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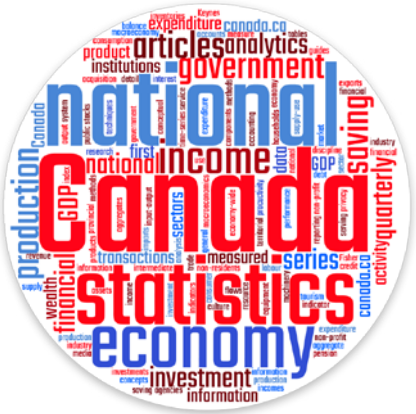

by Laurie Reedman and Andrew Brennan

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Estimating cannabis consumption using markers in wastewater: Methodological paper

by **Laurie Reedman** and **Andrew Brennan**

Abstract

In the fall of 2018, Canada legalized recreational cannabis. Given this major change in policy, Statistics Canada wanted to update and improve its cannabis consumption estimates and, ideally, estimate any changes in consumption that coincided with legalization.

Estimating illicit drug use with traditional surveys presents a challenge because respondents are likely to under-report their consumption. Furthermore, the degree of under-reporting could change as the drug is legalized, complicating a comparison of before and after legalization.

To supplement the surveys, Statistics Canada piloted the emerging science of wastewater-based epidemiology (WBE). This approach involves measuring wastewater in sewers for trace concentrations of a cannabis metabolite that is created and excreted after cannabis is consumed. The amount of cannabis metabolite in the wastewater can be used to compare cannabis consumption over time, and to compare consumption across different regions. With some additional information, this measurement can also be extended to estimate the total quantity of cannabis consumed in Canada. A high-quality WBE estimate of cannabis consumption would be useful to calibrate cannabis surveys or, when combined with data about legal cannabis sales, to help estimate the size of the illegal cannabis market.

This paper examines the parameters needed to calculate the mass of cannabis metabolites in wastewater, and the additional parameters needed to estimate the total quantity of cannabis consumed. This paper discusses the sources of error for each parameter, their effects on the final estimates and our methods for validating the results. We identify the excretion rate, which is the fraction of the consumed drug excreted as a metabolite, as the key source of uncertainty in the WBE estimates of total cannabis consumption. We are seeking feedback and additional research to improve the utility of WBE.

Keywords: cannabis; metabolite; wastewater based epidemiology; excretion rate; potency; uncertainty

Summary

This paper describes the progress made during the first nine months (March through November 2018) of the pilot project to estimate cannabis consumption based on cannabis metabolites in wastewater. It supports the previously-released data (see "Wastewater-based estimate of cannabis consumption, March to August 2018") by discussing the methods and parameters used to obtain those results. Specifically, this paper focuses on the parameters required to estimate cannabis consumption, the sources of uncertainty associated with each parameter, the overall uncertainty in the WBE estimates and our result validation methods.

Project objectives

The objective of the pilot project was to demonstrate the feasibility of estimating the quantity of cannabis consumed in Canada by measuring cannabis metabolites in wastewater samples. When cannabis enters the body, its main psychoactive ingredient—tetrahydrocannabinol (THC)—is processed into a number of non-psychoactive metabolites, of which 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol (THC-COOH) is among the most common and stable.

Beginning a few hours following cannabis consumption and continuing for a few days or weeks, THC-COOH is excreted into wastewater via urine and feces (Huestis 2007; Gracia-Lor et al. 2016), which provides trace evidence of the cannabis consumption. Because THC-COOH is created only in the body, its presence in the wastewater specifically indicates that cannabis was consumed, not just grown or processed. Wastewater-based epidemiology (WBE) involves sampling the wastewater that enters a treatment facility to measure trace quantities of a drug metabolite and then—using a number of model parameters—extending these measurements to estimate the corresponding quantity of drug consumption within the service area.

