

Evaluation and Comparison of Online Equianalgesic Opioid Dose Conversion Calculators

This article will review the substantial differences among the available opioid conversion calculators.

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Opioids are among the most used analgesics for moderate-to-severe chronic pain management.¹ Opioids can be given via virtually every route of administration, which affords significant dosing flexibility. Although oral administration generally is the preferred route when possible, opioids may be administered via oral, transmucosal (sublingual, buccal, intranasal), transdermal (passive, iontophoresis), spinal (intrathecal, epidural), rectal, topical, and intra-articular routes.¹ Generally, it is not possible to define maximum opioid doses for individual patients because the dose is adjusted based on the intensity of pain and level of opioid tolerance from previous and regular exposure.² When pain is not adequately controlled

despite increasing doses of the opioid or because the presence of intolerable adverse effects influences compliance, switching opioids or changing the route of administration may be indicated.^{3,4} Therefore, variable analgesic potencies of different opioids may be considered, with specific attention paid to analgesic effect, and the potential for overdosing or underdosing, the worst outcomes of which could be death or withdrawal, respectively.

Although opioids are one of the oldest therapeutic classes of medications, conversion from one or more opioids to another remains haphazard and variable. Considerable confusion persists about the process of opioid conversion when medications are rotated, or switched, which can be necessary to realize the most favorable balance of therapeutic effects and

side effects in patients who require opioid analgesic therapy as a component of overall pain management.⁵ Opioid rotation, defined as “a change in opioid drug or route of administration with the goal of improving outcomes,”⁶ begins with the selection of a safe and effective starting dose for the new opioid.³ Once initiated, the new therapy must be individualized via dose titration and treatment of adverse effects. Given the large differences in potency among opioids, receptor variability and affinities, polymorphic receptor variation, and individual tolerability, the selection of a starting dose must be conservatively estimated, giving careful consideration to the relative potency between the existing opioid(s) and the new one.⁷ Ideally, clinicians should switch with an initial dose that does not result in adverse effects or abstinence but maintains efficacy. In clinical practice, however, determination of optimal initial doses when rotating opioids is a challenge.

Clinicians generally calculate doses for opioid rotation using equianalgesic dose tables, but published data for conversion frequently are inconsistent.¹ Primary and secondary literature, company package inserts, and online sources for opioid conversions have conflicting equianalgesic dosing guidelines.⁴ Some conversion tables refer to older studies using single-dose designs rather than chronic dosing at steady state.¹ The extrapolation of the results from single-dose studies to the context of chronic opioid dosing is, therefore, not valid.¹ Moreover, the various tables often indicate different conversion ratios,⁴ which further complicate conversion calculations for opioids.

Aside from potential drug interactions and compromised organ function, providers must consider interpatient and inpatient polymorphic variability, genetics, and physiological differences.⁸ Important considerations

in converting from one opioid to another also include demographic factors, comorbidities, and drug interactions. In considering which specific opioid should be tried next, clinicians should weigh a patient’s history of any drug sensitivities or experiences with specific drugs; drug characteristics that may increase or decrease safety or efficacy, given the patient’s clinical status; drug characteristics that may offer previously unrealized benefits unrelated to pain relief (eg, convenience, improved adherence, less reliance on oral administration, or access to a regular non-opioid drug in a combination product); and problems related to financial issues or insurance coverage.⁷

If a clinician selects an opioid that requires enhanced knowledge for safe prescribing, such as methadone or transmucosal fentanyl, they should ensure that their skills are adequate, obtain appropriate consultation, or refer to persons with expertise in prescribing these drugs. To reduce the risk of unintentional overdose when pain intensity may be changing quickly or when rapid titration is needed, opioid rotation in the setting of acute pain management should employ a short-acting opioid, rather than an extended-release formulation or methadone.⁷

Although opioid rotation is a common practice, there are substantial limitations in the standard of care. To reduce the risk of unintentional overdose, the conversion ratio calculated for a patient undergoing opioid rotation should be adjusted based on clinical assessment of risk. Since it is unlikely that a standard algorithm could be developed to meet all of the considerations outlined herein for every patient, opioid rotation remains both art and science, requiring experience and skill.⁷

At the time of manuscript submission, there were eight equianalgesic conversion calculators available online.

Unfortunately, there are substantial differences in availability, quality, complexity, features, and limitations among the eight. While calculators can help prevent computational errors, clinical judgment and individualization of treatment are necessary to switch a patient safely and effectively from one or more opioids to another.

