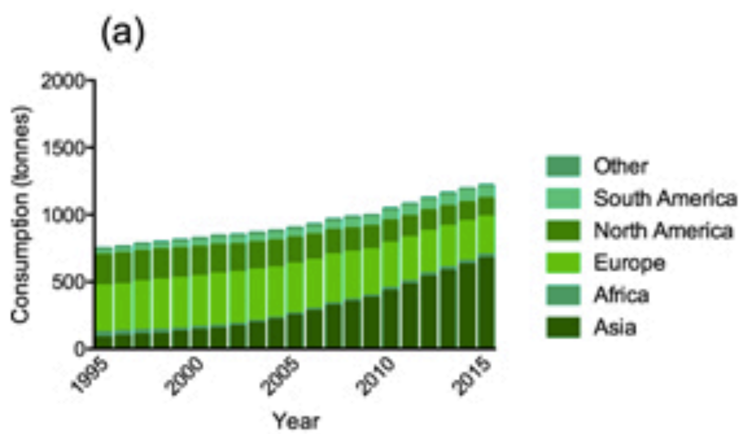


Figure 4 Global trends in carbamazepine consumption, Oldenkamp et al. (2019).

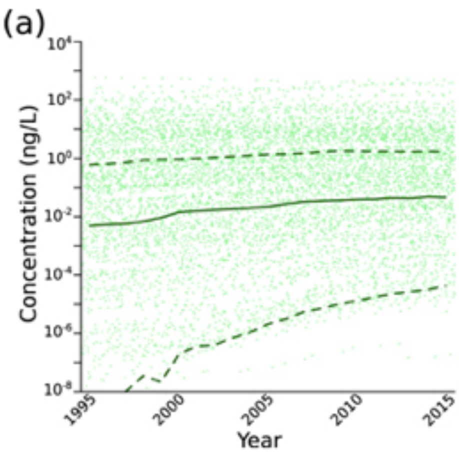


Figure 5 The environmental concentration of carbamazepine over time, Oldenkamp et al. (2019)

DEET

Usage and Prescription

DEET (chemical name, N,N-diethyl-meta-toluamide) is the active ingredient in many insect repellent products. It is widely used to repel biting pests such as mosquitoes and ticks. Every year, an estimated one-third of the U.S. population use DEET to protect them from mosquito-borne illnesses, and it is suspected that usage exceeds sales. There are a variety of products containing DEET including liquids, lotions, sprays, roll-ons and towelettes. DEET is designed for direct application to people's skin to repel insects.

Metabolism and Excretion

The primary metabolites of DEET N,N-diethyl-m-hydroxymethylbenzamide (BALC) and Nethyl-m-toluamide (ET). The recovered DEET metabolites were observed significantly more from children (1,116 µg) than from adults (446.2 µg) ($p < .001$). Small children are at increased risk of excessive absorption of DEET applied to the skin because of their relatively higher surface to volume ratio compared to adults (DrugBank, 2021b). DEET is principally excreted via the kidneys, where the initial phase is initially rapid but not more than 50% of the absorbed dose is excreted during the first 5 days

Wastewater Treatment

Marques dos Santos et al. (2019) state that degradation in WWTP processes is highly variable and removal rates range from 10 to 90%. Loss of a compound in a WWTP may be due to adsorption to sludge, volatilization during aeration processes, or biodegradation (aerobic or anaerobic). DEET can enter wastewater through the washing of laundry, showering and disposal of DEET down the drain. During recreational water activities DEET can also be introduced to the aquatic environment.

Environmental Occurrence and Risk

Among aquatic species, acute effect concentrations range between 4 and 388 mg/L. The chronic no-observed effect concentrations (NOEC) for daphnids and green algae range from approximately 0.5 to 24 mg/L (Weeks et al., 2012).

Trends

Seasonal variations in DEET are expected, as during the summer DEET usage accounts for almost 60% of all usage during a year, while during the winter months DEET usage accounts for <5%. DEET usage also varies by hour of the day with two maximums, one in the morning period around 09:00 and a second one in the late afternoon with peak around 17:00, which is important to bear in mind when taking monitoring samples. They also found that DEET concentrations in wastewater does not always correlate with sales data or resemble PEC which could be due to complex entry pathways and seasonal usage patterns (Marques dos Santos et al., 2019).

Diclofenac

Usage and Prescription

Diclofenac is used to relieve pain, swelling (inflammation), and joint stiffness caused by arthritis (Government of British Columbia, 2018). Diclofenac must be prescribed unless when sold as a single medicinal ingredient for topical use on the skin in a concentration equivalent to 2% or less of diclofenac for not more than 7 days.

Metabolism and Excretion

Diclofenac is mainly eliminated via metabolism. Of the total dose, 60-70% is eliminated in the urine and 30% is eliminated in the feces (DrugBank, 2021a). The primary metabolite is 4'-hydroxy diclofenac which is weakly active with one thirtieth the activity of diclofenac. Other metabolites include 3'-hydroxy diclofenac, 3'-hydroxy-4'methoxy diclofenac, 4',5-dihydroxy diclofenac, an acylglucuronide conjugate, and other conjugate metabolites.

Wastewater Treatment

Generally, diclofenac is poorly biodegradable which often translates into low elimination rates during biological wastewater treatment. Only a minor portion is adsorbed to sludge. Bioaugmentation could be used to enhance elimination, but this will require more research on the microbial communities that are able to degrade diclofenac (Vieno & Sillanpan, 2014). The minimum and maximum effluent concentrations found in Canada are 0.005 µg/L and 0.36 µg/L (Metcalfe et al., 2003).

Environmental Occurrence and Risk

Diclofenac is known to harmfully affect several environmental species at concentrations of ≤ 1 µg/l and is also chronically toxic. Based on these studies, Ferrari et al. (2003) calculated a predicted no effect concentration (PNEC) for DCF as 116 µg/l, i.e. 1000-fold higher than concentrations usually measured in the environment. It has the highest acute toxicity within the class of AIAPs (Aydin et al. 2018; Vieno and Sillanpää 2014). It can cause a decrease in the population of fishes and birds by causing renal failure (Oaks et al. 2004; Hoeger et al. 2005).

Ibuprofen

Usage and Prescription

Ibuprofen is often sold under the common brand names of Advil and Motrin. Ibuprofen can be used to 'relieve pain from various conditions such as headache, dental pain, menstrual cramps, muscle aches, or arthritis. It is also used to reduce fever and to relieve minor aches and pain due to the common cold or flu.' (Government of British Columbia, 2019b). Ibuprofen is the third most popular, highly prescribed and most saleable over the counter medicine in the world (Chopra & Kumar, 2020).

Ibuprofen must be prescribed unless:
a. An oral dosage form that provides 400 milligrams or less per dosage unit; or
b. A modified-release oral dosage form that provides 600 milligrams or less per dosage unit (Government of Canada, 2020b).

Metabolism and Excretion

Almost all of ibuprofen is metabolized, with 15% excreted unchanged (Chopra & Kumar, 2020). The elimination of ibuprofen is not impaired by old age or the presence of renal impairment (DrugBank, 2021c). Urinary excretion of the two major metabolites, carboxy-ibuprofen and 2-hydroxy-ibuprofen (and their corresponding acyl glucuronides), accounts for ~37 and 25% of an administered dose. Small amounts of other hydroxylated metabolites (3-hydroxy-ibuprofen and 1-hydroxy-ibuprofen) have also been detected in urine (Mazaleuskaya et al., 2015). It is important to note that these metabolites are more toxic that the parent compound.

Treatment in Wastewater

The removal efficiency of ibuprofen in wastewater can vary from 12% (Coagulation-flocculation) to nearly 100% (ozonation/AOPs), membrane bioreactor and attached growth treatment processes (Chopra & Kumar, 2020).

Future Trends

In recent years, ibuprofen intake has increased as reported in many European Union (EU) countries (Hudec et al., 2012; Parolini et al., 2011).

Metformin

Prescription and usage

Glucophage and Glycon are common brand names. Metformin is used with a proper diet and exercise program and possibly with other medications to control high blood sugar. It is used in patients with type 2 diabetes. Metformin must always be prescribed. The dosage is based on patients' medical condition, response to treatment, and other medications patients may be taking. Doctors may direct patients to start this medication at a low dose and gradually increase it. BC recommends that patients follow their doctor's instructions carefully. Metformin sometimes has an off label use to treat PCOS (Niemuth & Klaper, 2018) and is also used in cancer treatment.

It is understood that metformin has a low adherence, due to swallowing difficulties from large tablets, side effects and patients on metformin being prescribed to multiple medications (Christofides, 2019).

Metabolism and Excretion

Almost 90% of metformin is excreted un-metabolized from the human body in urine and therefore ends up in wastewater influent (Briones et al., 2018).

Wastewater Treatment

Metformin wastewater concentrations have been found to correlate with prescription figures in Germany (Scheurer et al., 2012). Guanlyurea is a transformation product of metformin. In WWTPs, metformin is aerobically biotransformed to guanylurea at rates varying from 41% to 98% (Briones et al., 2018).

Environmental Occurrence and Risk

There is some evidence that metformin is an endocrine disruptor at environmentally relevant concentrations. Studies have found that metformin can alter gene expression (Niemuth & Klaper,

2018) and cause fish to turn intersex (Niemuth & Klaper, 2015). In the latter study, the authors explain that the concentrations to cause these effects were similar to concentrations found in wastewater effluents, ranging from 10.6-47 µg L^{-1}. (Blair et al., 2013) (Scheurer et al., 2012) and (Ghoshdastidar et al., 2015).

Future Trends

The number of people with diabetes is expected to increase globally from 425 million (2017) to 693 million by 2045 (IDF, 2017). It is estimated that 1 in 3 Canadians have diabetes or prediabetes and that the percentage being diagnosed in Canada will increase by 30% between 2020 and 2030 (Diabetes Canada, 2016). It would therefore be expected that the amount of metformin entering wastewater would also increase, and that the concentration of its transformation product guanylurea would also increase.

Naproxen

Prescription and Usage

Naproxen is used to relieve pain from various conditions such as headache, muscle aches, tendonitis, dental pain, and menstrual cramps. It also reduces pain, swelling, and joint stiffness caused by arthritis, bursitis, and gout attacks (HealthLink BC, 2021). Naproxen must be prescribed except when sold for oral use with a daily dosage equivalent to 400 milligrams of naproxen base.

Metabolism and Excretion

66-92% of Naproxen is recovered as conjugated metabolite and less than 1% recovered as naproxen or desmethylnaproxen. Less than 5% of naproxen is excreted in the feces (DrugBank, 2021d).

Wastewater Treatment

Wojcieszyńska & Guzik (2020) state that the removal of naproxen in wastewater treatment plants is significantly different and ranges from its almost complete removal to only a 40% degradation level. It was observed that in the effluents of wastewater treatment plants, the concentration levels of naproxen ranged from 25 ng/l to 33.9 µg/l. Moreover, Suzuki et al. (2014) showed that the effluents of wastewater treatment plants also contain its major metabolite 6-O-desmethylnaproxen at a concentration of 0.56 µg/l.

Environmental Occurrence and Risk

Naproxen is a stable molecule and therefore has high environmental persistence. It can also bioacculmunate, with concentrations found in the bile of fishes being 1000 times higher than this detected in samples in the lake (Brozinski et al., 2013). Naproxen has demonstrated endocrine disruptor effects, with A 14-day exposure to 10 µg/L of naproxen resulted in an altered gene expression in the gill tissue of zebrafish (Q. Li et al., 2016). Xu et al. (2019) demonstrated a decrease in the thyroid hormone levels in zebrafish after exposure to naproxen.

Naproxen exposure can also cause some effects in synergy with other compounds. A NOEC was identified for multiple no-steroidal anti-inflammatory drugs. However, when the drugs were combined in mixtures there were observable adverse effects (Melvin et al., 2014). Jiang et al., (2017) also showed that a mixture of naproxen, diclofenac and ibuprofen led to an increase in bacterial diversity in a sequencing batch reactor.

Theophylline

Prescription and Usage

Always must be prescribed. Theophylline is used to treat lung diseases such as asthma and COPD (bronchitis, emphysema). It must be used regularly to prevent wheezing and shortness of breath. This medication belongs to a class of drugs known as xanthines.

Metabolism and Excretion

About 6% of a theophylline dose is N-methylated to caffeine. Caffeine and 3-methylxanthine are the only theophylline metabolites with pharmacologic activity (DrugBank, 2021e).

Treatment in Wastewater

Nanofiltration was found to be capable of removing theophylline and caffeine (Egea-Corbacho et al., 2019).

Valsartan

Prescription and usage

Must always be prescribed. Valsartan is used to treat high blood pressure and heart failure. It is also used to improve the chance of living longer after a heart attack. In people with heart failure, it may also lower the chance of having to go to the hospital for heart failure. Valsartan belongs to a class of drugs called angiotensin receptor blockers (ARBs). This drug may also be used to help protect the kidneys from damage due to diabetes (Health Link BC).

Metabolism and Excretion

Valsartan is known to be excreted largely as unchanged compound and is minimally metabolized in man with the only notable metabolite is 4-hydroxyvaleryl metabolite (4-OH valsartan).

Wastewater Treatment

Bayer et al. (2014) found that the elimination of the substances with related structures (sartans) varied from 17 % for olmesartan to 96 % for valsartan. Monitoring data for these drugs in wastewater effluents of six different sewage treatment plants in Bavaria and at eight rivers, showed a median concentrations for valsartan of 1.1 µg L(-1). For valsartan and irbesartan AC filtration is also a significant removal mechanism (Bayer et al., 2014).

In a drinking water treatment plant valsartan acid is not prone to ozonation but is effectively removed by activated carbon filtration (NNDDIN et al., 2013). Biological treatment was also found to be more effective by Huang et al. (2018) in China, but removal rates were higher in August than November. Valsartan acid is a transformation product of valsartan formed in the activated sludge of WWTP, which is more persistent than valsartan. Although low concentrations of valsartan acid were detected in the raw sewage, significantly higher concentrations were detected in the treated effluent.

Environmental Occurrence and Fate

Nödler et al. (2013) found that Valsartan acid was frequently detected in German surface waters where it demonstrated high persistency. It was also detected in drinking water.

Trends

There is evidence that valsartan usage is increasing. For instance, the consumption of valsartan increased in Germany by more than 250 % from 2002 to 2009 to a total amount of 56 tons per year (Bergmann et al. 2011). Bayer et al. (2014) calculated the PEC for valsartan in German wastewater influent as shown in Figure 6.

Environ Sci Pollut Res (2014) 21:10830–10839 10835

Table 3 Comparison of predicted (PEC) and measured environmental concentrations (MEC) of the sartans in wastewater influent (WWi), wastewater effluent (WWef) and freshwater (FW)

	PEC_{WWi} [$\mu g\ L^{-1}$]	PEC_{WWef} [$\mu g\ L^{-1}$]	MEC_{WWef} median [$\mu g\ L^{-1}$]	MEC_{WWef} maximum [$\mu g\ L^{-1}$]	PEC_{FW} [$\mu g\ L^{-1}$]	MEC_{FW} median [$\mu g\ L^{-1}$]	MEC_{FW} maximum [$\mu g\ L^{-1}$]	Frequency of quantification [%]
Candesartan	1.00	0.81	0.46	0.82	0.08	0.06	1.10! (0.22)	48
Eprosartan	4.51	2.57	0.73	6.50	0.26	0.02	0.28	30
Irbesartan	4.52	3.21	1.25	2.60	0.32	0.08	0.80! (0.31)	66
Losartan	2.04	–[a]	0.21	0.45	–[a]	0.02	0.12	12
Olmesartan	1.08	0.90	0.74	1.20! (0.83)	0.09	0.07	2.20! (0.30)	74
Telmisartan	1.57	–[a]	0.68	1.40	–[a]	0.07	0.70! (0.30)	60
Valsartan	8.10	0.32	1.10	6.00	0.03	0.11	0.77	70

At MEC, the exclamation point marks the outlier at this sampling site, and in brackets, the next highest measured value is showed

[a] Data for losartan and telmisartan could not be calculated because of missing elimination data during wastewater treatment

Figure 6 Calculated PEC and MEC for Valsartan, (Bayer et. al, 2014)

Interestingly, the concentrations of valsartan acid and carbamazepine correlated well ($R^2 > 0.95$) in both river systems indicating an equivalent persistency and tracing capability for wastewater in surface waters.