Compared with survey-based cannabis consumption estimates, the WBE approach has several advantages: it is low-cost, it is fast and it reduces response burden. Also, the WBE approach is not as susceptible to the under-reporting or misreporting that results from stigma, hesitance to report illegal behaviour, or unknown total consumption within the reference period. The decreased under-reporting is particularly important for measuring changes in behaviour at a time when willingness to report cannabis consumption may be changing because of the *Cannabis Act*, which legalized recreational cannabis in Canada. Even if true cannabis usage did not change, surveys may indicate increased consumption as respondents become more willing to share their experiences. However, wastewater measurements would not be affected by this change.

The WBE approach is not without challenges. It is only able to estimate aggregate cannabis consumption within an area and cannot estimate the number of consumers, the average quantity consumed per user, the frequency of consumption, or consumption by personal characteristics (e.g., age, gender, income). In addition, WBE is a new science and it suffers from high uncertainty in parts of the process, such as the pharmacokinetics of cannabis processing in the body. These uncertainties can hopefully be improved with continued research.

With those strengths and weaknesses in mind, we have several specific aims for the WBE approach to estimating cannabis consumption. First, we want to track changes in cannabis consumption over time, including around the time of legalization, when reporting behaviours could change. Second, we want to compare consumption across different regions or cities. Third, we hope that WBE estimates could be used to adjust more accurately total national cannabis consumption estimates from monitoring and health surveys. Fourth, we want to estimate the quantity of cannabis acquired from illegal sources after cannabis legalization by subtracting the known legal purchases from the WBE estimates of total cannabis consumption.

The first two aims are relative comparisons and, in most situations, can be achieved by comparing the average rate at which the metabolite is excreted into wastewater, known as the metabolite load per capita (MLC). The last two aims require absolute estimates of total cannabis consumption. This additional step adds substantial uncertainty, which makes cannabis consumption less certain than MLC.

Project description

The project covered 15 wastewater treatment facilities from five cities: Vancouver, Edmonton, Toronto, Montreal and Halifax. It encompassed 8.4 million people, which is over 20% of the Canadian population. Data were collected every month from March 2018 onward and will continue until the spring of 2019.

External partners included the staff at the wastewater treatment plants and the Department of Chemical Engineering at McGill University, who performed the chemical testing of wastewater samples and provided expertise in the science of WBE. Within Statistics Canada, the project was a collaboration between the Macroeconomic Accounts Branch, Strategic Data Management Branch, Methodology Branch, and health analysis experts.

Wastewater samples were collected during the second week of every month. We followed a strict sample collection protocol to prevent spoilage and to ensure samples were representative of the wastewater and free of contamination. At most wastewater treatment plants, the wastewater was sampled every 30 to 60 minutes, inversely proportional to the flow rate, so that slower flow resulted in longer times between samples. This flow-proportional sampling ensured that the water passing through the facility was equally represented in the sample. However, at a few of the smaller sites, the wastewater was sampled on a regular schedule (time-proportional). In both cases, the small samples were combined into a daily aggregate and frozen at the end of the day. At the end of the sampling week, the daily aggregates were sent to McGill for chemical analysis, and the recorded volume of wastewater flow was sent to Statistics Canada. At McGill, the daily aggregate samples were thawed and combined into a weekly composite sample proportional to the daily flows to preserve the equal sampling of the wastewater. From this weekly composite, three extractions were drawn and analyzed for THC-COOH and metabolites from other drugs that are not discussed here. The concentration data were then sent to Statistics Canada via secure data transfer.

Computing the metabolite load per capita (MLC) (Equation 1)

MLC is the average rate at which people excrete THC-COOH into wastewater. It is a step in the calculation of total cannabis consumption, and it is also useful on its own for relative comparisons of drug use. For example, MLC can be used to track changes in cannabis consumption over time and to compare consumption across different geographical areas.

The rate at which THC-COOH arrives at a wastewater treatment plant during the data collection week can be computed as the product of the concentration of THC-COOH (nanograms per litre [ng/L]) and the flow rate (litre per week [L/wk]). We then need to account for potential losses of THC-COOH between entering the sewer system and arriving at the treatment facility. Finally, we want to scale this quantity by the number of people serviced by the wastewater treatment plant so that we can compare geographical areas of different sizes. To put these all together, MLC can be computed as follows:

Equation 1

$$MLC = concentration \times flow \times \frac{1}{1 - losses} \div population$$

We will now explore this equation in depth to describe the sources of uncertainty for each term.

