Morphine Milligram Equivalent (MME) Calculator: Frequently Asked Questions (FAQs) for HEAL Researchers

Topics:

****Please note that this tool is intended for RESEARCH PURPOSES ONLY. It is not intended for clinical use.**

What is Morphine Milligram Equivalent (MME)?

MME is a standardized metric to report prescribed opioid use for pain management. It is used to estimate the analgesic profile and/or overdose potential of prescribed opioid medications. MME equates different opioids into one standard value, based on morphine and its potency. MMEs are not appropriate for opioid analgesics that serve as Medications for Opioid Use Disorder (MOUDs). This tool should not be used for research participants using MOUDs.

What are the HEAL requirements for collecting MME data?

The NIH HEAL CDE program requires clinical pain studies that involve human subjects to collect data at two timepoints (e.g., baseline and a later timepoint to be determined by the study team, based on their specific needs/goals) on prescribed/dispensed opioid use for participants using opioids for pain management. For participants not using opioids, studies should explicitly report that the participant was not taking any opioids at the specified timepoint. Studies are required to collect and report opioid use data as daily MMEs. Studies must report: the name of the opioid; the dose; prescription duration; total days exposed; days elapsed during follow-up, hospital stay, or enrollment; the MME conversion factor; and the calculated MME values.

The Case Report Form (CRF) and CDE for MME are available for download at the HEAL CDE Repository here: https://heal.nih.gov/data/common-data-elements-repository?combine=MME&questionnaire=All&domains=All&file_language=All&copyright=All

A REDcap template is available on request, contact the HEAL CDE team (heal_cde@hsc.utah.edu).

Why am I being required to collect MME data in my study?

There are four different ways to standardize MME calculations, which vary by study design and intent of the study (overdose risk vs analgesic profile). We are requiring HEAL-funded studies on pain management in human subjects to report on opioid data that are used to calculate daily MMEs to automate values based on these standardized MME calculations. This way, an end-user could compare MME values across HEAL-funded studies, regardless of the intent of the trial. Reporting the underlying variable data used to generate the MME value also ensures that if MME calculations change in the future (based on guidelines or literature), we already have access to the necessary data to re-calculate MMEs.

How can I easily convert prescription opioid use to MME for the purposes of my study and HEAL data requirements?

Since reporting MME requires calculating an MME value from several variables related to opioid name/dose/duration/etc, researchers at Wake Forest University, University of Utah, and

the National Institute of Health collaborated to develop an online calculator that researchers can use to generate the MME value more easily from study data. The tool is available for free here: https://research-mme.wakehealth.edu.

Who should use the MME online calculator tool?

HEAL-funded clinical pain studies that involve human subjects funded in FY23 and beyond should use this tool. The tool is meant to be used by researchers to convert participants' prescription opioid use into a variable that can be compared across studies, and to be able to compare the different MME per day calculations to each other. **The tool is not meant to be used clinically or used to estimate opioid doses for treating Opioid Use Disorder.** Additionally, the tool is designed to be used by research staff, not individual participants.

Can the MME calculator be used for intravenous opioids?

No. The conversion factors used to convert opioid medications to MME have only been validated for oral medications or other specified formulations (e.g., topical patch, buccal administration, nasal spray).

How does the MME Calculator work?

Medication exposure can represent actual exposure (opioid medications taken, e.g., in an inpatient setting). MME could also represent potential exposure (e.g., for outpatient medications, the calculation is most often based on the opioid prescriptions with an assumption that the person "could" have taken all the prescribed medications). Medications dispensed for "as needed" (PRN) use are assumed to have been consumed.

For each opioid medication, the total actual or potential exposure to that medication within the timeframe under review is calculated as:

dose * number of doses per day * duration in days

The total exposure to the opioid is multiplied by a conversion factor that converts the amount to total MME for the exposure.

The total MME exposure is converted to MME per day according to 4 possible definitions, as described in: Dasgupta N, Wang Y, Bae J, Kinlaw AC, Chidgey BA, Cooper T, Delcher C. Inches, Centimeters, and Yards: Overlooked Definition Choices Inhibit Interpretation of Morphine Equivalence. Clin J Pain. 2021 Aug 1;37(8):565-574. doi: 10.1097/AJP.0000000000000948. PMID: 34116543; PMCID: PMC8270512.

Definition 1—Total Days Supply. The numerator is the sum of MME across all prescriptions. The denominator is the sum of durations across all prescriptions.

Definition 2—On-therapy Days. The numerator is the sum of MME across all prescriptions. The denominator is number of unique calendar days across all prescriptions. When prescriptions overlap, each calendar day is counted only once.

Definition 3—Fixed Observation Window. The numerator is the sum of MMEs across all prescriptions. The denominator is a time window that is defined at the study level, such as a follow-up window, time or time elapsed during a hospital stay or beneficiary enrollment. For example, opioids taken during the past 90 days.

Definition 4—Maximum Daily Dose. The highest single-day MME exposure, irrespective of days supply.

How do I access the calculator?

Visit the website: https://research-mme.wakehealth.edu. This tool is available to researchers. However, please note that researchers/users will need to login with their ORCID ID to access the calculator. If you are having problems accessing the calculator, you may need to reach out to your institution (since security levels range by institution) to get permission to access the tool for research purposes.

What information do I need to use the calculator?