2.2.2 Chemical Properties Table

For wastewater treatment, it is important to note that although the behavior of compounds in wastewater cannot be definitively predicted, certain chemical properties can provide an estimation of how compounds may fare. The chemical properties table (Table 1) was created for this report with the values sourced from literature.

Sorption of compounds to the solid phase can be estimated using the K_{OW} values which reflects the equilibrium of partitioning the organic solute between the organic phase, or the octanol and the water phases. For compounds with log K_{OW} < 2.5, the sorption to activated sludge is not expected to contribute significantly to the removal of the pollutants via excess sludge withdrawal. Between log K_{OW} 2.5 and 4 moderate sorption is expected and values higher than 4.0 indicate high sorption potential (Das et al., 2017).

The degradation constant can also be investigated, but this will vary significantly for compounds and on the local bacterial conditions of the WWTP biological treatment process. For this, more information would be required on Metro Vancouver WWTPs to find degradation constants for compounds under similar conditions. Complex structures with aromatic rings, and the presence of chlorine groups can reduce the degradation constant. Compounds with a biological degradation constant of <0.0042 L/gss/h are not expected to be removed significantly (<20%), whereas compounds with rate constants >0.4 L/gss/h can be transformed by >90% (Das et al., 2017).

Das et al. (2017) propose three classifications for how compounds are treated in wastewater:

1. Compounds which are easily removed by both Conventional Treatment Process (CTP) and Membrane BioReactor (MBR) (e.g. ibuprofen);
2. Compounds not efficiently removed in both systems (e.g. clofibric acid, diclofenac); and
3. Compounds not satisfactory removed by CTP but well removed by MBR (e.g. ketoprofen, mefenamic acid and naproxen).

PKa is important because the protonation state of compounds can influence sorption and degradation processes. There is a better removal rate of deprotonable compounds at lower pHs. The better removal rate of deprotonable micropollutants from wastewater can be achieved at low pH value, the protonation state influencing both sorption and degradation processes.

Table 1 Chemical Properties of Pharmaceutical Compounds in Wastewater

COMPOUNDS	FAMILY AND USAGE	PK_A	LOG K_{OW}	WATER SOLUBILITY MG/L	MOLECULAR WEIGHT	REFERENCE
Acetaminophen	Analgesic	9.9	-0.78	1000	180.2	(Al-Mashaqbeh et al., 2019)
Caffeine	Stimulant	14	-0.07	$2.16x10^4$	194.19	Pubchem
Carbamazepine	anticonvulsants	13.9	2.45	18	236.27	DrugBank, PubChem
DEET	Insect repellent	-1.37±0.7	2.02	912	191.27	Pubchem, ChemicalBook
Diclofenac	NSAIDs	4.15	4.51	2.37	296.1	Pubchem
Ibuprofen	NSAID	5.3	3.97	21	206.28	Pubchem
2-hydroxy-ibuprofen	Metabolite	SA(4.63), SB(-2.7)	-	0.3	222.28	Pubchem DrugBanK
Metformin	anti-diabetic	12.4	-2.64	Freely soluble	129.16	Pubchem
Granylurea	Metabolite	1.8 and 8.2	-	50 (soluble)	102.10	NIH
Naproxen	NSAID	4.15	3.18	15.9	230.26	Pubchem
Theophylline	methylxanthines	8.81	- 0.02	7,360	180.16	Pubchem
Valsartan	angiotensin receptor blockers	4.73	4.00	1.406	435.5	Pubchem
Valsartan Acid	Metabolite of valsartan	-	-	-	266.25	Pubchem

3. Jurisdictional Scan Literature Review

This section is a literature survey of three jurisdictions: Sweden, Switzerland and King County USA that have had various successes in preventing, monitoring, and managing pharmaceuticals in wastewater. All three jurisdictions have drug take back programs that are either relatively successful or are trialing new approaches to improve the program. This scan informs the recommendations for improving the drug take back program in the Metro Vancouver region.

3.1 Sweden

Sweden was chosen for the jurisdictional scan because:

1. There is considerable research on the success and improvements within the drug take back program (which is one of the most successful in Europe)
2. There is a National Pharmaceutical Strategy to tackle pharmaceutical pollution
3. There is a successful systematic monitoring program in place.

National Pharmaceutical Strategy

The Swedish government, the Swedish Association of Local Authorities and Regions and a range of pharmaceutical actors are developing and continuing the implementation of Sweden's National Pharmaceutical Strategy, NPS (Government of Sweden, 2020; Swedish Medical Products Agency, 2020d). Under the NPS, target area 3 is addressing the socio-economic and environmentally sustainable use of medicines. This includes ensuring the use of medicines that are environmentally sustainable and have a limited impact on the environment.

As part of this strategy, the aims of the Swedish Medical Products Agency (MPA) include ensuring that environmental considerations are considered when approving and regulating pharmaceutical products and that information is provided on the environmental impacts of pharmaceuticals. To offer an incentive to producers to consider the environmental impact of their drugs, the Swedish government set aside 19 M Swedish Krona (approximately 2.8 M Canadian Dollars) in 2020 for a pilot project to award drug companies that can demonstrate effective pollution control during the manufacturing of their products (Centre for Antibiotic Resistance Research CARe, 2020).

The Swedish MPA is also creating a Knowledge Centre on Pharmaceuticals in the Environment 'with the vision to protect people, animals and the environment from harmful effects caused by pharmaceuticals, now and for future generations.' Although this is a Swedish initiative, the Centre intends to have an international outlook and contribute to both Sweden's environmental goals and the Global Sustainability Goals defined by the UN (Swedish Medical Products Agency, 2020b).

Drug Take Back Program

In Sweden the drug take back program is coordinated by the Swedish Medical Products Agency and through Sweden Apoteket, a state-run pharmaceuticals retailer. The federal government funds the program, with €1,444,442 budgeted for its operation in 2006. It is therefore mandatory for pharmacies to participate in the scheme, with 100% currently participating. This contrasts with Canada where waste/garbage (including post-consumer pharmaceuticals) is regulated at the provincial level and each province has a slightly different approach. The Swedish program has been in operation since 1970, and current collection points are pharmacies, as well as online pharmacies and recycling centers. The pharmaceutical waste collected was 1010 tonnes or 0.1 kg/capita (Volha Turlo, 2017).

Any drugs returned to pharmacies are incinerated, and the Swedish Medical Products agency advises that drugs are not disposed in household waste or flushed down the toilet. They treat pharmaceutical packaging as a municipal issue, so the packaging disposal policy may vary by local jurisdiction. However, it is stated that if the drug packaging has visible residues it should be returned to pharmacies as well, making them one of the few national jurisdictions to suggest this (Swedish Medical Products Agency, 2020a).

Research on the Drug Take Back Program

Sweden has conducted considerable research to understand how the drug take back program operates. In a study conducted by Persson et al. (2009), the Swedish Association of the Pharmaceutical Industry AB together with Apoteket AB surveyed the public in 2001, 2004 and 2007 to investigate their understanding of drug disposal practices. 85% knew that correct disposal of unused medicines was to return them to a pharmacy with 43% doing this in the last 12 months. Of patients who saved their medicines, 55% indicated that they would return it to a pharmacy in the future. When asked of reasons of why medications were returned, 50% answered environmental reasons, with 42% stating that they worry about the environmental impact of medicines. This demonstrates that even in 2009, there was a considerable public awareness of the environmental impacts of pharmaceuticals and the correct disposal methods.

To understand the types of pharmaceuticals that were returned and the motivations for returning pharmaceuticals, pharmacists conducted semi-structured interview with patients returning medications (Ekedahl, 2007). The most common reasons cited for retuning drugs were:

1. Passed expiry date
2. Death of patient (so were handing in medications on someone else's behalf)
3. Improved condition or therapy changes.

The relative importance of the reasons to patients who cited more than one reason was not established. Patients may also ascribe different reasons to returning different drugs, which was not investigated in this study.

The authors also differentiated between two types of drugs being returned by 408 patients: ongoing medication and former medication. Ongoing medication was defined as either medication the patient was intended to use on the day the medicines were returned or as medicines a deceased patient was prescribed to take at the time of their death. These consisted of 37% of returned medications. All other returned medications (63%) were defined as 'former medication.' This shows that patients were more likely to return drugs that they could no longer use.

Policy Interventions in the drug take back program

Sweden have trialed multiple policy solutions that intend to improve the drug take back program. They also have certain healthcare policies that indirectly improve the drug take back program and preventative policies that aim to reduce the amount of pharmaceuticals prescribed.

Ease of Return

Pharmacies in Sweden supply special transparent plastic bags with informational text where unused drugs preferably should be placed, and customers also do not have to queue when returning drugs (Persson et al., 2009). It is unclear whether promotional materials are used to communicate these instructions to patients. Patients can also return drugs at recycling centers or at online pharmacies, giving more locations and avenues to return drugs if access is an issue.

Promotion and Messaging

When the drug take back program was being developed an overall promotion message was agreed upon – that there was a risk of polluting drinking water for future generations of humans. Secondly, the message was altered to appeal to specific target groups, whilst ensuring the multiple messages did not contradict each other to ensure consistency. The messages were widely circulated on major TV news studios and in Sweden's largest morning paper in 2005 (Gunnarsson & Wennmalm, 2008).

Patient Support

This is not an example of a policy intervention to directly improve the success of drug take back programs, but a healthcare policy designed to improve patient adherence, which presents opportunities for engaging and educating patients about the environmental impacts of pharmaceuticals. Montgomery et al. (2008) conducted a study on the follow up rates Pharmaceutical Care (PC) services in Sweden. PC services are longer term patient counselling by a pharmacist. Its aims depend on the individual patient, but can include a combination of monitoring patient adherence, counselling, practical help with medication, lifestyle advice and addressing drug related problems. As of 2002, these services were available at 240 out of 870 community pharmacies in Sweden. Anyone on prescription drugs who needs continuous support is eligible for the service. Although the compliance effectiveness was not evaluated, this service presents a promising opportunity to educate patients on environmental impact and encourage greater compliance which will be discussed in the recommendations.

Environmental Classification of Pharmaceutical Drugs

The original idea behind classifying drugs based on their environmental impact was to enable drug management decisions to be made on multiple levels by multiple stakeholders:

1. Drug producers
2. Doctors prescribing drugs (although this could be extended to pharmacists advising on medication)
3. Patient when choosing and using drugs (Gunnarsson & Wennmalm, 2008).

This classification system was established in 2004 as a collaboration between producers, authorities and the public healthcare (Wennmalm & Gunnarsson, 2009). The risk classification is closely related to EMEA guidelines and is expressed as the ratio between the predicted environmental concentration (PEC) of the active ingredient (AI) and its predicted no effect concentration (PNEC). However, risk assessment data were missing in 47% of AI (Wennmalm & Gunnarsson, 2009). Sweden has in the past used two main models to classify the environmental risks of drugs.

1. Stockholm model

This model attempts to classify environmental hazard inherently by estimating biodegradability (OECD guidelines or equivalent), potential to bioaccumulate, and toxicity to aquatic organism (across three tropic levels of fish, Daphnia (crustaceans) and algae). The three are added together, with biodegradability 0 or 3, potential to bioaccumulation 0 or 3 and toxicity to aquatic organisms (0-3). For instance, a drug that meets the first two criteria and has high toxicity will be scored 9. As of 2009, the results of the classification of around 350 active drug substances were available on the Stockholm County Council's website for pharmaceutical information (*www.janusinfo.se*).

2. Swedish model

For the risk assessment, the Predicted Environmental Concentration (PEC) is calculated based on the sold quantity of active substance (obtained from Apotoket), all of which is assumed to be consumed, excreted (using a default value of 200l person^{-1} day^{-1}) and diluted in sewage and to the water source (by a default factor of 10). The Predicted No Effect Concentration (PNEC) is the highest concentration that is considered harmless based on toxicological data. How the risk assessment is communicated depends on the stakeholder:

1. Patients
   PEC/PNEC ratio is verbally provided with a very short assessment on what this means. For example, if PEC/PNEC > 10 means that use of the medicine has been considered to result in high environmental risk.

2. Prescribers
   Additional classification on the degradation, bioaccumulation and persistence of the medication is provided.

3. Specialists.
   More extensive environmental data including: ecotoxicological, degradation, partition coefficient, carcinogenicity, mutagens, teratogens, pharmacological activity of metabolite, kg in sales, integration of data from risk and hazard, calculation of risk assessment.

Additional information on the system can be obtained from the LIF website (*www.fass.se*). The Swedish Medical agency also intends to undertake a study about customers' willingness to pay for environmentally assessed medicines to identify if patients would pay more for drugs with a lower environmental impact. The most recent version of the database *Pharmaceuticals and Environment* launched in 2016 (janusinfo.se) is a non-commercial, freely available web-based database of compiled environmental information for pharmaceutical substances. This can be used by prescribers to easily compare drugs on their environmental impact. The database contains environmental hazard and risk information, primarily gathered from regulatory authorities and pharmaceutical companies. There are also assessments comparing substances within some groups of pharmaceuticals. The database is used by the Swedish Drug and Therapeutics Committees to include environmental aspects when recommending pharmaceuticals for healthcare providers. Website viewing figures show that users primarily look for information on commonly used substances, e.g., diclofenac and paracetamol/acetaminophen. Major problems for the development of the database are lack of data, lack of transparency, and discrepancies in the available environmental information (Ramström et al., 2020).

Policies Interventions at the Prescriber Level

Healthcare Professional Education

The first attempt at medical education on environmental issues with pharmaceuticals in Sweden was undertaken by environmental coordinators in the regional hospitals who arranged seminars and lectures on pharmacology for hospital staff. In 2005, Apoteket/SCC published a book about drugs and the environment to be used in order to increase the knowledge of all stakeholders (Gunnarsson & Wennmalm, 2008).

The Swedish Medical Products Agency is now advocating for the following healthcare education initiatives (Swedish Medical Products Agency, 2020c):

1. Promote the development of guidelines for healthcare professionals on the prudent use of pharmaceuticals posing a risk to or via the environment.
2. Explore, in cooperation with relevant stakeholders, how environmental aspects could become part of medical training and professional development programs.
3. Foster best-practice exchanges between Member States on how environmental considerations are taken into account in the advertising and prescription of medicinal products and the choice of therapy more generally, where appropriate.

Aiding Prescribing Decisions

The pharmaceutical strategy makes it clear that patients will still get the required medication for their treatment when environmental concerns are considered. OECD Pharmaceuticals Residues in Freshwater: Hazards and Policy Responses reports that Sweden has a 'Wise List' of recommended pharmaceuticals for the treatment of common diseases that takes into account environmental impacts when comparing medications that are equally safe and equally suitable for the medical purpose. The Wise List sounds like a suitable solution for reassuring healthcare professionals that they do not have to sacrifice patient care to make more environmentally informed decisions, by giving them an easily accessible platform for this information.