Concentration

The concentration of metabolites measured in wastewater could be affected by both the collection and the chemical analysis of the wastewater sample.

Errors that arise from sample collection and preparation remain unclear at this time. Our procedures adhere to the Sewage Analysis CORe group Europe (SCORE) network's best practices for wastewater analysis (Castiglioni et al. 2016), which were developed to standardize and improve WBE. The wastewater treatment facilities are well managed and use high-quality equipment to sample proportionally to the flow from the centre of the incoming wastewater channel. We do not expect issues with freezing or shipping since the samples are typically still frozen when they arrive, and a single freeze-thaw cycle likely has very little effect on THC-COOH concentrations (Causanilles et al. 2017). However, THC-COOH losses have been previously reported during sample preparation (Been et al. 2016), and errors could be caused by imperfect proportional-to-flow sampling, by wastewater acidity affecting the behaviour of THC-COOH, or by a variety of other factors that can affect THC-COOH (Causanilles et al. 2017). We also introduced a step to combine the seven daily samples into a weekly aggregate to reduce testing costs while averaging over a longer period of time. Although this is a straightforward addition to the process, it still has the potential to introduce errors that have not been previously examined.

The chemical analysis of the prepared samples seems highly reliable. The McGill lab has strict protocols, high-performance equipment, rigorous quality assurance practices and methods that have been performance-tested by the SCORE network. The lab analyzes each weekly wastewater composite three times, and the three measurements tend to be similar to one another (coefficient of variation = 12%). However, errors may occur that bias the chemical analysis. Laboratory measurements of THC-COOH concentration in wastewater have been observed to be biased downward for reasons that are not yet understood (Gracia-Lor et al. 2016). Another potential issue is that the analyses for each month were performed at different times, so the analysis calibration could be different because of different operators, ambient lab conditions, equipment maintenance, or other factors that could lead to different results when the tests are spaced months apart.

We have planned several experiments to validate our procedures and to help us determine the magnitude of these potential errors. First, we are testing the effect of calibration errors, or errors resulting from the chemical analysis occurring at different times, by reanalyzing all the past samples for one site. All the months will have the same calibration for the retest, but potentially different calibrations for the original testing. Second, we are testing for possible biases in the chemical analysis by sending some samples to an independent lab. Third, we are testing the process of creating a weekly composite by analyzing the seven daily aggregates and comparing them with the weekly composite. Along with these planned experiments, we are considering a few other approaches to validate the concentration data. The THC-COOH concentrations tend to vary substantially from month to month, and it is not clear whether this variation arises from true differences in cannabis consumption, from different losses from one month to the next, or because the samples are not representative of the wastewater. In the latter case, we could improve our estimates by standardizing our measurements based on reference compounds that should remain fairly constant (such as ammonia, which is a component of normal urine). Other candidates for reference compounds are cotinine, a by-product of cigarette smoking, and codeine, a pain reliever. Both of these compounds are likely consumed at relatively stable and known rates. We have not yet measured these reference compounds, so we would need to either retest the previous samples or begin this standardization moving forward. Additionally, we want to test whether proportional sampling is being well executed at the wastewater treatment plants since non-proportional sampling could lead to biases in our estimates. To test this, we could compare the drawn samples' timestamps with high-frequency flow rate data to ensure that the timing properly produces flow-proportional sampling.

Flow

Wastewater treatment plant operators measure flow rate on a regular basis to understand and control how their sites are functioning, so these measurements should be high quality. We tested these data by comparing the flows with weather events in the city. In some of the treatment plants, the flow strongly and clearly responded to rain events. In other sites, the response was weak or not present, but this could be because of sewer systems designed to treat storm water separately. We also tested the flow data by comparing daily flows with ammonia concentrations at the wastewater treatment plants where this information was available. We found the flow was strongly negatively correlated with the ammonia concentration, as expected because their product should remain constant. At this point, there is no reason to be concerned about the quality of the flow data collected by the wastewater treatment plants.

