

# Inches, Centimeters, and Yards: Overlooked Definition Choices Inhibit Interpretation of Morphine Equivalence

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ND is a methods advisor to the RADARS System of Denver Health and Hospitals Authority. RADARS System does not use the metrics described herein.

[go.unc.edu/mme](http://go.unc.edu/mme)



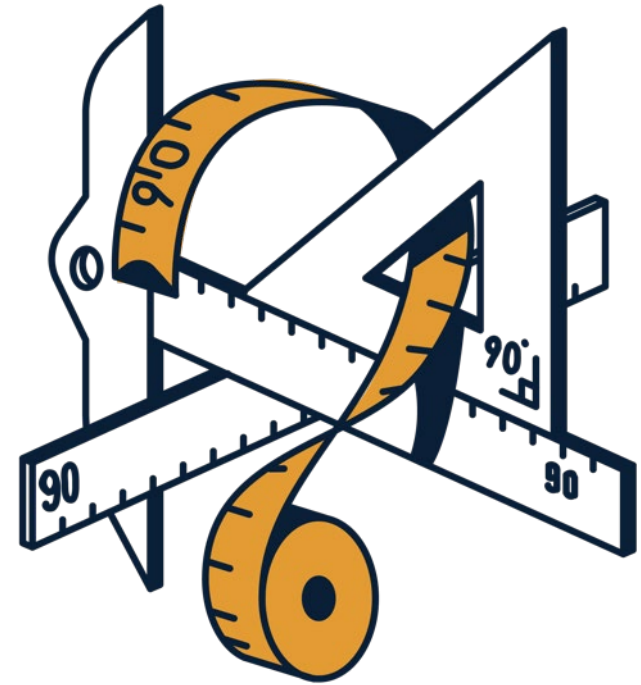
Slides, code, equations & accepted manuscript  
*Clinical Journal of Pain*

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# Introduction



# MME per day is enshrined in state laws, with the assumption that it is a standardized metric.



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## Laws Limiting the Prescribing or Dispensing of Opioids

Drug overdose is a nationwide epidemic. Opioids, both prescription painkillers such as Oxycodone and non-prescribed drugs such as heroin and fentanyl, are responsible for most of these deaths – nearly 47,000 in 2018 alone.<sup>1</sup> Provisional data show that overdose-related deaths have accelerated since then, with more deaths recorded in the twelve-month period ending May 2020 than in any other twelve-month period on record.<sup>2</sup> While the majority of opioid-related deaths are now caused primarily by illicit opioids such as heroin and illegally manufactured fentanyl, the number and rate of deaths related to prescribed opioids remains high.<sup>3</sup>

While the federal government has the exclusive authority to determine whether a medication will require a prescription and whether a prescription medication is designated a federally controlled substance, states have great autonomy in the regulation of medical practice within their states.<sup>4</sup> States have used that authority to enact a number of laws designed to reduce potentially inappropriate prescribing and dispensing of opioids.

One way states have attempted to regulate the use of opioid medications is by passing statutes or enacting regulations (collectively referred to in this document as “laws”) that impose enforceable limitations on the ability of medical professionals to prescribe or dispense those medications for pain treatment. The number of states with such laws has expanded rapidly, from ten in 2016 to 39 by the end of 2019.<sup>5</sup> The provisions of these laws vary between states and within states over time. At the end of 2019 the most common duration limit was 7 days, with a range of 3 to 31. Fourteen states imposed limits on the dosage of opioids that can be prescribed, ranging from 30 morphine milligram equivalents (MME) to a 120 MME daily maximum.

This document displays the characteristics of these laws as of December 31, 2019. The columns first provide information on when the state first enacted a law that restricted the prescribing or dispensing of opioids for pain, and when that law was last modified. The remaining columns provide information on the duration or amount limit on opioids prescribed for pain, which categories of substances are covered, whether the law only applies to the initial prescription, and whether there is a different restriction or requirement for minors. Finally, the Table displays whether the law contains exceptions for professional judgment, cancer treatment, surgical pain, palliative care, or other reasons. Extensive additional information is provided in the footnotes. The table also provides information on how these laws have changed over time. Previous versions of the law are detailed in gray-shaded rows; brown-shaded cells indicate what aspect of the law changed in the newest iteration.