Prescription Adjustments

The Swedish (MPA) is also intending to explore the possibility of reducing waste by optimizing the package size of pharmaceuticals so that medicines can be dispensed in quantities better matching needs, and by safely extending use-by (expiry) dates so that fewer medicines that are still usable have to be thrown away.

Prescription and Usage

From a source control perspective, it is important to understand prescription patterns and usage in Sweden. Even through Canada and Sweden have different demographics and populations, they are both developed and relatively wealthy countries. It is possible that usage patterns could somewhat correlate. The Swedish MPA provided statistics for annual usage in Sweden of the active compounds. The data includes pharmaceuticals sold over the counter as well as prescriptions. Sweden had 10,230,185 inhabitants as of 31 December 2018 (SCB, 2019; TemaNord, 2020).

Table 2 Pharmaceutical usage data in Sweden (TemaNord, 2020)

Active substance	mg/DDD	Millions DDD/ Sweden	kg sold/ year (2018)
Paracetamol	3,000	91	271,670
Lactulose	6,700	34	224,519
Ibuprofen	1,200	62	74,636
Carbamide*		18	17,636
Acetylsalicylic acid	160	96	7,381
Metoprolol	150	54	8,056
Omeprazole	20	162	3,243
Losartan	50	50	2,511
Chlorhexidine*		2	2,021
Furosemide	40	46	1,858
Atorvastatin	20	90	1,793
Enalapril	10	176	1,761
Diclofenac*		2	1,728

* *mg/DDDs not provided, only information about units sold.*
DDD refers to Defined Daily Dose, the assumed average maintenance dose per day for a drug used for its main indication in adults.

Sweden is in the top 5 of EU member states for anti-depressant usage, but the bottom five for cholesterol lowering drugs and antidiabetics. Fitch Solutions Group Limited (2020) forecast that pharmaceutical spending will increase in Sweden. They also predict that demand for prescription medicines in Sweden will grow because of an increasingly progressive attitude towards healthcare and the country's ageing population. An increasingly ageing population means that medicines commonly prescribed to this demographic will be more likely to increase disproportionally compared to other medications that are more predominant in younger age groups.

Wastewater treatment plants

TemaNord (2020) collated influent and effluent loadings from wastewater treatment plants in Sweden, providing information on treatment efficiencies of common pharmaceuticals during wastewater treatment. It is important to note that these loadings are not directly comparable to concentration data as presented in the results section, as pharmaceutical consumptions, interventions and wastewater treatment varies heavily between jurisdictions.

Table 3 Influent and effluent loadings of the most used pharmaceuticals in Sweden 2018 as kg/year (TemaNord, 2020)

Pharmaceutical	Chemical Biological (97%)		Untreated (3%)	Total	% of distributed parent pharmaceutical released from WWTP
	Influent	Effluent	Effluent	Effluent	
Sodium fluoride	70	70	2	72	76%
Omeprazol	31	31	1	32	1%
Acetylsalicylic acid	149	15	5	20	0.1%
Furosemide	1,009	1,009	31	1,041	56%
Metoprolol	234	117	7	124	2%
Amlodipine	37	19	1	20	3%
Losartan	97	49	3	52	2%
Candesartan	105	94	3	98	23%
Simvastatin	11	1	0	1	0.1%
Atorvastatin	35	17	1	18	1%
Levothyroxine sodium	0	0	0	0	0%
Diclofenac	17	15	1	16	1%
Ibuprofen	3,620	362	112	474	1%
Paracetamol	5,270	527	163	690	0.3%

Table 4 summarizes the three most common drugs found in influent or in effluent from this study. It is interesting to note the discrepancies here between the three factors, because they can help understand entry pathways. For example, as ibuprofen has high usage but is also heavily metabolized in the body, meaning that it may be less prominent in influent. As paracetamol has for a while been recognized as a key pollutant there are likely technologies already in place to remove it. The others in effluent either will not have treatment technologies designed for their adequate removal, or will be formed in wastewater as metabolites or transformation products.

Table 4 Three most prevalent drugs found in wastewater influent and effluent in Sweden

Usage	Influent WWTP	Effluent WWTP
Paracetamol, lactulose, ibuprofen	Lactulose, carbamide, paracetamol	Lactulose, carbamide, chlorhexidine

In 2014, Sweden undertook a 3-year project to evaluate Swedish WWTPs for their ability to remove various micropollutants and their environmental, economic and future sustainability (Baresel et al., 2019). The project reviewed contaminants detected in WWTP effluent and available technologies for their removal. This resulted in a list of micropollutants to be considered, their effects on recipients, sampling analyses strategies, selection of treatment technologies, cost-effectiveness and combinations to be further investigated. A simplified version of results from Baresel et al. (2019) is reproduced in Table 5. It is worth noting that these are all advanced tertiary technologies that come with considerable cost and time trade-offs.

Table 5 Technologies capable of removing pharmaceuticals and other properties

	OZONATION	BIOFILTER WITH GRANULATED ACTIVATED CARBON (GAC)	POWDERED ACTIVATED CARBON AND ULTRAFILTRATION	OZONATION WITH BIOFILTER WITH GAC	ULTRAFILTRATION & BIOFILTER WITH GAC
Pharmaceuticals	Good	Good	Good	Good	Good
Antibiotic Resistance	Moderate	Moderate	Good	Moderate	Good
Estrogenic Effects	Good	No Removal	No Removal	Good	No Removal

Environmental Prevalence

Although the pharmaceuticals can enter the environment through pathways other than wastewater, environmental prevalence can provide important insights for identifying persistent chemicals. For instance, some chemicals can leave wastewater at relatively low concentrations but are concerning pollutants because of their high environmental persistence. Environmental prevalence in Sweden can also be a good indicator of what environmental concentrations can be expected when there are policies in place to prevent pharmaceuticals from entering the environment.

A study was undertaken to investigate the concentrations of organic micropollutants in Sweden’s largest drinking water reservoir (Rehrl et al., 2020). These are likely compounds that have very high prevalence in wastewater effluent and/or high environmental persistence. It is important to note that compounds in effluent at the highest concentrations are not necessarily the same compounds that persist and cause the most issues in the environment.

Table 6 Concentrations of organic pollutants in Sweden's largest drinking water reservoir in ng/l (Rehrl et al., 2020)

POLLUTANT	AVERAGE	MINIMUM	MAXIMUM
3-(4-Methylbenzylidene)camphor	3.3	2.1	6.8
Diclofenac	2	1.6	3
Fluoxetine	1.4	0.77	4
Furosemide	1.2	0.95	1.8
Tolyltriazole	0.98	0.81	1.6
Caffeine	0.8	0.65	1.6
Valsartan	0.69	0.5	1.2
Daidzein	0.49	0.37	1
Methylparaben	0.31	0.23	0.47
Sulisobenzone	0.3	0.25	0.49

Seasonal variations were also observed. This is suspected to be a combination of lower degradation in winter, UV light affecting pharmaceutical breakdown and seasonal variations in prescription. This is very important to bear in mind when interpreting sampling results.

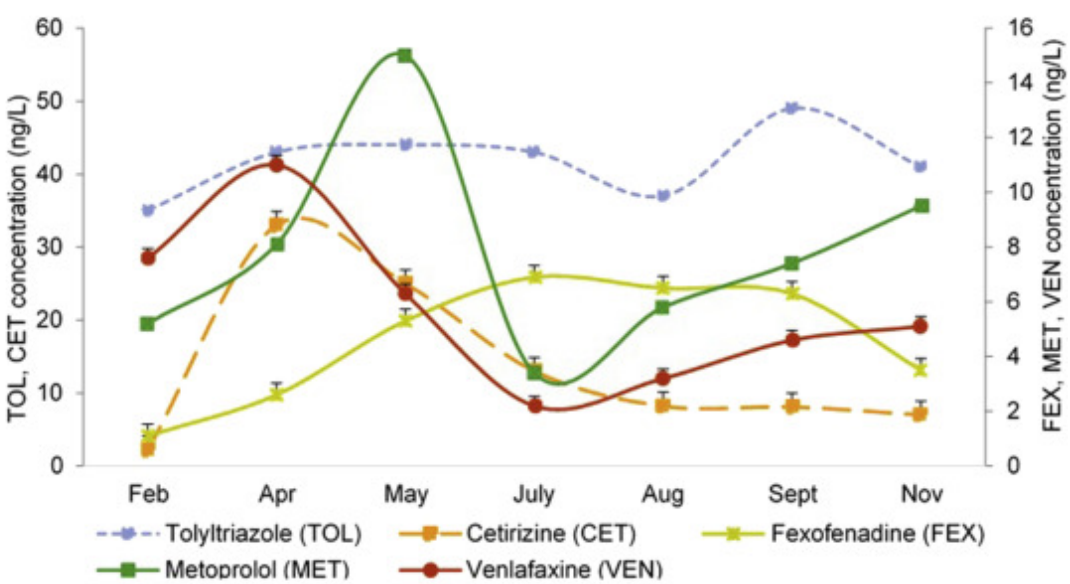


Figure 7 Seasonal variations of pharmaceutical compounds in the environment (Rehrl et al., 2020)

3.2 King County

Drug Take Back Program

In 2013, the King County Board of Health passed a Rule and Regulation to create permanent drug-take back programming for King County residents. This was funded by manufacturers and mandated by local health ordinances. In 2018 the secure Drug Take-Back Act came into law in Washington, which requires medicine manufacturers to create, fund, and operate a convenient state-wide collection and disposal program for unused medicines. The Hazardous Waste Management Program oversees the program to ensure regulatory compliance and safety.

MED-Project (Medication, Education and Disposal) is the approved stewardship plan operating in King County on behalf of the drug companies it represents. King County's program launched in 2017. This program appears not to be mandatory for pharmacies as there is an option for pharmacies and hospitals to sign up for a safe deposit box on the website.

Operation

120 Secure Medicine Return drop-boxes are located throughout King County at participating pharmacies, hospitals and law enforcement offices. There is no cost to residents to use this service. There is a search tool where customers can type in their address or look on the map to find their nearest location. There is also a no cost mail-back service for 'residents that are homebound or have limited mobility.' This includes inhalers and injectors.

Figure 8 Secure Disposal Box in King County

Substances accepted are Medicines sold in any form, both prescription and non-prescription, controlled substances and pet medicines. Substances not accepted include Herbal remedies, Vitamins, illicit drugs, personal care products, medical devices and iodine containing products. 44,780 pounds of medicines were collected in 2019 (Hazardous Waste Management Program, 2019).

Promotion and Messaging

King County departments and partners developed the "Don't Hang on to Meds" campaign, which featured real-world stories on how secure medicine storage and disposal saves lives by preventing inappropriate access to medicines in the home. This provides multiple infographics to use as well as a video. Importantly, these infographics are targeted at different groups. They also highlight the social risks of keeping drugs round the house rather than the environmental ones. For example, a campaign video stresses that returning medications can help prevent suicides.

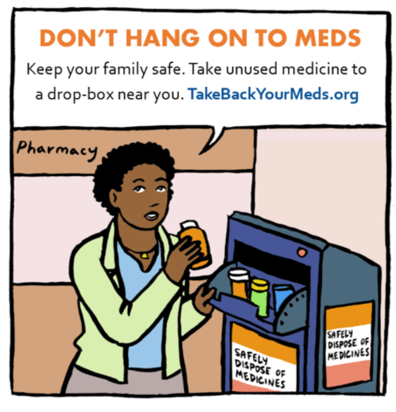


Figure 9 Promotional material for the drug take back program in King County

Tag lines used in infographics include:

1. Get unused medicine out of the home, keep your family safe.
2. Kids and pets can get into them, even with child resistant lids.
3. Someone might take pills without you knowing
4. Medicine can look like candy and bottles aren't always childproof
5. Getting rid of unused medicines is free and easy
6. Over 100 drop boxes in King County

The messaging appears to target caregivers by highlighting the social dangers of keeping medications and convince people how easy it is to return them. The infographics all direct people to the website MedicineReturn.org. Importantly, the messaging also tells people to return the drugs to a drop box instead of telling them not to dispose of them down the toilet.

Patient Education

King County are also attempting to educate residents on medication storage and disposal with the messaging of 'Keep those you love safe from accidental poisoning and overdose.' They make the following recommendations on their website:

1. Pick a storage place children cannot reach.
2. Put medicines away after each use.
3. Make sure the safety cap is locked.
4. Teach children about medicine safety.
5. Safely dispose of the medicines you no longer need.

Take Back Events

National Prescription Take Back Day is on the 24th October. Public Health Insider reports that past national drug take back events have been popular to raise awareness and promote action about medicine safety. In the fall of 2019, households across the country disposed of 882,919 pounds (over 441.5 tons) of unused and expired medication at DEA take back day events during a single day. Washington State residents dropped off 15,624 pounds (Public Health Insider, 2020).

Prescription Trends

Washington State releases prescription data on an open-source platform (Washington State Department of Health, 2021). This includes the number of prescriptions by drug class over time. Prescription numbers can also be found for specific drugs by year. This data base is collated and open access to reduce incidences of drug misuse. This data could be used to calculate PEC. BC Pharmanet provides similar data to this that may allow identification of prescriptions trends and provide prescriptions figures to calculate PEC.

Wastewater Management

Policy

King County is currently developing its Clean Water Plan to improve the resilience of their wastewater systems and ensure that the best outcomes for human health, habitat and wildlife are achieved. The following decision areas with relevance to pharmaceutical pollutants are:

1. Preventing pollution at the source
2. Preventing pollution from historical activities
3. Managing stormwater and combined sewer overflows.

In 2020, King County conducted scoping of options that could address the above issues. These options were developed with community-participatory input and were reviewed by relevant stakeholders, including local government. In 2021, actions are grouped into wider strategies which again incorporate input from community stakeholders. The strategies are then available for public comment. Importantly, water quality was raised as a key stakeholder priority indicating that people are being increasingly aware of water quality and pollution. The plan also incorporates equity concerns and is translated into multiple languages to allow for greater accessibility. King County are conducting multiple wastewater improvement initiatives.

3.3. Switzerland

Wastewater Management

Upgrading Wastewater Treatment

At the start of 2016, new regulations came into effect in Switzerland requiring roughly one hundred of the country's municipal WWTPs to be upgraded over the next 20 years to remove micropollutants, such as pharmaceuticals. This required the implementation of advanced treatment technologies including ozone based Advanced Oxidation Process after tertiary treatment is completed, with the aim of achieving an overall reduction of 80% in the micropollutants discharged (Eggen et al., 2014).

Public support appears to have enabled this policy, with the average willingness to pay per household being found to be CHF 100 (US$ 73) annually for reducing the potential environmental risk of micropollutants to a low level (Logar et al., 2014).

Monitoring

The Swiss micropollutants strategy establishes a set of indicator compounds by which to monitor micropollutants. The 12 compounds were selected for their low biodegradability and resistance to removal in conventional wastewater treatment. The indicator selected compounds are easy to analyze, so that they can be detected regularly and compared with influents and effluents in treatment plants. With this monitoring strategy it also easier to regularly test the effectiveness of interventions, including new wastewater technologies and policies. The aim of the Swiss regulations is to achieve 80% removal across the plant as a whole. The regulation focuses on dissolved compounds. Accordingly, indicator compounds involve compounds that have not yet been substantially degraded at the biological treatment stage. The 12 pharmaceutical indicator compounds can be assessed in a single laboratory test, using a combination of high-performance liquid chromatography and tandem mass spectrometry offering a relatively efficient and cost-effective monitoring option (Bourgin et al., 2018; Eggen et al., 2014). Research also exists to help design schemes for monitoring the most relevant pharmaceuticals in hospital effluents based on predicted concentrations and environmental toxicity data (Daouk et al., 2015).

Drug Take Back Program

Pharmaceutical waste can be returned to community pharmacies or designated disposal points. It is estimated that 237 tonnes/million capita in Switzerland is returned, making it the country with the highest return rate in Europe.