Losses

Losses account for THC-COOH that was excreted into the wastewater but never reached the treatment plant. THC-COOH can degrade in wastewater under some conditions (Ramin et al. 2016; Ramin et al. 2017). However, the rate of degradation differs by site because it depends on the established populations of microbes in the wastewater system, similar to how the biology in one person's gut is different from everyone else's (McCall et al. 2016). This complicates comparisons between sites and cities. We do not currently have any information about how degradation differs between wastewater treatment plants in our pilot study, and we do not know the typical degradation rates for wastewater treatment plants in Canada. However, degradation has been estimated to be under 10% in most cases (Castiglioni et al. 2016), so we are proceeding as though there are no losses. We would like to revisit this idea when more information becomes available.

Scaling by population

To compare sites or cities of different sizes, we would like to scale the quantity of THC-COOH by the number of people who are contributing to the wastewater.

One way to estimate the population contributing to the wastewater is to use census data to count the number of people living within the physical boundaries of the wastewater treatment plant catchment area. Census data provide accurate information for people's permanent place of residence at the time of the census. These counts can then be updated to reflect changes since the census—for example, by measuring the changes in the number of dwellings in the area and projecting the population accordingly. However, the population permanently living in a region is not the same as the population contributing to the wastewater at any given time. There are commuters and travellers who do not live within a region but who contribute to its wastewater, or people who live in the region but are away and do not contribute to the wastewater. Also, waste from portable toilets and septic tanks in other regions can be deposited into a city's wastewater treatment system, inflating the contributing population by an unknown amount. Nevertheless, we expect these effects to be small compared with the number of permanent city residents who contribute to the wastewater every day. Therefore, we are using population estimates based on the 2016 Census that have been updated to reflect the latest dwelling growth as of March 2018.

An alternative population estimation method involves using evidence of human biomarkers within the wastewater itself. Lai et al. (2011) used measurements of prescription pharmaceuticals to estimate the number of people contributing to the wastewater. They chose Atenolol, a medication used to reduce blood pressure, which is used by 1% to 3% of the local population. They also raised the idea that the population estimate can be based on multiple compounds in parallel for increased accuracy. This population estimation method improved their precision for estimating per capita drug consumption compared with using census information.

Been et al. (2016) took a hybrid approach where they used census data to estimate the mean population, but used biomarkers in the wastewater (ammonium concentrations) to estimate how much the population fluctuated. They then included these fluctuations as uncertainties when calculating cannabis consumption per capita. We have not yet explored the possibility of using human biomarkers in the wastewater to estimate the contributing population.

Extrapolating to national cannabis consumption (Equation 2)

MLC can be used to examine trends across time and to compare different geographical regions, but it does not tell us the size of the overall cannabis market. A WBE estimate of national cannabis consumption could be used to calibrate cannabis surveys and to estimate the size of the illegal cannabis market after legalization.

To estimate the rate of cannabis consumption in Canada based on MLC, we need to know the following three factors: the cannabis's THC potency, the THC-COOH excretion rate for a given dose of THC, and the relationship between cannabis consumption within our measured areas and the rest of the country. The relationship is as follows:

Equation 2

$$national\ cannabis\ consumption = MLC \times \frac{1}{mass\ excretion\ rate} \times \frac{1}{THC\ potency} \times effective\ population$$

We will now expand on each term in this equation, including what is known and uncertainties.

Mass excretion rate

The mass excretion rate is the mass of THC-COOH excreted compared with the mass of THC in the cannabis product consumed. Its inverse is often called the correction factor. The excretion rate is often presented as a molar excretion rate, which is the number of THC-COOH molecules excreted compared with the number of THC molecules in the cannabis product. To convert from a molar to a mass excretion rate, we need to account for the different molar masses of the two substances, which is a ratio of 0.91 for THC to THC-COOH (Gracia-Lor et al. 2016).