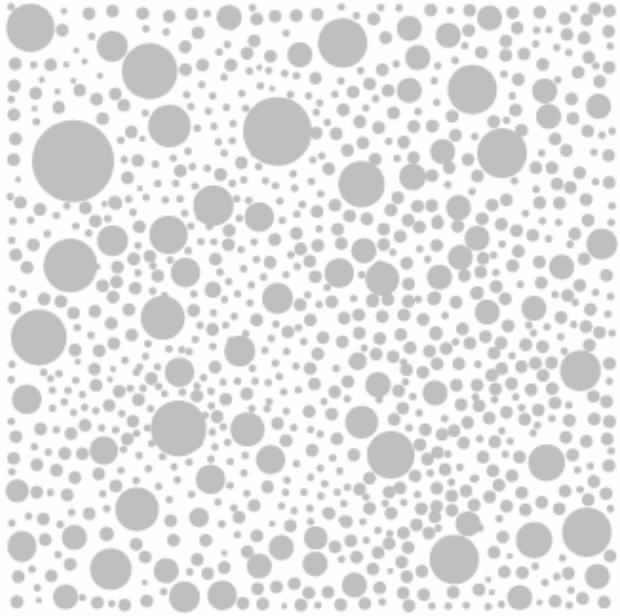
The wide variety in these laws between states and within states over time is notable. Research is needed to determine whether these laws are effective in improving prescribing practices and reducing opioid-related harm, and what impact these variations may have. It is also unknown whether limitations on the prescription of opioids for pain may have unintended negative consequences, such as increasing harm related to heroin and other non-prescription opioids, as has been found with some prescription drug monitoring program (PDMP) laws.<sup>6</sup> Research is also needed to determine whether these laws contribute to the burden of untreated or inadequately treated pain.

1

imposed limits on the dosage of opioids that can be prescribed, ranging from 30 MME to a 120 MME daily maximum.

4

states



Same dataset  
Same patients  
Same prescriptions  
Same conversion tables  
Same threshold (90 MME)