Comparison of Online Calculators Methods

Primary and secondary literature, manufacturers’ package inserts, and online sources for opioid dose conversions have conflicting equianalgesic dosing guidelines and recommendations. This disparity creates considerable confusion about the process of opioid conversion, rotation, and switching. Since providers and pharmacists often use questionable equianalgesic conversion tables or easy-access opioid conversion calculators as tools for converting opioids, we present an updated comparison.

This project aimed to compare and contrast the various online opioid conversion calculators, identify the mathematical disparities in conversion, compare automated conversions against manual calculations, reveal potential risks to the end user, and make recommendations to health care providers for practical and safe approaches when predicting opioid conversions. We hypothesized that there is a wide disparity among available online calculators, which presents potential risks to patients, providers, and pharmacists.

After conducting an online search for calculators using PubMed, Google, and Google Scholar, we found eight equianalgesic conversion calculators available online and comprehensively evaluated them to determine their advantages, disadvantages, unique features, and potential risks to users. We then compared the calculators with respect to the following characteristics: opioid

Table 1. Available Online Opioid Dose Conversion Calculators

	WA State Agency	MedCalc	Pain Research	Pain Physician	Hopkins	Palliative Care	Global RPh	PPM
Opioid dosage calculator		X	X	X	X	X	X	X
Equianalgesic table displayed			X	X	X	X	X	X
Can convert multiple opioids to a single alternative			X	X	X	X	X	X
Acute vs chronic dosing for morphine and methadone							X	X
Transdermal fentanyl	X			X	X	X	X	X
Transdermal buprenorphine						X		X
Methadone	X	X	X	X	X		X	X
Tapentadol							X	X
Dose reduction for incomplete cross-tolerance				X			X	X
Availability for smartphone					X	X	X	X

Based on references 18-25.

PPM, Practical Pain Management; WA, Washington

conversion computation accuracy, specific option to convert to/from transdermal fentanyl, specific option to convert to/from methadone, up to date with newly FDA-approved opioids, reduction for incomplete cross-tolerance, and availability for smartphones. (Transmucosal fentanyl conversion options were not included because with one exception, they are not interchangeable to or from other opioids at any dose, nor are they anticipated to be used for “chronic pain.”) We included in the project all available online opioid conversion calculators accessible to the public without a fee and any comparative clinical studies evaluating online opioid conversion calculators, and excluded any online calculators with exclusive access to professional society members (blocked from public access) or those requiring fees. Studies that are non-comparative also were excluded.

We performed manual calculations referencing the opioid analgesic comparison tables sanctioned by

the American Pain Society guidelines and Pereira et al.^{9,10} All calculations performed manually also were computed using each of the eight available online opioid dose conversion calculators. Since we used the same reference tables to compare all calculator dose computations against all manual calculations, they served as a control across all manual calculations; this allowed a fair comparison in terms of percent difference between and among the calculators tested. We then measured the percent variation for the calculators compared with the manual calculations to determine the mathematical conversion disparities among the eight calculators.

Results

Table 1 lists the online opioid conversion calculators that were compared in this project and elucidates several disparate features among them.¹¹⁻¹⁸ For example, the Washington State Agency calculator does not convert from one opioid to another, but merely

provides the morphine equivalents.¹¹ The MedCalc calculator is used for initial dosing, or non-steady state, which is an oral to intravenous (PO:IV) morphine ratio of 6:1,¹² whereas the other calculators use a PO:IV morphine ratio of 3:1, i.e., chronic dosing.¹¹⁻¹⁸

The MedCalc calculator was an outlier and represented the largest disparity in answers; therefore, it was excluded from the data presented herein.¹² The other calculators listed in Table 1 were more similar for the purposes of this study. Some of the calculators provide different safety warnings, some exclude certain opioids, and some provide the option to dose reduce for incomplete cross-tolerance. Percent variation compared with manual calculation was noted, and it ranged from -55% to +242%. Two of the opioids most notably responsible for the wide range in percent variation were methadone and fentanyl. This is because their equivalencies are not necessarily bidirectional, and methadone conversion, in particular, has not traditionally

Table 2. Selected EDRs: Morphine-to-Methadone Conversion

Morphine Dose (mg/d)	30-90	90-300	300+	Important note: These ratios should NOT be used in reverse—that is, for converting from methadone to morphine.		
Morphine:Methadone EDR^a	4:1	6:1	8:1			
Morphine Dose (mg/d)	30-90	90-300	300+			
Morphine:Methadone EDR^b	4:1	8:1	12:1			
Morphine Dose (mg/d)	<100	101-300	301-600	601-800	801-1,000	>1,001
Morphine:Methadone EDR^c	3:1	5:1	10:1	12:1	15:1	20:1

^aBased on reference 20.