The excretion rate for cannabis is complex and difficult to quantify. It depends on the consumption method (e.g., inhalation versus oral ingestion), the consumer's biology and even the smoking technique (Gracia-Lor et al. 2016; Huestis 2007). It could also depend on the frequency of consumption, the product type (e.g., dried leaf versus hashish), co-consumption with other drugs and the user's adiposity. From the scientific literature, we have different estimated excretion rates only for smoking dried cannabis (molar excretion rate = 0.5%, Gracia-Lor et al. 2016) and eating cannabis products (molar excretion rate = 2.2%, Gracia-Lor et al. 2016). This does not reflect the full range of product types, consumption methods (e.g., vaping) or consumption frequencies. Even these excretion rates are based on little pharmacokinetic research—only one study of 16 participants examined the excretion rate after smoking. Furthermore, most of the research has been done on healthy white male adults (Gracia-Lor et al. 2016), and excretion rates could vary systematically by race, gender and age.

Another important issue with excretion rate research is that it has mostly focused on measuring metabolites in urine, not feces, even though feces is the main route by which cannabis metabolites are excreted from the body (Huestis 2007). While THC-COOH may not be the primary metabolite in feces (Huestis 2007), it can still be present in substantial quantities in some circumstances (Gracia-Lor et al. 2016). THC-COOH excreted in feces is likely to dissolve into the wastewater and contribute to wastewater-based measurements (Been et al. 2016; Gracia-Lor et al. 2016). For edible cannabis products, the fecal excretion rate has been estimated to be more than four times higher than the urinary excretion rate, but the fecal excretion rate has never been measured for smoking (Gracia-Lor et al. 2016). Ultimately, we need a wastewater excretion rate for THC-COOH, which we define as the fraction of the consumed THC that ends up dissolved in the wastewater as THC-COOH. The wastewater excretion rate seems to be the sum of the excretion by the two routes, urine and feces, the latter of which is currently unknown and could be as high as or higher than the former.

Considering all of these factors, the excretion rate is a major source of uncertainty. More clinical research is needed to determine an excretion rate for urine and feces, for other demographic groups and consumption frequencies, for different product types and consumption methods, and to test for the effects of co-consumption (e.g., with alcohol).

Conceptually, it is possible to combine distinct excretion rates into a composite rate that captures average excretion. For example, inhalation and ingestion excretion rates could be combined if we knew the fraction of THC that was inhaled versus ingested. This can likely be approximated using survey data, including the 2018 National Cannabis Survey (Statistics Canada), the 2017 Canadian Cannabis Survey (Health Canada) and the 2018 Canadian Tobacco, Alcohol and Drugs Survey (Statistics Canada). However, this approach presents several challenges. Survey respondents may have a tendency toward under-reporting, which could be more pronounced in users of some products over others. In addition, many consumers of edibles do not know how much cannabis they have consumed, so they report their consumption in terms of gummy bears or brownies, which can vary widely in strength from around 5 milligrams of THC per serving to over 200 milligrams of THC per serving (Friese et al. 2017). We would also need to convert concentrated products to equivalent dried flower quantities, which is a complex

task that has not been completed at this time. These factors make it difficult to determine what fraction of THC was consumed through inhalation versus ingestion, which highlights the need for better data on the consumption patterns of Canadians.

While we await additional research on excretion rates, we will approximate using the best information available. Since the majority of cannabis users consume dried flower or leaf by smoking (77.6%, coefficient of variation = 2.94, National Cannabis Survey wave 1, Statistics Canada), we will proceed as though smoking is the dominant form of cannabis use. We will consider only excretion via urine since that is all that is available. Thus, our provisional mass excretion rate is 0.5% ÷ 0.91 = 0.55%, leading to a correction factor of 1 ÷ 0.55% = 182. This correction factor is likely an upper bound; including edibles or fecal excretion would result in higher excretion rates of THC-COOH and a lower correction factor.

THC potency

MLC multiplied by the correction factor equals the mass of THC consumed per capita. To calculate the cannabis mass per capita, we need to know the average potency, which is the fraction of the dried cannabis that is THC. Average THC potency is challenging to estimate because it varies widely across products, from under 5% to over 20% (Ontario Cannabis Store 2018). Even the same product can vary substantially from one batch to the next, as reflected in the wide ranges for each single product (e.g., Northern Lights THC = 9% to 15%, Ontario Cannabis Store 2018). Moreover, illicit cannabis often does not come with potency information, so the potency would be unknown to the consumer.

