ODPRN suggested calculation of opioid milligrams of morphine equivalents

About the ODPRN

The Ontario Drug Policy Research Network (ODPRN) is a province-wide network of researchers who provide timely, high quality, relevant drug policy research to decision makers. We conduct research to determine real-world drug utilization, safety, effectiveness, and costs of drugs in Ontario, and have developed partnerships that allow us to engage in cross-provincial comparisons of drug safety and utilization.

We are funded to conduct pharmacoepidemiologic and drug policy research as part of an initiative to provide evidence to inform policy at the Ontario Ministry of Health (MOH). As such, the ODPRN works closely with the Drugs and Devices Division (DDD) of the Ontario MOH and other stakeholders to select key priority areas and topics for analysis. The work was also supported by ICES, which is funded by an annual grant from the Ontario MOH.

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Background

Opioids are a group of drugs commonly prescribed to treat pain. Some opioids are also used as cough suppressants or as treatments for opioid use disorder. The safety of prescription opioid use and the rate at which these medications are being prescribed is of considerable concern. In particular, studies have shown that opioids are being increasingly prescribed, and that higher doses and co-prescription with other substances (such as benzodiazepines, alcohol, or gabapentin) can increase the risk of overdose.[1-4]

Opioids used for pain include a number of different drugs with different formulations that vary on a chemical level. These differences affect how much of the drug a person needs (i.e. potency) to reach the same desired analgesic effect. To allow us to compare and combine all opioid drugs, we calculate dose in milligrams of morphine or equivalent (mg MEQ; this may also be referred to as MME [milligrams morphine equivalent] or mg MED [milligrams morphine equivalent dose]), which is a standardized measure of the total amount of opioid dispensed on a single prescription or more broadly into the community. This is calculated by adding up the total number of milligrams of drug contained in every opioid unit (e.g., tablet, capsule, liquid or patch) dispensed, and then converting this into an equivalent morphine dose. This allows us to estimate the total amount of opioids dispensed, incorporating the dose of drug, the type of formulation, and the potency of the particular opioid. This method has been used in several public reports and scientific papers.[5-7]

MEQ

Milligrams of morphine or equivalent (MEQ) is a standardized measure for opioid content that allows for the comparison of drugs with different strengths by converting them all to their equivalent amount in milligrams of morphine.

Table 1: Relevant Ontario Data Sources

Data	Description
Ontario Drug Benefit (ODB) Database	The ODB database contains data for prescription drugs received under the Ontario Drug Benefit program, from April 1991 onwards. This program covers prescriptions drugs for all residents in Ontario with a valid health card who are over the age of 65. Residents under the age of 65 can also qualify for this program if they are in financial need (Ontario Works), receive disability support or home care, have high drug costs relative to household income, or reside in a long-term care home. This dataset contains prescription details including the Drug Indentification Number (DIN), quantity, day supply, and route administered.
Ontario Narcotics Monitoring System (NMS) Database	The NMS database collects data on dispensed prescriptions for narcotics, controlled substances and other monitored drugs, irrespective of whether the prescription is paid for under a publicly funded drug program, through private insurance, or by cash. This dataset contains information on filled prescriptions from July 2012 onwards, and includes prescription details including the DIN, quantity, day supply, and route administered.
NMS Monitored Drug List	The NMS Monitored Drugs List (MDL) provides a list of products that the Ontario Ministry of Health has selected for monitoring. In general, drugs captured within this list include opioids, benzodiazepines, antihistamines, stimulants, and testosterone that were dispensed in the province from July 2012 onwards. The MDL can be downloaded in Excel or XML format here. To calculate MEQ, the NMS Monitored Drugs List (MDL) should be limited to opioid medications, and the following elements should be added to the list: • **Drug Class**: Classifies opioids into drug type (e.g. Oxycodone, Fentanyl, Hydromorphone, etc.) • **MEQ Flag**: indicator to determine whether a morphine equivalence (MEQ) conversion is available for a particular opioid. Generally, dose calculations are only performed for oral and transdermal opioid formulations (injections are not included), and where there is a dose conversion factor (Table 2) • **Strength**: A numeric strength value for each drug. This can be derived from the character strength value included in the drug list (For example, convert character value '30mg' to '30').

Background

An MEQ can be calculated for an opioid when there is a valid MEQ conversion (**Table 2**). The basic MEQ dose calculation for an opioid claim is computed using the following equation:

*dose=quantity*strength*conversion_factor*

average daily dose=dose/day supply

Where *quantity* is the quantity on the claim from the prescription database (i.e. ODB or NMS dataset) and the *strength* is the value for the DIN from the NMS Monitored Drug List. The strength value in the NMS Monitored Drug List will have to be converted to a numeric form prior to using in the calculations. Each opioid has a conversion factor and strength. Note that Fentanyl is handled differently from all other opioids due to its form of administration (see notes below). The average daily dose in MEQs can be calculated by dividing the dose by the days supply on the claim recorded in the prescription database (i.e. ODB or NMS dataset).