3.4 Drug Take Back Program in the Metro Vancouver Region

In BC, including Metro Vancouver, the drug take back program is managed by the Health Products Stewardship Association, the national producer-funded product stewardship association for pharmaceuticals, sharps and other health products for several provinces across Canada. HPSA were interviewed to understand more about the program operation.

In BC, the provincial Recycling Regulation requires producers of pharmaceuticals to manage their waste and prevent it from entering solid or liquid waste disposal systems. Across Canada, in provinces with similar regulations, pharmaceutical producers have coordinated their take back programs by creating the not-for-profit Health Products Stewardship Association (HPSA) – it is producer funded instead of government funded.

Metro Vancouver runs the Unflushables campaign, which communicates what items should not be flushed down the toilet. There is a poster specifically for pills and a video for medications. Metro Vancouver promote the campaign primarily on social media. Separately, HPSA has their own promotional materials, which pharmacists can request to display in their pharmacy. These include posters that convince people not to throw out their medications in bins or toilets, but instead return them to pharmacies for correct disposal.

Figure 10 Promotional materials for drug take back programs. Left and center HPSA, right Metro Vancouver

4. Research Methodology

The research methodology consisted of the data analysis of the monitoring data from Metro Vancouver and interviews with pharmacists, HPSA and prescribers. The data analysis was undertaken to provide an initial assessment of the pharmaceutical concentrations entering wastewater, to estimate removal efficiencies of pharmaceuticals in wastewater and to identify what type of pharmaceuticals were entering wastewater. These data insights were used to inform future recommendations in monitoring and prevention strategies. The interviews were used to understand how the drug take back program operated within Metro Vancouver. The interviews focused on the program operation, including potential limitations and improvement. These were also used to identify how successful policies identified in the jurisdictional scan could be applied to Metro Vancouver.

4.1 Data analysis of wastewater data

The data was collected by Metro Vancouver as part of their monitoring programs and provides concentrations of various pharmaceuticals and metabolites obtained from the following locations shown in Figure 11:

1. Iona WWTP (2018, 2019)
2. Northwest Langley WWTP (2017, 2018)
3. Jervis Pump Station (2019)
4. A maintenance hole located on North Arm Interceptor, MacDonald Street Section (2019)
5. Harbour Pump Station (2019)

For locations 3-5 sampling took place on 4 dates within an 11-day period in July. The influent and effluent samples from Northwest Langley in 2017 were taken on 5 sampling days between the 18th June – 8th July. The influent and effluent samples from Northwest Langley in 2018 were taken on 5 sampling days between 12 November-2nd December. The influent and effluent samples from Iona in 2019 were taken on 5 sampling days between the 16-29th July. It is expected that sampled concentrations will vary by day, which is why averages, maximum and minimums were used for the analysis. It is also important to consider that there may be slight seasonal variations in the concentrations of pharmaceuticals, but this data would be insufficient to confirm if this is the case.

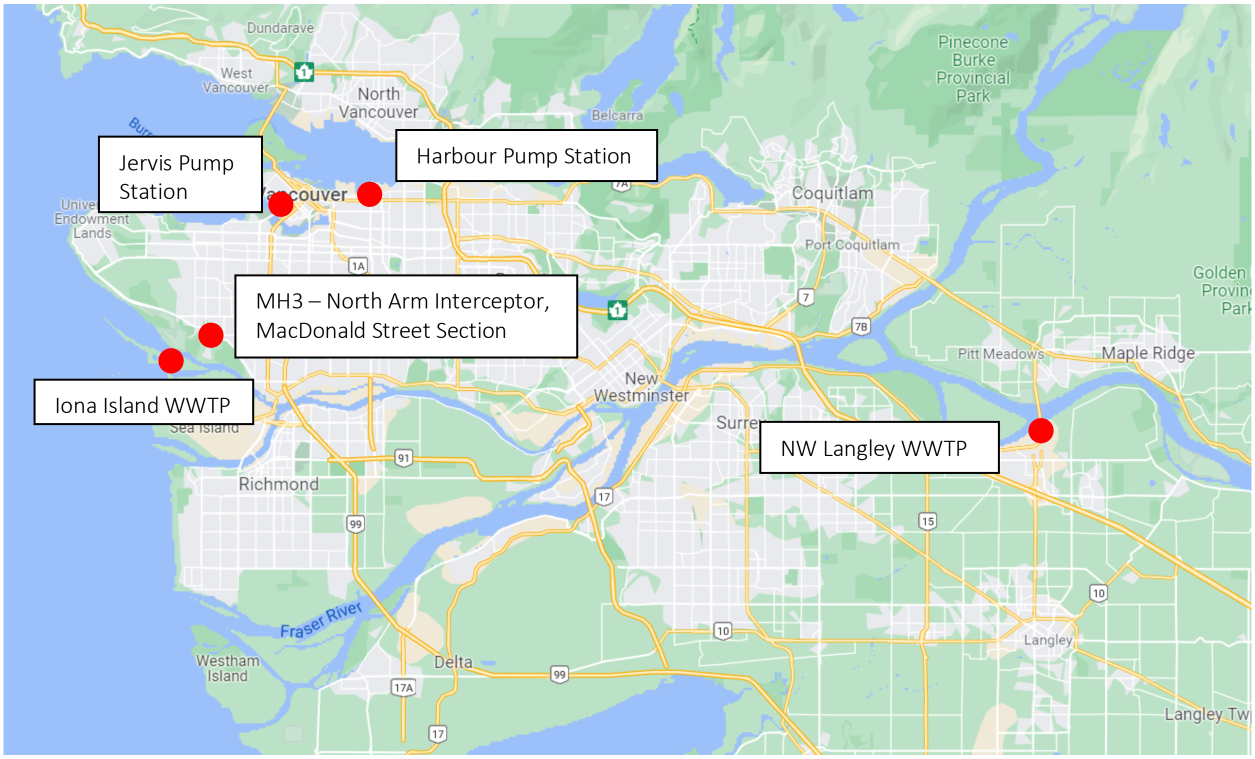


Figure 11 Sampling Locations

For the two WWTPs, multiple influent and effluent concentrations were recorded for each compound. Due to the large volume of data and significant time limitations this analysis was treated as a first step exploratory study identifying any initial inferences, trends and insights from the data that could be investigated further. Therefore, the data was also organized to be a reference spreadsheet to enable concentration monitoring data to be looked up quickly and easily in the future. Concentrations (MECs) can be compared to the predicted environmental concentrations calculated from prescription and usage data to identify any discrepancies, which could indicate that another pathway in addition to consumption significantly contributes to the wastewater value. Both MEC and PEC can also be compared to the Predicted No Effect Concentration (PNEC) values to identify the likelihood of environmental risk. This is also useful as are very few regulations for pharmaceutical substances within aquatic receiving environments (water, sediment, biota). In absence of regulatory information, other metrics (such PEC and PNEC comparison) may be used to help inform decision-making on pharmaceuticals and other compounds of environmental concern.

Inferences were made to attempt to understand the significance of the data. Primarily, this was done by putting the data in context, informed by insights from the literature reviews and interviews. However, it is important to note that there are significant limitations when drawing inferences from this data, which will be acknowledged and discussed.

4.2. HPSA Interviews

Two HPSA representatives participated in a one-hour semi-structured interview where they answered questions about the program operation, promotion, and assessment metrics within Metro Vancouver. These questions and responses went on to inform the pharmacist questions.

4.3. Phone Survey

The original plan was to get 2-3 pharmacist interviews lasting 30 minutes through a combination of cold calling and pharmacists referred to Metro Vancouver through HPSA. However, it was found that the cold calling approach was ineffective because pharmacists stated that they were too busy to give half-hour interviews during working hours. The methodology for cold calling instead changed to a 5-minute short phone survey with key questions. These were designed to supplement the longer interviews conducted and to investigate if any insights were shared between multiple pharmacies.

Pharmacies in the Metro Vancouver area were cold called and asked if they would be willing to answer a few questions about how the drug take back program operated in their pharmacy. Three pharmacists agreed to answer questions. Names of pharmacies were recorded, but the names of respondents were not.

4.4. Pharmacist Interviews

HPSA arranged contact with two pharmacists. These interviews lasted approximately 30 minutes. A base list of questions was asked, with the freedom to allow for follow up questions if required.

4.5. Prescriber Interviews

Due to difficulties in finding prescribers for interviews, only two were contacted and were only able to give a brief statement on the extent to which they considered the environmental impact of drugs when prescribing. Longer form prescriber interviews would be beneficial for a future investigation.

5. Findings

5.1 Pharmaceuticals in Metro Vancouver Wastewater

5.1.1. Pharmaceuticals Entering Wastewater Influent

Average Concentrations

The average concentration of pharmaceuticals entering Northwest Langley WWTP in 2017 and 2018 and Iona WWTP in 2019 are shown in Figure 12. The 10 pharmaceuticals with highest measured concentrations are shown in the graph. The 10 most prevalent pharmaceuticals are not the same as the pharmaceuticals reviewed in 3.1.2, notably because these were selected for analysis based on literature suggesting that they were highly prevalent and high risk, and the prevalence of pharmaceuticals will vary between jurisdictions.

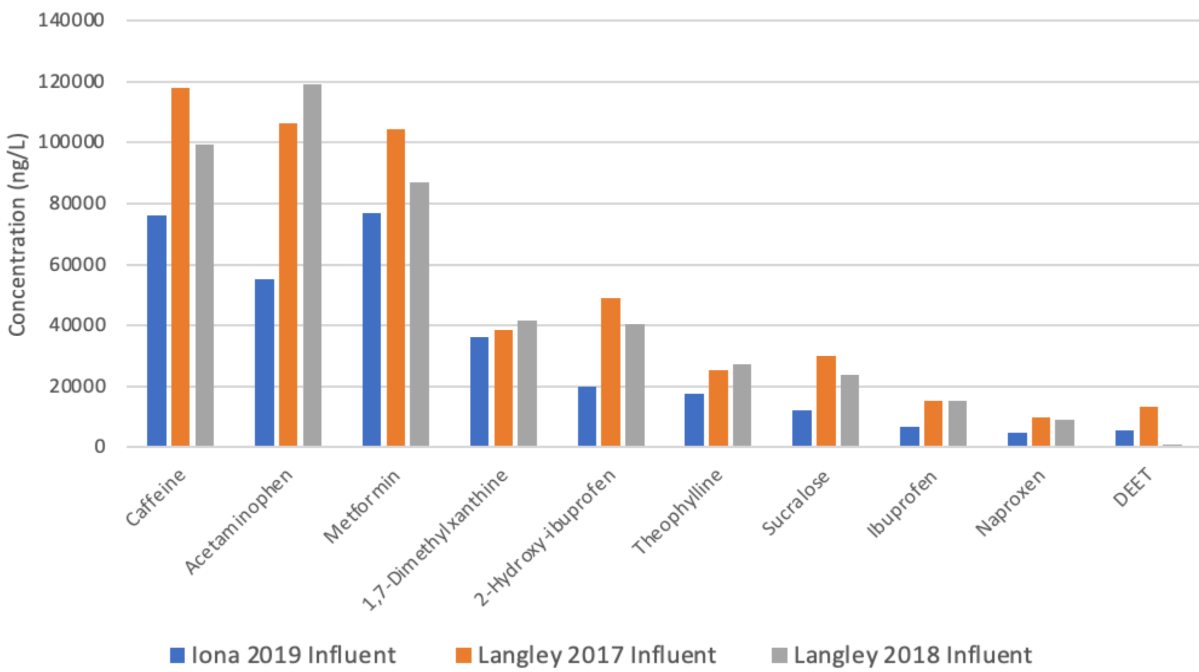


Figure 12 Average Influent Concentrations of Pharmaceuticals at two Metro Vancouver WWTPs

Iona WWTP has lower influent concentrations for the most prevalent compounds likely because it receives wastewater from a combined sewer system and, therefore, concentrations of compounds are diluted by large volumes of stormwater. The two years of data from the small catchment served by the Northwest Langley WWTP show roughly similar concentrations between the two datasets. It is important to understand what factors can affect influent concentration both to identify reasons for different influent concentrations between WWTPs and different compounds including differences in the collection network (e.g., combined versus separated systems) and different entry pathways. It should be noted that the analysis is only limited to the two years of data from two of the five wastewater treatment plants in the Metro Vancouver region and does not provide a full picture of pharmaceuticals in Metro Vancouver wastewater.

Below are listed the different entry pathways of pharmaceuticals into wastewater influent, and the factors that can affect the proportion that each entry pathway contributes to the final influent concentration, and how high that concentration will be.

1. Human Consumption: prescription rate, prescription dose, sales rate, usage rate metabolism, local manufacturing
2. Veterinary Consumption: prescription rate, sales rate, usage rate, metabolism, surface runoff (farm-land use)
3. Incorrect Disposal: adherence, awareness of correct disposal, disposal method (flushing or bin)
4. Local Manufacturing: distance from sampling site, type and volume of chemicals manufactured
5. Hospital effluent: distance from sampling site, number of patients treated, effluent treatment technologies, disposal practices.

Even though the limitations in the dataset mean that there is not a conclusive way to identify either of the above, certain factors can be investigated to aid the pathway characterization.

Human Consumption

1. Prescription or sales data, and any discrepancies between PEC and MEC

If a drug is highly prescribed, or highly sold, then it is likely to be in influent concentrations at a high concentration. The PEC can be calculated based on prescription or sales data and compared to the MEC to identify discrepancies, which could be due to incorrect disposal, seasonal trends or local manufacturing.

2. Amount of metabolized drug compared to parent drug in influent

If a drug is consumed a proportion of it will be metabolized, so if a drug metabolite is present in influent consumption usage and excretion will be contributing pathway. If a metabolite is present at high or comparable levels to the parent compound then the parent compound is either highly metabolized or incorrect disposal pathways may only be a minor contributing entry pathway.

3. Prescribed dose

If the compound is prescribed at a high dose, it may well appear in influent at a high concentration even if the prescription rate is lower.

4. Population density and stormwater

Higher population density can mean that there are more drugs being consumed, excreted and/or incorrectly disposed of. However, other impacts such as the contribution of stormwater in combined sewer systems and industrial sources of pharmaceuticals may outweigh population density effects.

5. Seasonal Trends

Uses of different pharmaceuticals may fluctuate in different seasons. For example, if samples are taken summer months DEET usage will potentially be higher and medication usage for coughs and colds is potentially lower.

Veterinary Consumption

1. If veterinary specific drugs are found in influent, then this is a contributing entry pathway. This was the case with the Metro Vancouver dataset, which will be discussed later.

Incorrect Disposal

1. Awareness of correct disposal

Although this will be discussed in detail later in the report, the pharmacists interviewed raised that they were more likely to talk about drug disposal to patients that were switching or ending a prescription. Therefore, medications that are more likely to be switched or ended, potentially those with bad side effects, low adherence, or medications for chronic conditions could be more likely to be handed in. Over the counter drugs could be less likely to be disposed of correctly because the pharmacists said that they didn’t usually speak about the drug take back program to patients buying over the counter medications.

2. Adherence

Prescription drugs with lower reported adherence will be more likely to be incorrectly disposed of, and therefore incorrect disposal may be a more significant contribution to their influent pathway than drugs with generally higher adherence.

Local Manufacturing and Pharmaceuticals Usage

1. Local Manufacturing

A scan for the presence of local chemicals manufacturing can identify if any pharmaceuticals can potentially enter influent through discharge from these plants. This was undertaken in Metro Vancouver, and none was found.

2. Industry Disposal

It was beyond the scope of this project to investigate the disposal of pharmaceuticals in industry (research, veterinary surgery disposal, farming.)