ElSohly et al. (2016) found that the potency of illicit cannabis plant material seized in the United States had risen from 4% in 1995 to approximately 12% in 2014. Been et al. (2016) quote an average potency of 11% for seized cannabis products in Switzerland. While reliable potency information for cannabis products in Canada is currently a data gap, we are using an approximate value of 12% and will carry the uncertainty of this value through the calculation when we quantify our combined uncertainty. It would be helpful to have an up-to-date Canadian value, based on scientific evidence, to reduce the uncertainty in this parameter.

Extrapolating to the unmeasured population

The final term in Equation 2 is the effective population, which can be calculated as the population covered by our wastewater treatment plants divided by the national share of cannabis they consume. This term can be understood as two steps. First, the per capita cannabis consumption multiplied by the study area population equals an estimate of the total cannabis consumed within the study area. If we want to extend this estimate to the entire country, we need to scale by the fraction of the national cannabis consumption that occurred within the study area. If the rest of the country used cannabis at the same rate as the study area, the effective population would simply be the national population. However, if, as an extreme example, nobody used cannabis outside the study area, the effective population would be the population covered by the wastewater treatment plants.

The simplest way to estimate the effective population is to assume cannabis consumption at our sites was representative of the rest of the country, so the effective population is then equal to the national population. However, our pilot sample is not a representative sample of people: it includes five major cities across the country and is far more urban than Canada as a whole. Even within the selected cities, our sample areas may not be representative of the entire city. Toronto, Montréal and Halifax all include wastewater treatment plants in their downtown areas, but these plants do not capture the entire metropolitan areas' wastewater. Some evidence from surveys suggests that consumption patterns are not the same in urban versus rural areas (Rotermann and Pagé 2015). However, for now we will proceed with the assumption that cannabis consumption at our sites is representative of the country as a whole and will revisit this assumption when more information becomes available.

Utility of MLC versus cannabis consumption

Ultimately, we would like to work with cannabis consumption rather than MLC, but estimating cannabis consumption requires the excretion rate and drug potency. These factors add a huge amount of uncertainty to our estimate. Therefore, it is helpful to know what we can learn from the relatively more certain MLC.

MLC can be used for relative comparisons, such as changes over time or across locations, where MLC estimates are available for both points of the comparison. For a difference in MLCs to correspond to a difference in drug consumption, the parameters linking the MLCs to the corresponding drug consumption (potency, excretion rate and degradation in the sewer) need to be the same for both points of the comparison. While this condition may not be satisfied exactly—as degradation could differ between sewer systems, and a shift toward edibles would change the composite excretion rate—it is likely close in many situations. Thus, MLC can often be used for comparing WBE estimates across different times and locations. In fact, the international WBE community typically does not compute cannabis consumption, but instead compares results in terms of MLC.

Quantifying uncertainty

We have discussed many sources of uncertainty: creation of a composite water sample for the week, chemical analysis of the water sample, flow measurement, degradation in the sewer system, excretion rate, fraction of cannabis consumed by product type and method, THC potency, number of people who contribute to the wastewater, and similarity between the cannabis consumption in our study areas versus the rest of the country. In addition, there is uncertainty associated with sampling the water (i.e., analyzing only a sample of water rather than all the water that passes through, and sampling one week out of every month). Some of these uncertainties are quantifiable with repetition and experimentation, such as the sample preparation and chemical analysis. However, other uncertainties are not currently quantifiable with our methods or the existing research, such as the excretion rate (since the fecal excretion rate has not been measured for smoked cannabis) and THC potency (because there is little research to work from). For these factors, we need to estimate the uncertainty based on expert opinion until there is more research.

With the uncertainties for each parameter, we want to compute an overall uncertainty for the WBE estimate of cannabis consumption. Lai et al. (2011) proposed a linear method for estimating overall uncertainty. The equation for estimating national cannabis consumption, obtained by substituting Equation 1 into Equation 2, is a product of many terms, each with an associated uncertainty. Lai et al. (2011) estimate the variance of that product using a first-order approximation. This approximation performs well as long as the coefficients of variation are relatively small for each parameter—around 30% or less. However, some of our terms have high uncertainty, which makes this approximation underestimate the true variance.