^bBased on reference 22.

^cBased on reference 21.

EDR, equianalgesic dose ratios

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Table 3. Comparison of Proposed Morphine to Fentanyl Conversion Parameters

Oral 24-h Morphine, mg/d²⁵	Fentanyl Transdermal, mcg/h²⁵	Oral 24-h Morphine, mg/d²⁶
60-134	25	30-90
135-224	50	90-150
225-314	75	151-210
315-404	100	211-270
405-494	125	For every additional 60 mg/d of morphine, give an additional 25 mcg/h of fentanyl.
495-584	150	
585-674	175	
675-764	200	
765-854	225	
855-944	250	
945-1,034	275	
1,035-1,124	300	

Based on references 25-28.

been calculated with an equation until recently.¹⁹ Various opioids with -55% variation could place the patient at risk for withdrawal and/or an underdose. Fentanyl and methadone, which had calculated percent variations of 100% and 242% respectively, could conceivably place the patient at an increased risk for an overdose and possibly even death (Figure 1).

Discussion

The wide range in percent variation for methadone is presumably due to the conversion schematics heretofore proposed for converting morphine to methadone.²⁰⁻²² Table 2 provides a comparison of three proposed morphine-to-methadone conversion strategies.²⁰⁻²³ These three published schematics used 3 to 6 breaking points, the

result of which are precipitous drops in dosage equivalents at the break points.²³ In 2012, Fudin and Fudin proposed a mathematical model (Fudin Factor²⁴) to eliminate the peaks and troughs previously published by Ripamonti (1998), Ayonrinde (2000), and Mercadante (2001).^{8,20-22} The newly proposed mathematical model was used to develop the methadone conversion in *Practical Pain*