Hospital effluent

1. Patient Use

If a hospital is upstream of a WWTP this will likely mean a higher concentration of pharmaceutical drugs entering influent due to patient usage.

2. Disposal

Hospitals must dispose of their unused and expired pharmaceuticals. It is beyond the scope of this report to investigate how this is done in Metro Vancouver hospitals. Metro Vancouver has also implemented a bylaw that restricts the discharge of unused pharmaceutical from hospitals.

Types of Pharmaceuticals in Influent

Each drug found in either of the WWTPs was ranked based on measured concentration to investigate whether certain classes of drugs were more prevalent in wastewater. Proportional concentration refers to the summed average concentrations of each class of drugs taken as a proportion of the total. The number is the different type of drug classes present in influent. This is to demonstrate that the highest concentration class of drugs may not be the same as the drug types with the highest number.

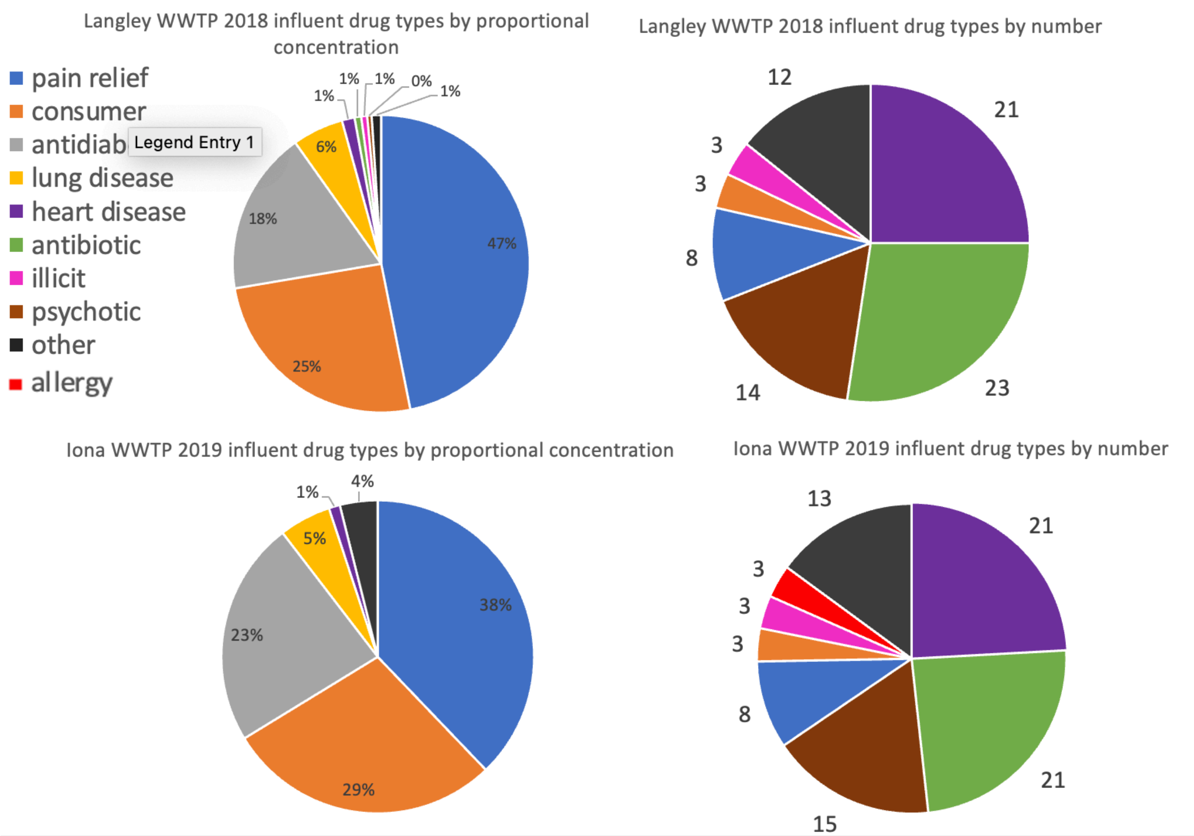


Figure 13 Influent drug types by number and concentration (Metro Vancouver, 2019)

Eight pain relief drugs (including acetaminophen and ibuprofen) made up a high proportion of the influent concentrations in both plants which was closely followed by consumer products (caffeine, DEET, sucralose), and the singular anti-diabetic metformin. By number, the highest number of drug types found in wastewater were those used for heart disease, closely followed by antibiotics and psychotics. However, these drugs appeared at lower concentrations so even combined were not at a significantly higher proportion by concentration.

The presence of certain drugs points to pathways beyond human consumption and improper disposal. Trenbolone, a steroid used on livestock to increase muscle growth and appetite was found in Langley 2018 influent, indicating that the use of this drug in farmland is significant enough for it to enter wastewater presumably through surface runoff. The presence of drugs only expected to be from hospital effluent is also contributing to wastewater influents. In Northwest Langley WWTP samples from 2018, iopamidol (x ray contrast agent), Diatrizoic acid (radiographic contrast agent), and tamoxifen (cancer chemotherapy) were all detected in influent. In Iona WWTP samples from 2019, iopamidol and diatrizoic acid were present in influent.

Antibiotic Drugs in Influent

Antibiotic drugs in influent were investigated further, due to the evidence that they can cause significant problems in wastewater and that it is preferential that they do not enter WWTPs at all. Both Northwest Langley and Iona WWTP data had measurable concentrations of antibiotics in their wastewater influent, which is concerning as it was noted in the literature that even small concentrations are sufficient to give rise to antibiotic resistance.

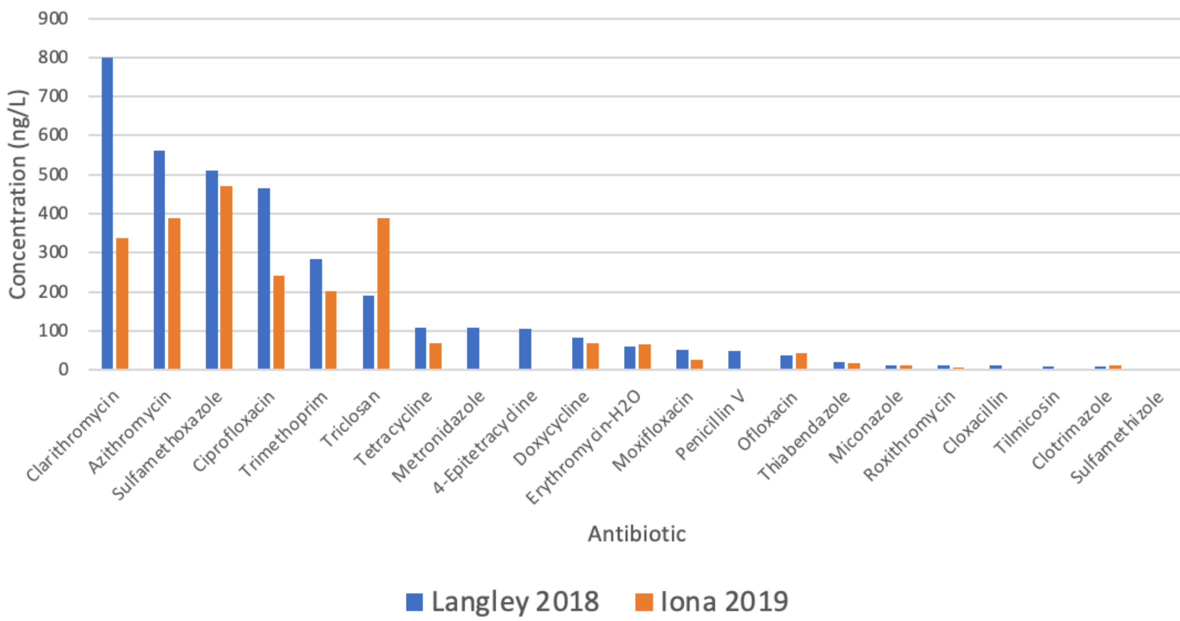


Figure 14 Antibiotic influent concentrations (Metro Vancouver 2018, 2019)

5.1.2. Influent and Effluent Comparison

Reasons for Difference in Influent and Effluent Concentrations

Concentrations were sampled from the influent and effluent of Iona and Langley WWTPs. For each WWTP the influent and effluent concentrations for each compound was averaged, and the minimum and maximum sampled concentration recorded to give a range, as the sampled concentrations varied significantly. For some compounds, a concentration of 0 was recorded on some repeats presumably due to the sampled concentration being under the limit of detection. This calculation method differs from Metro Vancouver's convention of using the detection limit value or ½ detection limit. The averages and maximum and minimums were therefore only calculated from the measured values. (e.g. if the sampled readings were 0, 4, 0, 3) the minimum was taken as 3, the average as 3.5 and the maximum as 4.) It is important to consider what changes between the influent and effluent concentration can mean. For different compounds, certain scenarios were observed:

1. The effluent concentration was lower than the influent concentration
2. The influent and effluent concentration were very similar
3. The effluent concentration was higher than the influent concentration

In scenario 1, it can be assumed that the compound is being transformed or removed during wastewater treatment. The current data is not sufficient to identify specific removal processes. Further investigations are recommended to identify treatment mechanisms and why treatment is effective on certain pharmaceuticals more than others.

In scenarios 2 and 3, it can be assumed that the compound is not being removed from the influent during treatment. The below reasons are hypothesized to contribute to this:

a) The wastewater treatment technologies are not capable of removing this compound. Further insights may be gained by comparing the technologies in use in Iona and Langley WWTPs to literature on these technologies and their removal efficiencies for the investigated compounds. Comparison to structurally similar compounds may be used if published information on the exact compounds cannot be found.
b) The compound may be partially removed, but at the same time more of the compound is being made through metabolism or transformation processes of other compounds.
c) There are variations in the recorded sample concentrations which could be due to variations in flow rate, removal efficiencies and influent concentrations because of usage trends, temperature and sunlight. Sunlight is particularly important as UV radiation acts to break down certain compounds.

Comparison of influent and effluent concentrations

The graphs below show the influent and effluent concentrations for the compounds with the highest prevalence in influent at Langley WWTP in 2017 and 2018. The error bars refer to the minimum and maximum concentrations for influent and effluent respectively. This shows that the concentrations did vary quite heavily.

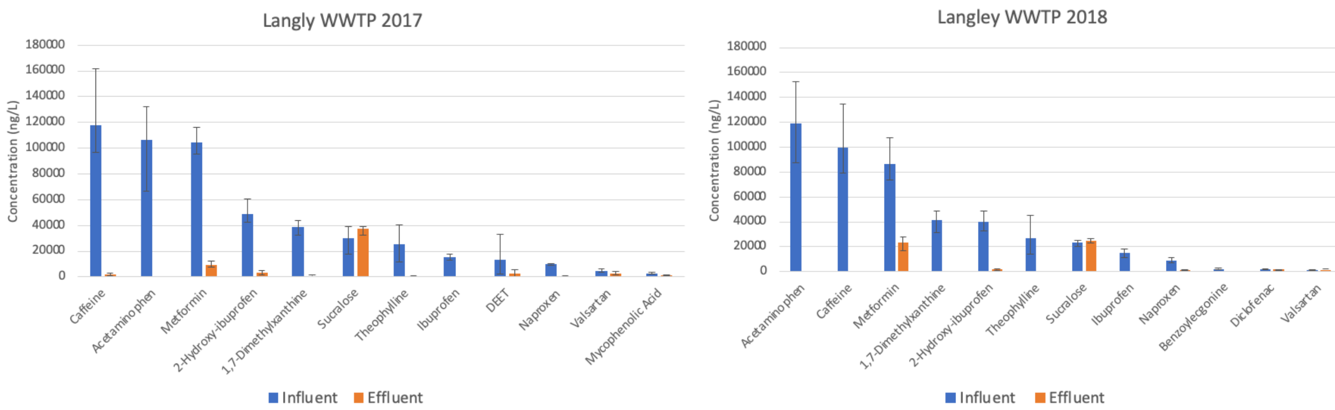


Figure 15 Average concentrations of the most prevalent compounds found in influent and effluent samples at Northwest Langley WWTP. Error bars refer to the minimum and maximum concentrations.

The Northwest Langley WWTP treats the waste of approximately 30,000 people in northwest Langley and is a secondary treatment facility. Northwest Langley WWTP appears to be partially removing many of the compounds at high influent concentrations. However, the reduction in ethe ffluent concentration of metformin could be due to its conversion to its metabolite granlyurea which was not sampled for.

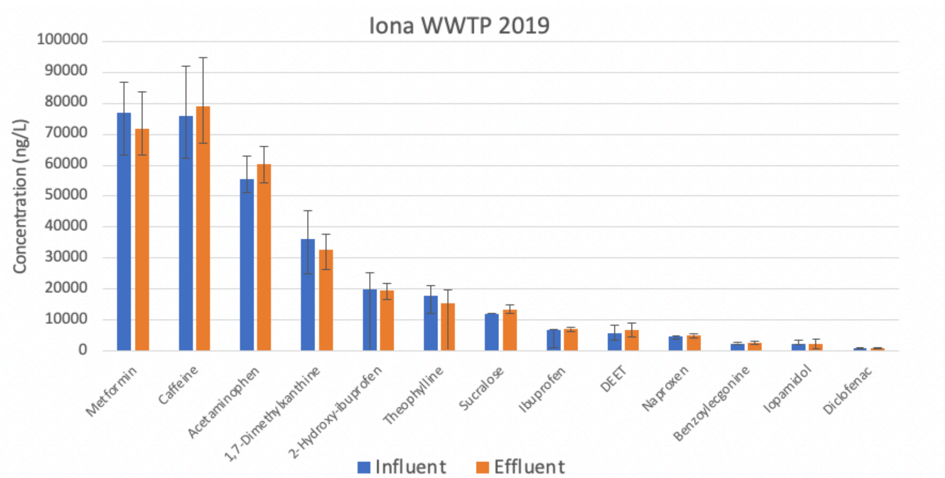
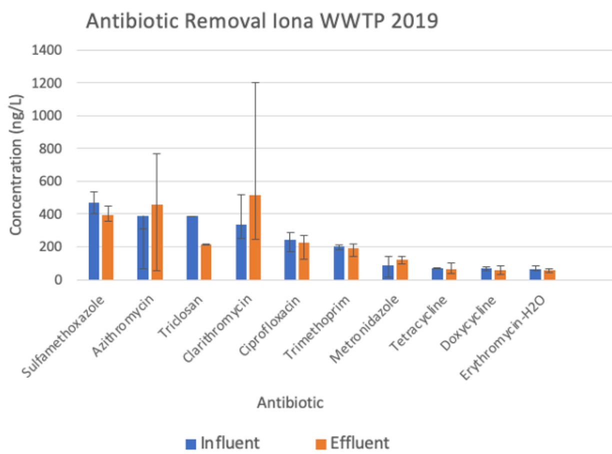


Figure 16 Average concentrations of the most prevalent compounds found in influent and effluent samples at Iona WWTP. Error bars refer to the minimum and maximum concentrations.

Iona WWTP is a primary treatment facility that treats the wastewater of 600,000 residents in Vancouver, the UBC Endowment Lands and parts of Burnaby and Richmond. It treated about 200 billion liters of wastewater in 2020 (Metro Vancouver, 2020). In Iona WWTP samples, there is either an increase or no significant change between the influent and effluent concentrations, which may suggest that secondary treatment is significantly better at removing compounds. Of the most prevalent compounds, there are no major differences between compounds removal efficiencies.