Because of the potential inaccuracies of the linear approximation for these purposes, Jones et al. (2014) proposed the more general approach of estimating the variance using Monte Carlo simulation. This method involves characterizing each term by a statistical distribution that reflects the uncertainty about its value. Ideally, this distribution would be based on data, but expert opinion can be used if data are unavailable. Values for the individual terms are then simulated at random from each of the distributions, and the back-calculation is performed using these simulated values. This procedure is repeated many times to obtain a simulated distribution for overall cannabis consumption, from which credible intervals can be calculated. The authors caution that it is crucial to recognize that there is also potential for systematic error (bias) in each parameter estimate.

Jones et al. (2014) also proposed a Bayesian Markov chain Monte Carlo method that extends the Monte Carlo method in two ways. First, it can be used to explicitly model variation in MLC at different points in time, reflecting the idea that metabolite flows in the wastewater could vary day by day or month by month because of differences in drug consumption. Directly modelling this variation improves the accuracy of the uncertainty estimation when the periods have different drug loads. Second, the Bayesian Markov chain Monte Carlo method can be used to pool multiple estimates of the same quantity to create a unified estimate. For example, instead of measuring only THC-COOH, we could measure two metabolites of THC, each of which would give an estimate of THC consumption. The Bayesian Markov chain Monte Carlo method is able to combine these estimates in a principled way and characterize the resulting uncertainty. Been et al. (2016) used this idea to combine WBE estimates with survey

estimates of cannabis consumption. They acknowledged the potential errors in the survey data, including the under-reporting of regular and occasional users and the possible increased rate of non-response for heavy users. They also acknowledged potential errors in the wastewater analysis, particularly the lack of scientific research about fecal excretion rate.

At this time, we are still exploring options for quantifying the uncertainty of our estimates. We will likely try both the Monte Carlo simulation, for its generality and simplicity, and the Bayesian Markov chain Monte Carlo method, for its ability to model variation in metabolite loads across time.

Validation

We can validate our results by comparing them with other sources. At the MLC level, we can compare our results with previous wastewater-based cannabis studies across Europe and around the world, many of which were done as part of the SCORE program (SCORE 2017). At the cannabis consumption level, we can compare our results with surveys of Canadian cannabis consumption (PBO 2016; Macdonald and Rotermann 2018; Cannabis Economic Account 2018; Provincial and Territorial Cannabis Economic Accounts 2018). To compare our results with surveys, we must estimate the annual total volume of dried cannabis consumed across all of Canada to ensure that we are using the same concepts and definitions.

We can also compare our results with local data near our pilot sites, rather than only with national aggregates, although these data do not typically have the same reference period. These data sources include the National Cannabis Survey; Canadian Community Health Survey; Canadian Health Measures Survey; Canadian Tobacco, Alcohol and Drugs Survey; and previous research by MacDonald and Rotermann that combines various survey data (Macdonald and Rotermann 2017; Macdonald and Rotermann 2018). Formal methods have not yet been developed for this phase of validation.

Demonstration of cannabis consumption calculation

The following example calculation shows how we plan to proceed and highlights which uncertainties are more important than others. We invite feedback on the parameter values we are using and encourage additional research on some of the critical values. In this illustration, we are aggregating all the wastewater treatment plants, but the same methods could be used to calculate MLC and cannabis consumption at the level of a city or wastewater treatment plant.

The typical measured concentrations of THC-COOH are approximately 140 ng/L. The total flow across all pilot sites is 33.5 billion L/wk. The population base across all the sites is about 8.4 million people. We assume that losses are negligible.