Transdermal Fentanyl Conversion Notes:

- The use of fentanyl patches may vary per person. Generally, a single fentanyl patch is used over a 3 day period, however sometimes individuals may use a fentanyl patch for only 2 days. If an individual is using a patch for 3 days, they are receiving 3x the dose on the patch (same dose for 3 days). If they use the patch for 2 days, they receive 2x the dose on the patch.
- By using the day supply and quantity field in the prescription database (i.e. ODB or NMS dataset), we can identify prescriptions that suggest a patch is being used for 2 days. This is calculated as the day supply divided by the quantity field. If this value equals 2, we assume that the individual is using a patch for duration of 2 days. In all other cases we will assume an individual is using a patch for 3 days.
- If an individual is deemed to be taking a patch for 3 days (day supply/quantity not equal to 2), we adjust the day supply value to equal 3 when this value is less than 3. This is to account for overestimating the dose received if the day supply field is incorrect. MEQ for fentanyl is then:

*dose=quantity*fent_equiv*fentfactor*

Table 2: Oral Opioid Analgesic Equivalence Conversion Table

Opioid	Number Mg	Ratio (Opioid:Morphine)
Morphine[1]	30 mg	1:1
Codeine[1]	200 mg	1:0.15
Oxycodone[1]	15-20 mg	1:1.5
Hydrocodone[2,3]	30 mg	1:1
Hydromorphone[1]	6-7.5 mg	1:5
Meperidine[1]	300 mg	1:0.1
Tramadol[4]	300 mg	1:0.1
Transdermal fentanyl[1] (routeadm is PATCH or TRANS PAD, or Trans Patch)	12.5mcg/h→30-67morphine* 25mcg/h→60-134mg morphine 37.5mcg/h→135-179mg morphine 50mcg/h→180-224mg morphine 75mcg/h→270-314mg morphine 100mcg/h→360-404mg morphine If 12.5mcg/h then Fent_Equiv = 1 If 25mcg/h then Fent_Equiv = 2 If 37.5mcg/h then Fent_equiv=3 If 50mcg/h then Fent_equiv=4 If 75mcg/h then Fent_equiv=5 If 100mcg/h then Fent_equiv=6 *12.5 was assumed based on a 3.8 meq/ug Mid-points were used for ranges	If day supply/quantity=2 then: Fent_equiv=1 → 1:48*2 Fent_equiv=2 → 1:97*2 Fent_equiv=3 → 1:157*2 Fent_equiv=4 → 1:202*2 Fent_equiv=5 → 1:292*2 Fent_equiv=6 → 1:382*2 If day supply/quantity is not equal to 2 then adjust fentanyl day supply when <3 days to equal 3 and use the following conversion: Fent_equiv=1 → 1:48*3 Fent_equiv=2 → 1:97*3 Fent_equiv=3 → 1:157*3 Fent_equiv=4 → 1:202*3 Fent_equiv=5 → 1:292*3 Fent_equiv=6 → 1:382*3
Other fentanyl formulations[4]	**Fentanyl buccal or SL tablets, or lozenge** (routeadm= “BUC STRIP” or “TAB SL” or “EFF TAB”)	1:0.13
	Fentanyl film or oral spray (currently not in drug list)	1:0.18
	Fentanyl nasal spray (currently not in drug list)	1:0.16
Methadone	Dose equivalence between methadone and other opioids has not been reliably established	Excluded from analyses
Buprenorphine	Dose equivalence between buprenorphine and other opioids has not been reliably established	Excluded from analyses

1. All conversions (except for hydrocodone and tramadol) are adapted from the National Opioid Use Guideline Group (NOUGG) guidelines available at: **http://nationalpaincentre.mcmaster.ca/documents/opioid_guideline_part_b_v5_6.pdf**
2. The conversion for hydrocodone is not available in the NOUGG guidelines. Therefore, the conversion is derived from the CDC and American Guidelines available at:
    - **https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf**
    - **http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf** (**Table 5**)
3. The NOUGG guidelines and a review (Nielsen, Suzanne, et al. “A synthesis of oral morphine equivalents (OME) for opioid utilisation studies.”) suggest using a conversion factor of 5 for hydromorphone. However, the CDC guidelines and American Guidelines recommend a factor of 4 for converting hydromorphone. Will monitor the suggested conversion when the revised Canadian guidelines are released and decide if any changes are needed. **http://onlinelibrary.wiley.com/doi/10.1002/pds.3945/abstract**
4. Conversions for newer fentanyl formulations (non-transdermal) and tramadol were adopted from United States Centers for Medicaid and Medicare Services (CMS) recommendations: **https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Opioid-Morphine-EQ-Conversion-Factors-March-2015.pdf**

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