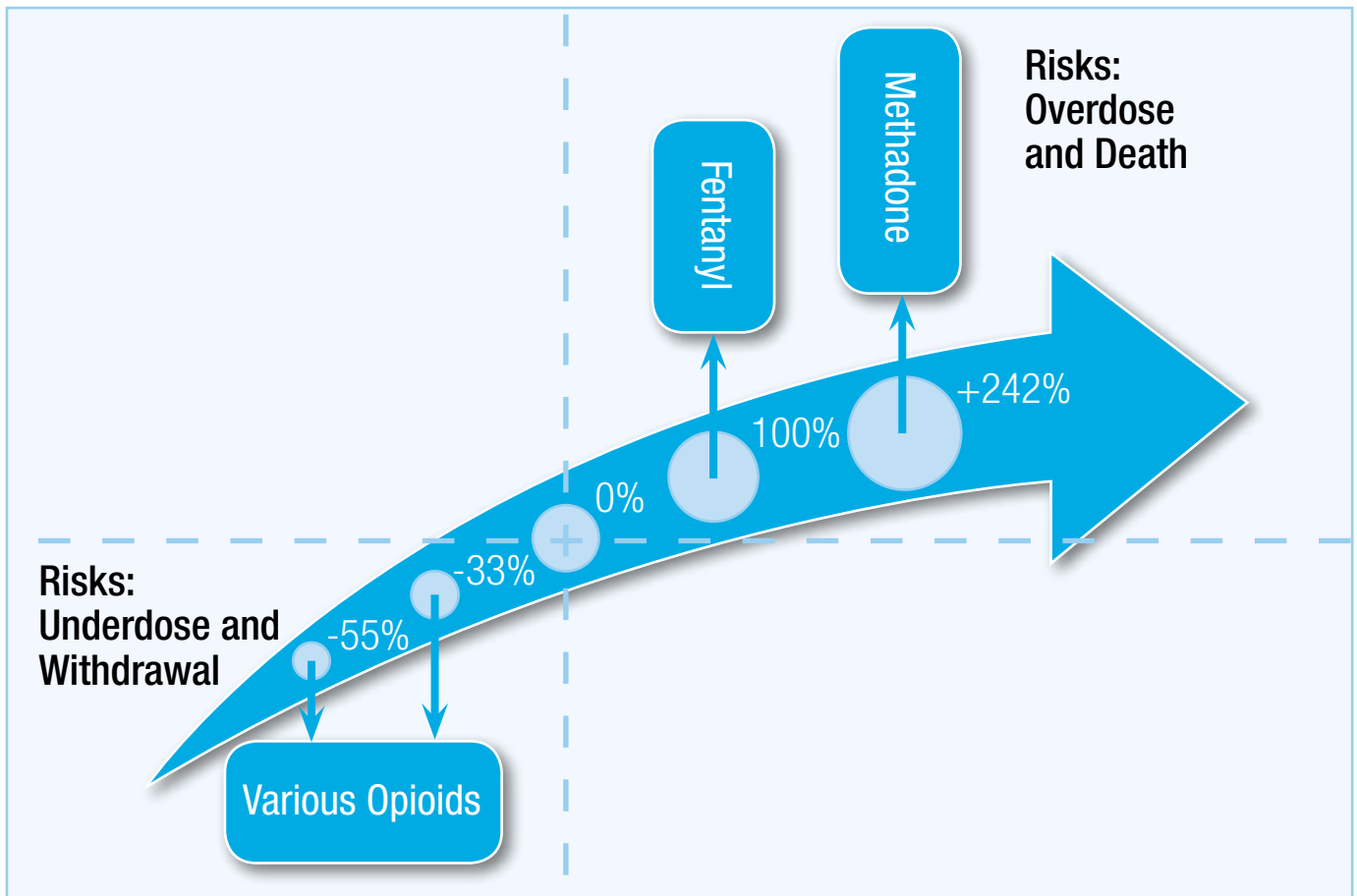


Figure 1. Percent variation between electronic and manual calculations.

Management's (PPM's) recently released online calculator.^{23,24} At the time of this study, no other calculator incorporated the Fudin Factor for methadone conversions; however, GlobalRPh incorporated it into their online calculator in April 2013.¹⁷

Another reason for the wide range in percent variation is due to the conversion from morphine to and from fentanyl. Table 3 shows the comparison of proposed morphine to fentanyl conversion parameters.²⁵⁻²⁸ Most of the opioid equianalgesic conversion calculators available reference the package insert, an approach that has been criticized because the package insert often has morphine ranges that are broad, conservative, and are based on opioid conversions that also have been faulted.^{25,29} Complementary available literature, such as Donner et al,

also provide conservative ranges, but they are less conservative compared with the manufacturers' recommendations.²⁶ However, conservative dosing in one direction begets potentially liberal results in the opposite direction. In an assessment of serum concentrations following multiple applications of a fentanyl 100 mcg/h patch, there was significant variation in the amount of fentanyl that was absorbed, which makes converting from morphine to fentanyl much more difficult.^{25,29}

Conclusions

Opioid rotation remains an option in cases where pain cannot adequately be controlled despite increasing opioid doses or when there are intolerable adverse effects. Several calculation tools including dose tables exist to support clinicians, but they must be used with

caution. Variability in patient response to individual opioids and conflicting data regarding equianalgesia contribute to the difficulties seen when making opioid conversions. *PPM's* most recently published online calculator may mitigate some of the issues regarding methadone and fentanyl outlined above because it uses a methadone equation rather than schematics of the past, as well as two separate fentanyl conversions to keep the calculations conservative in both directions.^{8,18,24} This study provides a contemporary review of online opioid equianalgesic dose conversion calculators, which is especially important when considering the ubiquitous use of the Internet and smartphones.

The authors wish to call attention to the disclosure statements herein because of direct involvement in the

development of the PPM calculator and the methadone conversion equation. Also, we acknowledge that ideal features for a calculator have yet to be determined. Some calculators purposely may exclude certain features as a safety measure. For example, the potential dangers of offering a methadone and/or fentanyl conversion are elucidated herein. Additionally, transdermal buprenorphine, a partial agonist/antagonist, presents yet another whole set of risks when one considers the potential for opioid displacement and withdrawal upon conversion to or from a pure opioid agonist. Finally, we conclude that there is a wide disparity among the eight available online equianalgesic opioid dose conversion calculators.

Opioid calculators may serve as useful tools when converting from one opioid to another, but all conversions need to be double checked by the end user for accuracy. There is significant and potentially dangerous inconsistency in certain calculated doses among various online calculators, most particularly with fentanyl and methadone. There is no standard reference for converting from one or more opioids to another; therefore, dosing tables and opioid conversion calculators only should serve as aids for determining an estimated target equianalgesic dose. While calculators may help prevent computational errors, they also can compute a fatal equivalency. Slow titration, clinical judgment, and individualization of treatment are necessary to safely and effectively switch a patient from one or more opioids to another. ■

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