First, we use Equation 1 to compute MLC.

$$MLC = concentration \times flow \times \frac{1}{1 - losses} \div population$$

$$= 140 \frac{ng}{L} \times 33.5 \cdot 10^{9} \frac{L}{wk} \times \frac{1}{1 - 0} \div \left(8.4 \cdot 10^{6}\ people\right)$$

$$= 560\ \mu g / \left(person \cdot week\right)$$

Next, we use Equation 2 to estimate the total national cannabis consumption. We will use a molar excretion rate of 0.5%, leading to a correction factor of 0.91 ÷ 0.5% = 182 grams of THC consumed per gram of THC-COOH excreted. We will use a potency of 12% and an effective population equal to the national population of 37 million, which assumes the cannabis use in our sites is representative of the country as a whole.

$$national\ cannabis\ consumption = MLC \times \frac{1}{mass\ excretion\ rate} \times \frac{1}{THC\ potency} \times effective\ population$$

$$= 560 \frac{\mu g\ THC-COOH}{person \cdot week} \times 182 \frac{g\ THC}{g\ THC-COOH} \times \frac{1}{0.12} \frac{g\ cannabis}{g\ THC} \times 37 \cdot 10^{6}\ people$$

$$= 31 \frac{tonnes\ cannabis}{week} \times \frac{365 \frac{days}{year}}{7 \frac{days}{week}}$$

$$= 1600 \frac{tonnes\ of\ cannabis}{year}$$

This estimate is high when compared with survey-based estimates of cannabis consumption. Most current estimates of national cannabis consumption are based on the 2012 Canadian Community Health Survey—Mental Health and are updated using different methodologies. For example, the Office of the Parliamentary Budget Officer estimated 2018 cannabis consumption to be between 378 tonnes per year and 1,017 tonnes per year, with a point estimate of 655 tonnes per year (PBO 2016). Macdonald and Rotermann (2017) estimate 700 tonnes were consumed in 2015; extrapolating the upward trend for the annual volume of consumption, we could expect between 750 and 850 tonnes of cannabis consumed in 2018. The Provincial and Territorial Cannabis Economic Accounts provisionally estimated 21.1 grams of cannabis consumed per capita in 2017, which projects to about 770 tonnes of cannabis consumed in 2017 (Provincial and Territorial Cannabis Economic Accounts 2018). Finally, from the Cannabis Economic Account in the second quarter of 2018, the estimated size of the market ($5.7 billion per year) and the price of cannabis ($6.74 per gram) together imply a total annual consumption of 850 tonnes in 2018 (Cannabis Economic Account 2018).

Keep in mind, our wastewater-based estimate is highly sensitive to some of the uncertain parameters, especially the high uncertainty of the excretion rate. When both urine and feces are combined as routes of excretion into wastewater, the wastewater excretion rate is likely higher than 0.5%. While this rate is currently unknown for inhaled cannabis, it could reasonably be 2% or higher, given the high fecal excretion rate for ingested cannabis. A combined excretion rate of 2% would reduce our national estimate to 400 tonnes of cannabis per year. This sensitivity highlights the need for new research on cannabis excretion rates.

We can avoid the excretion factor by validating the MLC. Our estimated MLC of 560 µg/(person·week), or 80 µg/(person·day), is consistent with the typical loads measured in Europe, which commonly range from 30 µg/(person·day) to 150 µg/(person·day) (SCORE 2017). This suggests our procedures and analyses are reliable, and gives us confidence that our data can be compared across time and cities to discern trends.

Conclusions

Wastewater management is an old science (for example, notice the drainage systems in Greek ruins); however, wastewater-based epidemiology is relatively new. It was originally used in the 1990s to monitor the environmental impact of liquid household waste. Wastewater analysis has demonstrated its potential as a useful complement to established monitoring tools for illicit drug use. It has some clear advantages over other approaches as it is not subject to response and non-response bias, and can better identify the true spectrum of drugs being consumed, as users are often unaware of the actual mix of substances they consume. This methodology also has the potential to provide timely information in short timeframes on geographical and temporal trends (European Monitoring Centre for Drugs and Drug Addiction 2018). In this paper, we are attempting to be fully transparent about the methods we are using and considering. We invite feedback and additional research to help improve our estimates and the science of back-calculating cannabis use. We would like to appeal particularly to the scientific community for better data on cannabis excretion rates, potencies, consumption by method and product type, and degradation in sewer systems.

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