For each opioid medication applicable to the participant: Medication, amount per dose, number of doses per day, number of days/duration of the medication

Study-specified fixed time window (e.g., 7 days, 30 days, 90 days) is needed for definition 3.

Does the calculator store any data that is entered into it after the MME values are generated?

No, the calculator does not store any data, nor does it track specific users or IP addresses. Users should export their data to Excel or CSV using the export function if they would like to save the MME data. The calculator will only track analytics on how many users access and use the tool.

What medications are included in the conversion calculator?

Buprenorphine
- Buprenorphine tablet/film (mg) sublingual
- Buprenorphine buccal film (mcg)
- Buprenorphine patch (mcg/hr) transdermal

Butorphanol (mg)
Codeine (mg)

Dihydrocodeine (mg)
Fentanyl
    Fentanyl buccal (mcg)
    Fentanyl oral lozenge (mcg)
    Fentanyl nasal (mcg)
    Fentanyl patch (mcg/h)
Hydrocodone (mg)
Hydromorphone (mg)
Levorphanol tartrate (mg)
Meperidine HCL (mg)
Methadone (mg)
Morphine (mg)
Opium (mg)
Oxycodone (mg)
Oxymorphone (mg)
Pentazocine (mg)
Tapentadol (mg)
Tramadol (mg)

The calculator uses mostly oral medication data, with a few transdermal medication options available (e.g. fentanyl patch transdermal). The calculator includes, where applicable, both short-acting and long-acting formulations. Please note that this calculator is only meant to be used to calculate MME data for the medications listed above, and is only applicable to these drug formulations at this point. **Scenarios involving methadone and buprenorphine for the treatment of Opioid Use Disorder should NOT use this calculator.**

Why does the calculator have a "with buprenorphine" and "without buprenorphine" filter?

The tool is intended only for research purposes where prescription data are used to calculate an equianalgesic MME. The calculator features options to analyze results with or without buprenorphine, accommodating its emerging role in pain research but recognizing that use of buprenorphine for pain management (vs Opioid Use Disorder treatment) is not universally accepted.

What is the difference between therapy days and observation window?

Therapy days (MME per day Definition 1—Total Days Supply and Definition 2—On-therapy Days) reflects the duration of the prescription. This will vary from patient to patient.

Observation window is defined for the study as a whole, and can reflect periods of time during which the participant had no opioid exposure. This calculation is typically used to accommodate fluctuations in opioid use/unstable opioid use for pain management.

For example, suppose a participant had a prescription for codeine for 5 days. The study does a 30 day follow up, examining opioid use during the follow up timeframe. The therapy days for this participant would be 5; the observation window would be 30.

How was this calculator developed, and what research was used to determine the MME for each medication? How was the accuracy determined for the calculator?

Extensive testing was done on the expected calculated response (determined a priori) and compared to actual response produced by the calculator. Extensive research was done on the conversion factors to be used for the calculator. For more information on the scientific methods used to develop this calculator, refer to the manuscript here: Adams MCB, Sward KA, Perkins, ML, Hurley RW, Standardizing Research Methods for Opioid Dose Comparison: The NIH HEAL Initiative Morphine Milligram Equivalent Calculator, PAIN, 10.1097/j.pain.0000000000003529

Have the standard conversion factors changed for opioid medications?

Some of the conversion factors have been updated. Please see the manuscript (above) for more details on the conversion factors and the research underlying updated conversion factors. This is also why it is important to collect the medication name, dose, and prescription duration (in addition to the MME value).

What is the difference between this calculator and previous MME calculators?

This online calculator incorporates a more comprehensive list of opioid medications, includes buprenorphine as an opioid analgesic for pain management, and is based on the most recent research/evidence for MME conversion factors.

How can data from the new MME calculator be integrated with existing datasets that used previous conversion factors or opioid measures? How should I reconcile differences between metrics?

If you have the input data (drug name, dose, prescription duration), you can apply the updated calculation to the previously collected data. It is recommended that you use the conversion factors embedded in the calculator tool to enable consistent cross-trial comparisons within the HEAL clinical pain research portfolio.

What will happen if research evolves and conversion factors are updated? What about experimental opioids that are in development – how will those be incorporated into the calculator?

As of right now, the calculator is locked, but it was developed to allow new medications and/or conversion factors to be added or updated in the future.

What information from the table needs to be collected for the CDE?

If the participant received or was exposed to any of the listed opioid medications for pain management (Yes/No).
If yes, the information used to calculate the total MME (medication, dose, number of medications per day, duration), and durations to calculate MME per day (the study time windows). Use of the MME conversion factors corresponding to the calculator is assumed; if other conversion factors were used to calculate MME, those conversion factors should be specified.

Note that this tool should not be used to inform clinical decision making nor should it be applied to opioid analgesics used to treat Opioid Use Disorder.

Can this calculator be used when studying specific pain conditions?

Yes. This calculator is not validated across specific diagnoses. Instead, it is meant to be broadly applicable for research where opioid medication data was collected since the calculator simply transforms the opioid medication data that was already collected. acc

Can this calculator be used to calculate MME from non-opioid substances?

No. This tool is only meant to be used for research purposes, with the list of opioid medications that are listed above.

Is it possible to integrate the tool with programming languages (such as R or SAS)?

Yes. The web tool has an application programming interface (API).

Who should I contact if I have questions or need help with the calculator?

Start with the HEAL CDE team (heal_cde@hsc.utah.edu). Be aware that they may refer your question to the developers at Wake Forest or the University of Utah.