Influent and Effluent for Antibiotics

The wastewater removal efficiency was also investigated for antibiotics. Looking at the wastewater removal efficiency, antibiotics were not significantly removed at Iona WWTP, a primary treatment plant or Northwest Langley WWTP, a secondary treatment plant, however Langley had slightly better removal rates indicating that secondary treatment is slightly more effective at removing antibiotics.



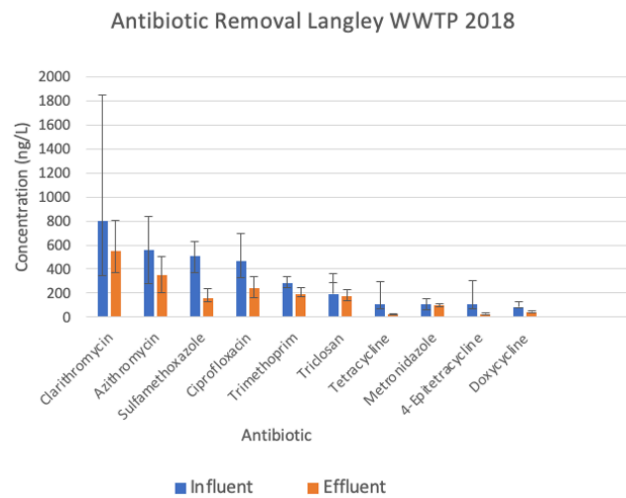


Figure 17 Average concentrations of antibiotics found in influent and effluent samples at Iona and Northwest Langley WWTPs. Error bars refer to the minimum and maximum concentrations.

5.1.3. Comparison of Metro Vancouver Concentration to Literature Values

To understand the significance of these concentration values it is important to put them in context to recorded concentrations elsewhere. Langley and Iona will have different effluent concentrations as Langley is secondary treatment and Iona is primary. It was challenging to find Canadian specific data for the effluent concentrations. However, the paper from Rogowska et al. (2020) records the highest ever recorded effluent concentration for a range for compounds from WWTPs in Europe and Africa. It should be noted that there may be significant differences in pharmaceutical prescription/consumption behaviors, influent concentrations, wastewater treatment technologies, and regulations between these regions and Metro Vancouver. Any comparison of effluent concentrations should take this into consideration.

Table 7 Comparison of Metro Vancouver effluent concentration values to maximum literature values

COMPOUND	MAXIMUM EFFLUENT CONCENTRATION 2019		MAXIMUM LITERATURE WWTP EFFLUENT CONCENTRATION (UG/L) (LOCATION)	REFERENCE
	Langley	Iona		
Caffeine	0.188	94.6	11.45 (Sweden)	(Gros et al., 2017)
Metformin	27.9	83.6	10.35	(Rogowska et al., 2020)
Granylurea	-	-	1.86 (Southern Germany)	(Trautwein & Kümmerer, 2011)
Acetaminophen	0.0351	65.9	11.73 (South-West England)	(Petrie et al., 2017)
Ibuprofen	0.445	7.8	9.20 (Sweden)	(Gros et al., 2017)
Valsartan	2.23	0.979	28.22 (Dresden, Germany)	(Gurke et al., 2015)
Naproxen	1.3	5.77	14.40 (KwaZulu-Natal Province, South Africa)	(Madikizela & Chimuka, 2017)
Theophylline	0.074 (minimum LoD)	19.8	3.17 (South-West England)	(Petrie et al., 2017)
Diclofenac	1.95	1.28	23.50 (KwaZulu-Natal Province, South Africa)	(Madikizela & Chimuka, 2017)
Carbamazepine	0.439	0.347	4.61 (Duisburg-Vierlinden, Germany)	(Deeb et al., 2017)

5.1.4. Collection System Samples Comparison

The most prevalent pharmaceuticals detected in collection system samples are shown in Figure 18.

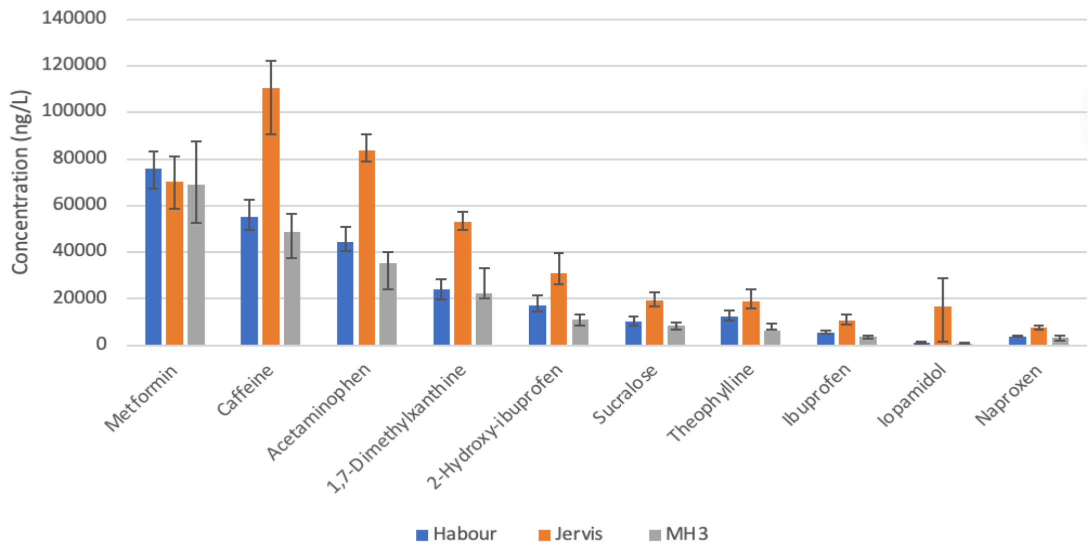


Figure 18 Average concentrations of antibiotics found in collection system samples. Error bars refer to the minimum and maximum concentrations.

Various steps were made to find possible explanations for the discrepancies between the different concentrations between the collection system sampling points:

1. Pharmaceutical manufacturing.

No significant chemical manufacturing was found in the postcode areas where the samples sites were located.

2. Population density.

The area around Jervis has a higher population density, suggesting that this could be an explanation for the higher concentrations recorded here.

3. Demographic.

As the elderly tend to have higher medication usage, the census data was used to compare the population age distributions in the areas served by the two WWTPs. However, this was inconclusive as there was no significant difference in age distribution and the census data covered different areas to those served by the WWTPs.

4. Land Use

Although this was not systematically investigated, it is possible that land use could be a determinant. Jervis is downtown and in a more urban location, meaning potentially more industrial land use.

5.2. HPSA Interviews

Operation

BC enforces compliance with extended producer responsibility for pharmaceuticals. For pharmaceutical producers to comply with EPR regulations, they must either join HPSA or set up their own take back program. HPSA's 150+ members jointly fund the drug take back program. However, HPSA will take back any medication regardless of whether the brand owner is a member. Medication packaging is not collected as part of the program, and due to its classification as health products also appears not to be covered under the BC packaging recycling regulations either. (Province of British Columbia, 2020) Customers are therefore instructed to return pills separate from their packaging in plastic bags.

Pharmacy participation is both free and voluntary. It is also free for consumers to dispose of their drugs. Pharmacies are chosen as take-back locations because they provide a safe and secure area to store medications and are not public spaces. It is also free for consumers to dispose of their drugs. Approximately 90% of retail pharmacies in BC are part of the program. HPSA also undertook a geoanalysis where the population of BC was over the HPSA network. This indicated that there was 99.2% coverage whereby a member of the public could access a take back location within 15km for an urban area or 30km for a rural area.

99.5% of collection sites are pharmacies. Drug take back events have been run in the past, but not during the Covid-19 pandemic. The locations for these were either police or fire stations to ensure there were appropriate safeguards for the medication waste container. Nurses have also reached out to HPSA to return drugs found at patients houses on home visits. Although HPSA does not have a standard protocol in place to accept these returns, this is practiced on a case-by-case basis.

Pharmacy Participation

Each month HPSA obtain a list of pharmacies from the College of Pharmacists of British Columbia and compare to the list of pharmacies in the HPSA network to identify which pharmacies are currently not participating. Outreach is conducted and pharmacies interested in participating are sent guidelines, which to be signed by a pharmacist. Initially the pharmacy will be sent a container to collect take back medication along with a welcome package with promotional materials and request forms for additional free promotion materials. HPSA also hosts digital promotional materials online. Some pharmacies request new supplies on a monthly basis but in more remote or rural areas the container takes longer to fill up. If after 18 months a pharmacy has not returned a container, HPSA will contact and ask for the container to be returned and send out new supplies.

Promotion to customers

HPSA doesn't have any requirements of 'best practice' for how pharmacies choose to promote the program because it is not mandatory. HPSA promotes to the public in general, but does not target specific patient groups. The messaging on HPSA promotional materials is relatively neutral and stresses the importance of safe medication storage and disposal, what is acceptable to return in pharmacies and how to do so.

Insights

Since 2012 in the BC program return volume has increased every year apart from during the COVID-19 pandemic. HPSA theorizes that this has correlated with increased customer awareness of program. HPSA does not compare volumes received between pharmacies. HPSA conducts an audit every 3 years to identify the proportion of prescription, over the counter and natural health products. This is a large undertaking, and they state that it would be extremely time consuming to work out which specific prescription products are returned, especially without packaging. The last audit was conducted in May 2019 and found that of the drug returned, 70% were prescription and 30% over the counter. There is seasonality in return rates, with more returns in Q1 and Q4, lowest returns in Q3. HPSA proposes that this is due to people being home more in winter months and may be more aware of medicine cabinets and more likely to clean them out during this time.

Future Targets

HPSA aims to improve the program by increasing consumer awareness and ensuring that it is easy for the public to know where to return drugs. They also want to ensure it is easy and painless for pharmacists to participate and to and work with stakeholders that can improve the success of the program.

5.3. Pharmacist Phone Survey

Program Operation

None of the three pharmacies were able to identify HPSA by name when asked whether they were part of the take back program. They only realized who they were when they were asked if customers were able to hand in expired medication to them. Pharmacies noted a number of drugs for a variety of different conditions were returned, with more tablets being returned than liquids.

Program Promotion

None of the three pharmacies actively promoted or used any posters, leaflets or pamphlets to promote the program to customers. Generally, the program is only discussed with patients in certain situations. Most common is when a patient's prescription is discontinued or changed, and they are told they can bring back their former medication in for correct disposal. Patient's prescriptions are discontinued or changed for a number of reasons including problems with tolerating it, switching to an alternative prescription or dosage adjustment. One pharmacy noted that they tended to discuss the take back program with regular customers more often, who were usually patients with chronic conditions on multiple medications. Another noted that they do not discuss the program with casual customers that just come in for one-time or over the counter purchases.

Discussion with Customers

Patients occasionally ask about the drug take back program, for instance to ask if expired medications are accepted. Customers have mentioned that they flush drugs down the toilet if not bought back in. Pharmacists said that they use both environmental concerns and social and safety reasons to convince customers of the importance of returning their medications. Patients also give environmental concerns as a reason for returning drugs, in addition to saying they do not need the drugs or that they have expired.

Support Wanted from HPSA or Metro Vancouver

The three pharmacies diverged on what support they would want from HPSA or Metro Vancouver to support them in program operation. One pharmacy said they were not interested in any specific support from Metro Vancouver or HPSA. The second said they would be open to receiving promotional materials, or more information on how to promote the program. The last pharmacy thought that support would not be necessary right now as they are a fairly new pharmacy, not busy and they have not filled up a HPSA return box yet. The interviewee questioned whether improving the program in their pharmacy would have much of an impact. However, they were open to receiving Metro Vancouver promotional materials in the future.

5.3. Pharmacist Interviews

The full transcribed interviews and the names and pharmacies of interviewees will be obtained by Metro Vancouver. Direct quotes are shown in italics.

5.3.1. Interviewee One

Program Operation

On average, it takes their pharmacy about 6 months to fill up one of HPSA's containers. HPSA request that the medications are returned to them

Program Promotion

HPSA materials, posters and brochures are on display to customers. Pharmacist does not hand materials to customers directly but promotes the program on their own Instagram.

Discussing the program with customers

The pharmacist stated that they would discuss the program with anyone who it seemed relevant to. They said that sometimes opportunities to mention the program come up in passing, for instance when customers mention that they have some unused medication at home. However, the most common situations in which the program is discussed with patients is when patients are discontinuing, changing or refilling a prescription.

Let's say you're on a blood pressure medication, and you have a side effect from it. And the doctor subsequently prescribes you medication about a week later. So I'll say, oh, you've got an adverse reaction to this so doctor will be prescribing a new medication. So when you pick it up, feel free to drop off previous medications.

An epi pen's typical shelf life is one year. So when people come in to get a refill of an epi pen or something like that, they mention you can bring your old one into dispose of properly.

Another common opportunity comes when pharmacists conduct a medication review, when they look at patients' prescriptions over the last six months and see how they are working.

And so we'll kind of go through and say, are you still taking [that medication] and then you kind of foray that into something. If you're no longer taking this medication, you know that … you can bring this medication back to us.

Communicating the importance of the program to customers

Patients are generally receptive when the importance of taking back their medication is explained to them. The pharmacist said that awareness of the program in their local area was generally high:

In my demographic here, a lot of people are aware of the fact that regardless of wherever you purchased the medicine, it can be brought into the pharmacy to be disposed of.

Environmental impacts of incorrectly disposed pharmaceuticals, including medication leaching into the wastewater or sewage system, as well as safety reasons such as the danger of kids accessing medication out of curiosity, are all reasons given to customers to return their medications. The pharmacist that when they ask customers to return their drugs, they communicate it like an obligation.

Returning Drugs

The pharmacist specified that they don't probe why patients return their drugs, and the most common reasons given are that the medications are just sitting in their cabinet. On occasion, a customer will return drugs on the behalf of another patient. They give the reasons of someone's passed away, or they are cleaning out someone's, often their elderly parents, medication cabinet or closet. Generally, more females than males return drugs. A diverse age range of customers return drugs, but the pharmacist specified that 80% of their customers demographic was likely between 20 and 50. Tablets are more likely to be returned than liquids, and over the counter and vitamins and minerals are slightly more likely to be returned than prescription. It is mostly adult medication that is returned, although some children's medication is also returned. The pharmacist thought that there were more medication returns in the spring, possibly due to people doing spring cleaning.

Support Wanted from HPSA or Metro Vancouver

The pharmacist wanted more messaging to customers to tell them how they should be returning drugs to meet HPSAs standards and avoid the extra unpaid labor.

Better messaging to the public saying, we take your medication, but you need to put it in a big container without your personal information, so that we don't have to have to scribble out and peel off the label. It's very time consuming, especially when I'm bringing my 30 bottles and the adhesive sticks on there and so you have to take a sharpie and opening those bottles. I don't get paid to do that or to pay my staff, myself to do something like that when I have other things to do that. So like some messaging for how you should bring it to the pharmacy without any personal information and in a big bag that we thought would be a time saver.

Health and Safety

The pharmacist mentioned that sometimes people return illicit drugs. They do take them but have to render them unusable so they can be disposed of at their own expense. They are not covered under the drug take back program.

Suggestions for program Improvement

The pharmacist suggested that more monetary support would be needed to improve the success of the program, and that the program as it is relying on a substantial unpaid workload from pharmacists.

I'll speak to you as a pharmacy owner, pharmacy manager. What monetary benefit am I going to get from this? Nothing? Right. I mean, putting a poster up fine, I could do that. But then if you *come in with certain bottles, and you're not a regular patient of mine, I'm already busy doing other things, and I'm not gaining anything from it. Yeah. You know, it's good for the environment, but as a pharmacy owner or a business owner, it is adding to my workload.*

The pharmacist explains that if they were paid for their time, they would be willing to potentially participate in a public drug take back event. They would also be interested in using Metro Vancouver's materials.

5.3.2. Interviewee two

Program Operation

The program operation was disrupted due to Covid-19, and this pharmacy, and others, did not accept returns for a time during this period because they were unsure of what the procedures were, especially for contamination issues. This could potentially lead to patients being unsure as to whether they are able to return medications.

For example, a week ago, one of our patients just called and said, are you guys ready for returns now? Because they know about the program.

Program Promotion

No promotional posters on display. Was not aware of Metro Vancouver promotional materials. Explained that the BC Pharmacy Association does some promotion blitzes in March and so does the Canadian pharmacy Association around the fall time. Both of these promotional blitzes bring in more customers returning medication.

Program Awareness

The pharmacist noted that disposal guidance has changed, and that at one point people were told to dispose of their excess drugs by flushing them down the toilet. Therefore, they reason that certain customers who experienced this prior messaging may not know the correct method of disposal. They also suggest that younger people may also have lower awareness as they do not require pharmacy services as much as the elderly. They also say they get many people coming in with drugs to the pharmacy and saying they don't know what to do with them, and on occasion people have mentioned flushing drugs down the toilet.

The pharmacist also suggested that people who obtained their pharmacy qualifications outside BC or Canada could have lower awareness of the program as it may not have been integrated into their training (or not the Canadian version of the drug take back program.) They also note that people in hospital practice might not know about the program as they have their own channels of disposal.

Discussing the program with customers

The drug take back program is not usually discussed with customers who just buy over the counter. They say that if a patient buys something that is either for a first aid kit or cold medicine travel kit they'll tell them that it should be good for a couple of years, but check expiry and if you haven't used it bring it back in. They explain that sometimes they get patients on prescribed pain medication, which because they understand as something that patients take only when they need they encourage them to bring any excess back.

They describe the typical way in which they would ask a patient to return medications:

If you have any expired drugs at home, just bring it back so we can get rid of it safely.

Returning drugs

Customers often return multiple drugs at the same time, and generally more pills are returned than liquids. Generally, drugs are not returned as HPSA instruct (in plastic bags with labels removed) so the pharmacists have to prepare the drugs for disposal which is a lot of work. Medications are sometimes returned on behalf of patients, especially by people clearing out loved one's areas. Home visiting nurses also frequently come into return. From their observations, they think that people return more in the spring, for spring cleaning, and during media promotional blitzes.

Doctors samples and the drug take back program

The pharmacist raised the issues of doctor's drug samples not being part of the HPSA drug take back program.

In Canada, for example, drug reps will go to a doctor's office and they will give them samples of medications. So there's actual product in the doctor's office, kind of like a mini dispensary. Those samples will expire if they don't get used. Alternatively, doctors can give a sample card to a patient and they can get the medication from the pharmacy, so there's less wastage. So the samples that are expiring will be at the office of a physician. And they don't have any way of getting rid of the medications. I often wonder why the samples are excluded from the program, when the drug companies are paying into the federal program.

Health and Safety

The pharmacist raised that they were concerned about the safety of the HPSA box. Firstly, they raise that it is a serious toxic hazard to have different chemicals mixing together over the almost a year period it takes to fill the box. They say that this is worsened by the open lid on the box, which allows toxic fumes to be released every time the box is opened, causing an inhalation hazard. Consequently, the pharmacists ask their staff to wear masks when they open it.

There's toxic brew happening in there already. And you open it and it's the size of a piece of paper. When you open that lid, it's dangerous. We tried to secure it on the side where nothing touches it …The [HPSA box] should not have an open lid. There should be like a screw top lid like almost like the size of a coffee cup where you can where you can pour [drugs in].

They also criticize HPSA for lack of a safety plan in dealing with the box, which is standard in any lab situation where chemicals mix together. They therefore say that the current set up shows a lack of concern for the safety of the individuals handing the products. They are also concerned the box is not locked, and there is therefore the potential of people taking medications from the bin.

It's not safe. The way it's set up. The lid is loose. If you knock down the box, you're screwed. There's not a safety plan in place even though there should be, like in labs, right? There should be a hazmat safety in place..disposing of certain chemicals, [if] you're gonna mix it in something will happen.

Some patients return sharps and drugs mixed together in the same bag. This is extremely dangerous for pharmacists.

So I tell our guys never reach into a [drug return] bag. Because especially if it's a palliative patient, there could be sharps in there, or there could be used patches. So that's dangerous.

The pharmacist says that they have a sharps disposal bin in their office from doing shots, so if they spot the sharp in the bag that can ask the customers to empty it in there. However, because the drugs and sharps are sometimes mixed together the sharps can end up in the HPSA bin.

Outreach and Promotion Opportunities

The pharmacy noted that as asking people to bring their unused drugs back was a one liner, they could easily raise it with more customers.

The pharmacist remembered medication safety being required by the Vancouver school board. They suggested the drug take back program could be linked with medication safety and Metro Vancouver could reach out to different schools with an education initiative. She also said that many schools have mandatory community projects in the social or health sciences.

They also recommended reaching out to the head offices of pharmacies and pharmacy regulatory colleges. They noted that the regulatory colleges may have interest in prompting that improve the drug take back program because their areas of concern include public safety surrounding drug use. They also meet twice early and host learning sessions. They also recommended that outreach could be undertaken with other Health Care Professionals, such as physiotherapists. Using this example, they say that someone might mention to their physios that their pain medication isn't working, meaning the physio could use this opportunity to tell them to bring any excess painkillers back to the pharmacy. However, they note that many physios may not be aware of the program or be aware that they can actively promote it.

HPSA Support

The pharmacist suggested that HPSA could invest in safer disposal boxes that destroy and render drugs unusable on site, like the RX destroyer. They say this is safer because the opening is smaller, and it avoids having *'a sinkhole of potential dangerous goods.'* They do acknowledge that this would cost more.

5.4. Prescriber Interviews

The prescribers interviewed here were not able to give long form interviews, but instead provided a short statement in response to the question below. It is discussed in the recommendations that longer form interviews would be beneficial to identify how certain recommendations and outreach programs could be implemented.

Do you ever consider environmental impact when choosing which drug to prescribe?

Prescriber 1 (hospital doctor and master's student in environmental studies): *On my end sure, though I am studying the environment and not necessarily representative of my group in the sense that I think I am more sensitive about stewardship when I prescribe but not everyone is. We often have to weight practicality against stewardship and it's not always straightforward.*

Prescriber 2 (hospital doctor): *Quite honestly, I've not considered it. I wouldn't even know where to look up that information. There's so many different meds we prescribe with so many different indications, I would need a comprehensive database with evidence based research if I were to make a decision based on that.*

6. Recommendations

Based on the research gathered through the literature review, jurisdictional scan, analysis of Metro Vancouver's monitoring data, and interviews with HPSA and pharmacists, this section provides recommendations for further studies and additional ways to reduce the presence of pharmaceuticals within wastewater. The recommendations are grouped into the following sections:

1. Monitoring and Pathway Characterization

How alternative monitoring strategies can help anticipate the amount and type of pharmaceuticals entering wastewater, identify priority compounds of concern and allow the assessment of any policy interventions.

2. Database Creation and Data Interpretation

Suggests strategies for organizing and interpreting data to help understand the different entry pathways, identify priority compounds, and allow a more contextual understanding of pharmaceutical risk in the environment.

3. Pathway Intervention

Suggests that intervening in pharmaceutical pathways to entry is more of a priority than fully understanding and characterizing entry pathways.

4. Drug Take Back Program Promotion

Suggestions for how the drug take back program in Vancouver could be promoted to increase its reach and ensure the messaging is persuasive.

5. Drug Take Back Program Operation

Suggestions for how the drug take back program can improve its operation in Metro Vancouver, particularly through addressing safety concerns and covering other pharmaceutical sources. This will need to be done in partnership with other organizations.

Monitoring and Pathway Characterisation

Do not use monitoring programs to place excessive focus on attempting to fully characterize and quantify pathways

It is extremely difficult to fully characterize and quantify pathways of individual pharmaceuticals into wastewater. Quantification in this context means attempting to calculate the relative contributions of several pathways into wastewater. Although quantifying pathways can provide the following benefits, these are outweighed by considerable limitations and higher benefits if resources are directed towards alternative management and preventative strategies. The major benefit of quantification is to develop a thorough understanding of the pathways of pharmaceuticals into wastewater and identify the key pathways by contribution to prioritize meaningful intervention. It can also allow the comparison of pathways between different pharmaceuticals and provide an easy way to assess the degree to which interventions are effective.

However, there are several limitations to quantification due to the availability of gathering complete and accurate data. Firstly, it is time consuming and extremely hard to identify and characterize all pathways for each pharmaceutical (manufacturing, veterinary use, disposal in waste and garbage receptacles vs toilets.) There is for instance no information on the ratio of pharmaceuticals disposed down bins vs toilets, which could help characterize the prominence of landfill leaching vs direct pathways. Prescription data also assumes perfect adherence. Veterinary use appears to be a particularly hard pathway to characterize as it includes there are so many variable factors including usage and dosage, location and environmental transport of pharmaceuticals. Therefore, it is suggested that accurate enough quantification cannot be achieved purely from literature. Accurate quantification would entail considerable primary research (local surveys on usage), ways to extrapolate from the limited literature data and a coordinated and long-term monitoring program. To put this data together would require some detailed modelling. Because of both the lack of literature information, monitoring information and usage information this would currently not be possible.

Calculate PEC as a metric to characterize pathways and anticipate trends

Attempts should be made to access BC PharmaNet prescription data, and more regional data if possible. This can be used to calculate predicted environmental concentration (PEC), using the methods described earlier in the report. PEC can also be used to:

- Estimate environmental concentrations for compounds with limited or absent monitoring data and/or analytical methods to measure concentrations.

- Estimate how influent, effluent and environmental concentrations have changed over time, and how they may change in the future.
- Compare to measured influent, effluent and environmental concentrations (MEC) to identify any discrepancies. Discrepancies can indicate that another pathway in addition to human consumption (incorrect disposal, manufacturing) is contributing to the influent concentration. This can allow for targeted prevention campaigns.

It must be noted that PEC can vary between areas, and that local prescription data will result in a more accurate estimate.

Improve the monitoring and information gathered for metabolites and transformation products

Certain metabolites or transformation products have a higher rate of formation under certain conditions and/or treatment technologies. It is recommended that a short review is conducted to compare the technologies and conditions currently in use at Metro Vancouver WWTPs to the literature on what metabolites and transformation products these conditions could give rise to. The next part of the review could collate any literature on the toxicity of these products. It is acknowledged that the literature on both the formation of and toxicity of these products is quite limited. If there are methods available, certain products could be selected for monitoring. Provisionally, it is recommended that valsartan acid (metabolite of valsartan), guanylurea (metabolite of metformin) and 2-hydroxy-ibuprofen (metabolite of ibuprofen) immediately undergo more stringent monitoring. This is because the parent compounds are present at high concentrations and valsartan acid and granylurea are currently not sampled, and all three metabolites have been identified as potentially more toxic than their parent compounds.

Consider a grouping strategy for more regular monitoring

Switzerland uses a compound indicator strategy to monitor improvements in wastewater technology more frequently than mass sampling compounds annually. Switzerland selected 12 indicator compounds to sample regularly in influent and effluent. (Bourgin et al., 2018; Eggen et al., 2014) detail the full decision of compound selection and the monitoring program operation. Metro Vancouver could adapt this strategy by also selecting a panel of representative compounds to monitor more regularly:

- Compounds that are diverse in structure
- Compounds in different therapeutic categories (e.g. antibiotic, heart disease drug, psychiatric drug)
- Compounds that are resistant to wastewater removal
- Compounds that are always present over the level of detection, and have reliable and accurate analytical methods

- Representative compounds of groups that either exhibit certain behaviors, or have concentrations that tend to correlate together (e.g. if the concentration of one increases, so does the other)

The advantage of more regular monitoring is that it is easier to see if certain interventions are having an effect, and it may be a more cost-efficient strategy to do regular monitoring.

Conduct a similar exploratory project for veterinary pharmaceuticals

Veterinary medicine, specifically veterinary antibiotic usage, appears to be a pathway that needs to be considered in source control. Further research on farmland and usage/prescription practices in Metro Vancouver can help with a broad estimate of how much this pathway contributes to wastewater entry compared to human pharmaceuticals. It is therefore recommended that another similar exploratory scoping project is undertaken for veterinary pharmaceuticals. Recommended components:

1. Scoping of potential sources for veterinary and human sources of pharmaceuticals (including meat processing plants, veterinary hospitals and other animal-based industries that can contribute to Metro Vancouver sewer inflow.
2. Literature review on pharmaceutical usage and dosing practices on farm animals, including likelihood of adherence and reasons for non-adherence, types of pharmaceuticals used, frequency of dosing and usual disposal methods of unused drugs.
3. Interviews with farmers on the above and veterinary or commercial prescribers on all of the above, and prescription behaviors.
4. Literature review on drug take back programs for veterinary drugs, including success metrics, promotion and operation.
5. Recommendations on limiting the use of animal antibiotics.

Database Creation and Data Interpretation

Consider a more holistic approach to risk

Chemical pollution risk needs to be considered more holistically by Metro Vancouver. By this it is meant that concentration on its own is not a sufficient risk metric, as sometime compounds present at high concentrations are not as risky as other compounds at lower concentrations. Only having data as concentrations can take away this nuance when designing interventions to reduce the risk and prevalence of certain compounds. The literature review also demonstrated that many pharmaceuticals have endocrine disrupting properties, meaning that they can be dangerous at low concentrations, and that antibiotics in WWTP can cause antibiotic resistance. To account for this, the creation of a new database is recommended.

Database Creation

It is therefore suggested that a database is collated with pharmaceuticals of concern and multiple risk metrics. The first part of the database should include relevant physical and chemical properties that can affect how chemicals are removed in wastewater.

1. K_{ow}
2. PKa
3. water solubility
4. Molecular Mass
5. Partitioning Coefficients
6. Rate of formation of known metabolites/transformation products

This has the extra advantage of compensating when detailed risk assessments have not yet been completed for chemicals, and there is a lack of literature on certain risks. It also allows safety to not just be judged on one factor.

Recommended information in risk database:

1. Concentration in Metro Vancouver influent, effluent and environmental
2. Any recorded endocrine disruptor activity
3. Any recorded carcinogenicity
4. Chronic affects
5. NOEC
6. Synergistic effects with other compounds
6. PNEC
7. ADI
8. Therapeutic dose
9. Bioaccumulation Potential
10. Environmental Persistence

This database should be updated as new drugs come onto the market. Compounds with particularly low NOEC, or as identified endocrine disruptors, chronic affects need to be removed even if their current concentrations are lower than others.

Pathway Interventions

Prioritize prevention

As much as possible antibiotics should not even be entering wastewater, because the treatment facilities provide ideal conditions for antibiotic resistance to spread. There is also evidence that mixtures of certain pharmaceutical compounds can also do more environmental damage than the individual compounds. Therefore, it is not good that numerous compounds are mixing together in wastewater. Any improvement in any prevention pathway is worth pursuing, even if it is a minor contributor compared to other pathways. Improved wastewater treatment that specifically targets micropollutants is also urgently necessary and WWTPs are being upgraded at Metro Van. During and after these upgrades are in progress, prevention has the potential to provide quicker and easier benefits which will be expected to be relatively cost-effective.

Find ways of assessing the impact of interventions that do not rely on quantification

Prioritizing quantifying pathways leads to thinking that reducing influent and effluent concentrations are the most important metric of success in managing pharmaceuticals at the source. It is important to note that even if pathways cannot be fully quantified, meaningful interventions can still be identified, and the success of said interventions can still be assessed. However, actual metrics of success may be less obvious and more contextual. For instance, improvements in drug take back programs may not be observable in influent concentrations if at the same time the prescription rate has increased. This is still however a meaningful intervention as it has prevented the influent concentration from rising further. Therefore, when an effectiveness of an intervention is being evaluated, it still must be considered that multiple pathways may be affecting the influent concentration.

Direct more focus towards prevention pathways, or pathways with more obvious interventions

It is already clearly apparent that without quantification there are ways to intervene in multiple pathways. There is enough evidence that these chemicals cause significant harm in wastewater systems and in the environment. The precautionary principle suggests that it is still worth acting to reduce this harm, even if there is still considerable uncertainty and unknowns. Many interventions can also target multiple pharmaceuticals at the same time. A summarized list of interventions and the pathways they impact is shown below:

1. Incorrect disposal
   Improved drug take back programs (greater awareness, improved access to disposal, pharmacy outreach, targeted promotion), extending drug take back program to samples and drug packaging

2. Human Consumption and Excretion

   Changing prescription behaviors (dose reduction, environmental impact considered when prescribing),

3. Veterinary medicine

Extending and promoting drug take back program to veterinary medicines

4. Manufacturing and Industry Usage

Does not appear to be a lot of chemicals manufacturing in Vancouver, but reducing industrial usage could be investigated

5. Hospital effluent

Intervention: data shows that this is contributing to wastewater influent, so stricter enforcing of bylaws could be required.

Be aware of future trends and act proactively

An increasingly ageing population will mean that the prescription rate of many pharmaceuticals will increase, but the ones for conditions that are more common in the elderly will increase disproportionately more. To identify prescription trends, permission could be requested to enter the BC PharmaNet database to see how prescription rates have changed over time. This should help give an estimate for how the prescription rate will change in the future for individual pharmaceuticals. It is recommended that a summary database is collated with pharmaceuticals of concern, their usage, the demographic rates of who usually has this condition, their adherence rate (or comment on adherence if one can be found) and prescription rate (and how this has changed over time).

As was recommended with the risk database, this summary database should be added to when new drugs come on the market. New drugs on the market should have an environmental assessment as part of their approval process in Canada, so this information should be accessible to enter into the risk database. The approval process will also display their usage.

Scoping project on the more environmentally focused prescription choices

Sweden has a database available to physicians that lets them compare medications for the same purpose on their environmental impact, so it is easier to consider environmental impact when prescribing. Reducing dosage could also be a promising avenue for reducing the prevalence of certain pharmaceuticals in the environment. One prescriber said that they would require an evidence-based database, similar to the one currently used in Sweden, to ensure they could incorporate environmental impact into prescription choice without impacting patient care. Although introducing a similar system to Sweden may be beyond what Metro Vancouver can achieve, it is possible that they could either work with other government bodies to achieve this or conduct an initial scoping review that could be taken further by other organizations.

Drug Take Back Program Promotion

Adjust Messaging to Match Pharmacist Messaging and Patient Concerns

Work with pharmacists to develop a best practice for how the program should be discussed with customers

Many pharmacists described how talking with customers was the main way of promoting the program, not posters or promotional materials. However, many pharmacist interviewees admitted that they generally only talked about the program to customers discontinuing or starting a new prescription. This has various consequences, including customers who only buy over the counters having a lower awareness of the program. Ideally, pharmacists would discuss the program with all customers, even if it is only a one liner. However, the way in which the program is discussed with customers should be different depending on their situation.

Take pharmacy input into promotional materials

Pharmacist input is also key to designing promotional materials going forward. Pharmacists should not just be bought in at the end stage to validate the materials already created, they should be part of the process from the beginning. This is both because of their experience talking to patients about drug take back programs, and their insight on knowing what patients understand about the importance of drug take back programs and what messages will resonate with them. They will be using these materials to talk to and give out to patients so the materials must be designed to support what pharmacists are saying to patients.

Consider using environmental and social messaging

Currently in the unflushables campaign, medications are mostly lumped together with other unflushables. Although this is a strong campaign to encourage people to think twice before they flush certain objects, the nuances and messaging specific to pharmaceuticals is missing. There is some strong messaging specific to pharmaceuticals which can 'nudge' people into feeling obligated to return them.

People can be encouraged to return their pharmaceuticals through two main messaging strategies: a) not disposing properly of pharmaceuticals harms the environment and potentially human health, and b) having excess pharmaceuticals in the home is unsafe due to risks associated with children/pets accessing them unintentionally, drugs being used for incorrect self-medication or suicide, and addiction. These messages in different ways stress the importance of the issue to customers and imply that it is not just an optional activity for them to return their drugs, but an obligation.

A potential avenue for Metro Vancouver could be to run a public focus group where a variety of social and environmental messages are proposed to people of varying demographics to see which messages would most encourage them to return medications. The results of this can inform the development of future materials, which should include both types of messaging.

Ensure Messaging Stresses Ease of Return

Customers need to be convinced that returning drugs is extremely easy and have no confusion about how they go about returning drugs. It should also be made clear that medications bought anywhere can be returned to a pharmacy.

Design messaging to ask customers to return drugs as HPSA instruct

A pharmacist interviewee raised that it was extremely time consuming to prepare the drugs for disposal, and that they were unpaid for this labor. They explained that HPSA would revoke their membership if drugs were not in the container correctly. They therefore recommended that more messaging should be used to show customers how to return drugs correctly (e.g. out of packets in a bag, no identifying information). A simple poster should be created to show this, and Metro Vancouver and HPSA could potentially look into ensuring plastic bags are available in pharmacies.

Extend Campaign to Veterinary Medicines

A pharmacist interviewee stated that they took back some veterinary medicines. Veterinary medicines were also found in Metro Vancouver influent. Promotion could be extended to ask people to return their unused veterinary medicines to pharmacies as well.

Make Messaging More Targeted

Target messaging depending on demographic

It is important to consider that different messaging will resonate with different demographic groups. For example, a parent may be more concerned of the risks that excess medication poses to children, whilst a young person may be highly concerned by environmental risks. King County's materials can be seen as a good example as varied and targeted messaging.

Target messaging for low adherence medications and associated conditions

Certain medications (including metformin, certain pain medications and heart disease medications) have a low adherence, suggesting these drugs are more likely to be unused and later disposed of incorrectly. Drug take back campaigns can be targeted to patients who take these drugs, as this will likely be more impactful. This may be most effectively done in partnership with patient groups. Pharmacists could also be asked specifically to talk to patients on prescriptions for low adherence drugs about the drug take back program.

Target Patient Support Groups

Patient support groups can range from casual organizations of patients with similar diseases that socialize and share information or be more formal organizations that keep patients and their families up to data with research, information and offer varying levels of support. Establishing links with these organizations can provide a way to reach a large number of patients from a source that they trust. Organizations to reach out to could include Diabetes Canada, BC Diabetes, Heart and Stroke Foundation Canada and the Mental Health Commission of Canada.

Seasonality Based Campaigns

HPSA said that more medications were returned in the winter months, potentially because people were more aware of their medicine cabinets. Therefore, a campaign for winter could encourage people to clean out their medicine cabinets and return any expired medications to pharmacies. DEET use dramatically increases in the summer, so a campaign for the summer could encourage people to either apply less DEET or buy alternative drug repellents.

Consider Additional Avenues of Promotion

Schools and Colleges

Pharmacist 2 noted that medication safety is a part of the Vancouver school boards curricula, so it is possible that Metro Van could look into what is required to be taught and potentially ask if the drug take back program could be integrated into the education. Alternatively, Metro Vancouver could go into schools to talk about the importance of the program. Pharmacist 2 also raised that many students are mandated to do community based projects in health and social sciences, meaning that Metro Vancouver could be a project partners and work with students to promote the program in their local communities.

Pharmacist Colleges

Metro Vancouver could undertake outreach in pharmacist colleges, to convince pharmacists in training of the importance of the program and how they can promote it so when they enter practice, they are more likely to engage in active program promotion.

Care Homes for the Elderly and Hospitals

Many studies pointed out that people more likely to return drugs are regular customers with chronic conditions that are more likely to be elderly. The elderly are less likely to be accessing social media where many of Metro Vancouver's campaigns are posed. Therefore, Metro

Vancouver may need to consider promoting the drug take back program in places frequented by this demographic, including community centers, hospitals, and care homes. It has been noted that medication returns are sometimes made on behalf of patients, either because they have died or because they are unable to access return services. Putting posters in care homes encouraging carers, family and friends to return patients medications could also be a promising promotion avenue. It would maybe be worth reaching out to a couple of care homes to query how they currently dispose of patient medications. Posters could also be displayed in hospital waiting rooms or wards.

Pharmacy Chain Head Offices and Regulatory Colleges

Pharmacist 2 said that many regulatory colleges would be interested in efforts to promote the drug take back program because their area of interest was drug safety. These colleges meet twice yearly and produce educational opportunities for pharmacies, making them ideal spaces for outreach. Another outreach opportunity could be the head offices of chain pharmacies to see if drug take back programs could be incorporated into company training or communicated to pharmacists in regular emails or notices.

Other Healthcare professionals

Other healthcare professionals, including physios and homecare nurses, all have opportunities to raise the drug take back program with patients. Interviews should be undertaken with a couple of each profession to identify ways in which they can promote the program to patients.

Social Media

As well as continuing to promote the program on their own social media, Metro Vancouver should reach out to other organizations or influencers that would be interested in promoting the program. This can expand the promotional each of the drug take back program and potentially generate some more followers for Metro Vancouver by introducing their messaging to new audiences. Some potential organizations of influencers interested could include:

- Local news
- Patient support or information pages
- Social organizations
- Local community pages and community organizations
- Environmental education and activism influencers or organizations
- Hospitals
- Veterinary Hospitals
- Local pharmacies or pharmacy chains

Pharmacist 2 noted that media blitzes were effective in increasing takeback, so media campaigns with increasing reach will likely be an impactful intervention.

Vet Surgeries

Posters could be displayed in the waiting rooms of vet surgeries.

Drug Take Back Program Operation

Invest in Pharmacy Outreach

For HPSA and provincial government to acknowledge that there are issues with how the drug take back program currently operates

The issues identified in this report cannot solely be rectified by Metro Vancouver. It is therefore crucial for these organizations to understand these issues and work with Metro Vancouver to find solutions. The health and safety issues need to be considered urgently by HPSA.

Acknowledge that there is an urgent need to communicate the importance of drug take back programs to pharmacists, not just customers

It is clear from the interviews that many pharmacies do not see the need to actively promote the program or see no reason why they should when they are not financially compensated for it. The reasons given for this include small size of pharmacy and believing that it won't make a difference and viewing drug take back programs as a low priority when they have multiple other tasks to complete. Therefore, serious work needs to be completed in convincing pharmacists of the importance of drug take back programs, and why they shouldn't just receive drugs from those who ask to return, but actively encourage customers to return them.

Actively send pharmacies promotional materials and plastic bags

HPSA currently allow pharmacies to request materials (as do Metro Vancouver) but do not send them to them directly. The drawback of this approach is it relies on pharmacies taking this initiative, even though the interviews demonstrated that pharmacists are very busy and requesting materials will likely not be a priority for them. Instead, it is suggested that MV send materials for pharmacies to display directly, or actively reach out and email pharmacies to ask them to display the materials.

Reach out to chain pharmacies

The main offices of chain pharmacies in the Metro Vancouver area could be a potential outreach avenue. These offices have the authority to reach out to individual pharmacies with certain messages. Potential outreach strategies that could be requested include:

1. Head offices sending an email to pharmacies reiterating the importance of promoting drug take back programs in the pharmacies and displaying posters
2. Chain pharmacies integrating the drug take back program into staff training
3. Chain pharmacies putting a message about the drug take back programs in the hold messages that customers here when they ring the pharmacy (current messages tend to include healthy eating and sunscreen application)
4. Chain pharmacies using their social media to promote the importance of drug take back programs, and asking their pharmacists, if they are comfortable, to do the same.

Involve Pharmacists in Program Monitoring

Monitoring Surveys

It will be important to have ways to monitor the success of introduced intervention strategies. One such way could be asking some pharmacies to conduct informal surveys of drug take back programs. A basic survey could simply monitor how many patients come into return medications on a daily, weekly or monthly basis. Expanded surveys could investigate if various promotional activities increase take back rate, or pharmacists asking patients why they are returning drugs and what drugs they are returning.

Consider operating in locations other than pharmacies

Public Drug Take Back Events

Pharmacist 1 said that if they were appropriately compensated, they would be happy to participate in a public take back event. King County demonstrated that these events could be highly effective, and it is maybe worth undertaking more research on what makes a successful drug take back event when organizing one. HPSA also mentioned that they were aware of Drug Take Back events at locations such as fire stations to alleviate the potential security concern.

Mail Back Services

King County provide a mail back service where residents can mail back their unused medication for correct disposal. Metro Vancouver could communicate with HPSA to see if there is any possibility of a similar program to set up. This could help address the discrepancies between rural and urban coverage and provide an easier avenue to return for disabled or elderly patients, for whom driving could be an issue which is especially important as it has already been established that this patient demographic does tend to have unused medications.

Expanding in home collection

HPSA said that they accept take backs from nurses visiting patients' homes. Instead of individual nurses contacting HPSA to get approval to this perhaps this could be communicated to nurses that they are able to pick-up unused medications up from patients' home and return them.

Address the Health and Safety Issues with the Program in partnership with pharmacists

Consider Changing the HPSA collection box design

Pharmacist 2 raised that the box design was extremely unsafe and an inhalation hazard. The welfare of pharmacists must be taken seriously going forward, and HPSA needs to consider the use of boxes that either destroy on site (such as the RX destroyer) or at the very least, boxes specifically designed for safe chemicals storage.

Develop a detailed health and safety practice code

Pharmacist 2 also raised severe health and safety concerns with the chemical storage in the HPSA box, which would not be acceptable in a lab setting. There should be detailed safety protocols in place for incidences including:

1. Spillage of chemicals
2. Sharp injury
3. Inhalation of chemicals
4. Spillage of box
5. Damage to box

Create clear messaging asking customers to separate sharps from drugs

Another health and safety concern was customers frequently bringing in sharps mixed with medications for disposal. This is a risk for the pharmacists who have to separate them under HPSA guidance. Therefore, more messaging is needed to communicate to customers that the two must be packaged separately for disposal.

Extending program to incorporate medications not covered by the program

Investigate why BC EPR regulations do not apply to drug samples

The pharmacist raised their frustration that drug samples were not covered under EPR, despite also be manufactured by the same companies that fund HPSA, meaning they had to fund the disposal of these themselves. Pharmacist 2 said they accepted them anyway, but were unsure of why they had to be disposed of separately. More investigation is required to why these samples are able to be excluded from the program.

Develop a protocol for accepting illicit drugs

Pharmacist 1 noted that they do on occasion accept illicit drugs, that they have to render unusable and pay to dispose themselves. This cost should not be put on pharmacies as it is a public health issue. Again, health and safety protocols should be designed for pharmacies safely disposing of illicit drugs, especially as these can also cause problems in the environment.

Veterinary Medications

Pharmacist 1 mentioned that they were already accepting veterinary medicines to dispose of correctly, although they themselves were unsure if this was covered under the HPSA program. Either way, it needs to be made explicit that pharmacists can accept these medications as they are contributing to pollution.

Drug packaging

Research has identified that drug residues left on incorrectly disposed of packaging can also enter wastewater and the environment from landfill leaching. However, HPSA current guidelines ask customers to separate packaging from the tablets and dispose of the packaging separately as this is not covered under the pharmaceutical manufacturers EPR. However, disposing with the packaging would first help separate the drugs from each other in the box and reduce the health and safety risk. It would also ensure the residues in the packaging are also safely incinerated.

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