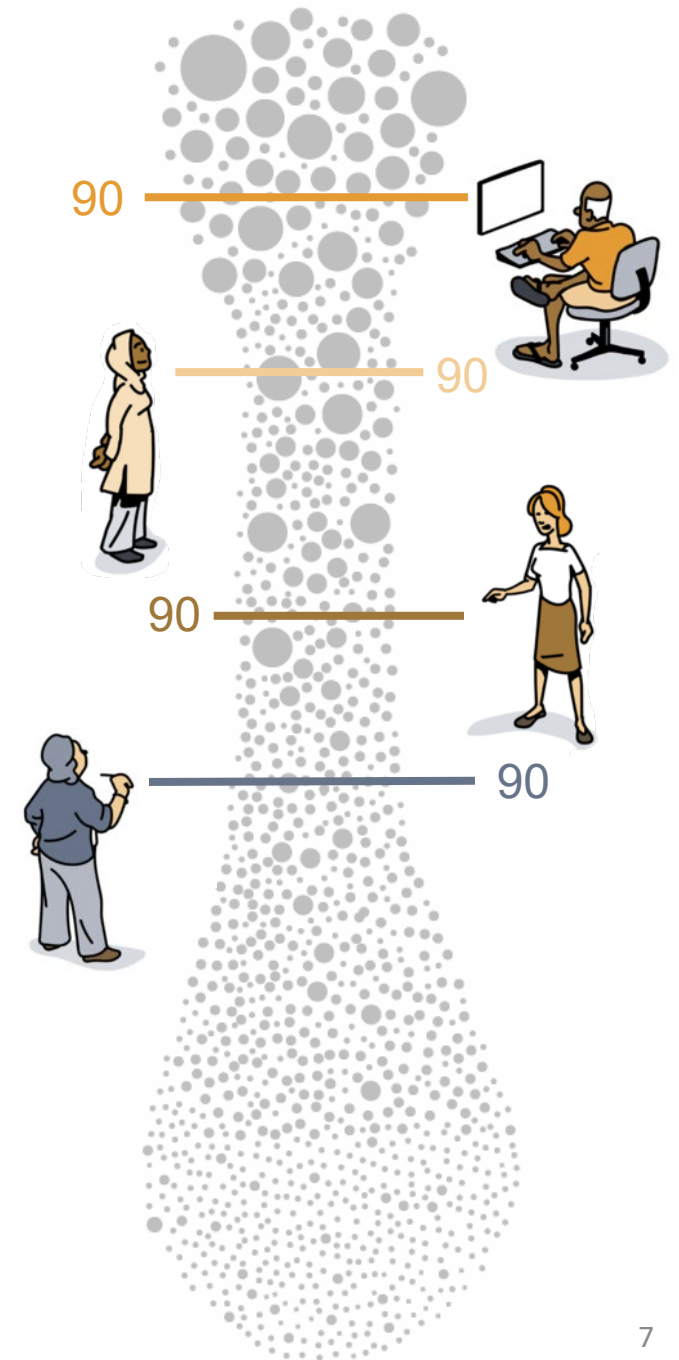
Identify the “high dose” patients



# There are at least 4 separate ways to calculate “daily MME.”

Same dataset  
Same patients  
Same prescriptions  
Same conversion tables  
Same threshold (90 MME)

Identify the “high dose” patients



# Is this a “high dose” patient?



30mg extended-release oxycodone twice-a-day for around-the-clock pain for 30 days (60 tablets) = 2,700 mg ME



One 5mg oxycodone twice-a-day as needed for breakthrough pain for the first 7 days (14 tablets) = 105 mg ME

Total MME = 2,805

Both prescriptions are dispensed on the first day of a 30-day month, with no refills observed.

Assume 1.5 for conversion factor. Use 90 MME to define “high dose” threshold.





# Even for this simple 2 prescription scenario, there is no agreement on the daily MME.

Using 90 daily MME as the threshold, two definitions would consider this a “high dose” patient, whereas the other two would not.

Studies used to establish the 90 MME/day threshold used 4 different definitions.

The “CDC Method” calculates MME per **prescription**, not MME per **patient**.

31.2 MME per day



75.8 MME per day



93.5 MME per day



105 MME per day

# Cohort Study of the Impact of High-dose Opioid Analgesics on Overdose Mortality

LESS IS MORE

## Opioid Dose and Drug-Related Mortality in Patients With Nonmalignant Pain

Tara C. Gomes, J. Michael Paterson

## A History of Being Prescribed Controlled Substances and Risk of Drug Overdose Death

## Transdermal Fentanyl Versus Sustained Release Oral Morphine in Strong-Opioid Naïve Patients With Chronic Low Back Pain

Laurie Allan

## Risks for Possible and Probable Opioid Misuse Among Recipients of Chronic Opioid Therapy in Commercial and Medicaid Insurance Plans: the TROUP Study

## A Randomized Trial of 2 Prescription Strategies for Opioid Treatment of Chronic Nonmalignant Pain

Bruce D. Naliboff, Quynh Pham, and Paul Shekelle

## Prescription Opioid Duration of Action and the Risk of Unintentional Overdose Among Patients Receiving Opioid Therapy

Matthew Miller, MD, ScD; Catherine W. Barber, MPA; Sarah Leatherman, PhD; Jennifer Fonda, BS; John A. Hermos, MD; Kelly Cho, PhD; David R. Gagnon, MD

## Opioid Prescriptions for Chronic Pain and Overdose

A Cohort Study

Kate M. Dunn, PhD; Kathleen W. Saunders, JD; Carolyn M. Rutter, PhD; Caleb J. Banta-Green, MSW, MPH, PhD; Joseph O. Merrill, MD, MPH; Mark D. Sullivan, MD, PhD; Constance M. Weisner, DrPH, MSW; Michael J. Silverberg, PhD, MPH; Cynthia I. Campbell, PhD; Bruce M. Psaty, MD, PhD; and Michael Von Korff, ScD

## A Feasibility Study of Transdermal Buprenorphine Versus Transdermal Fentanyl in the Long-Term Management of Non-Cancer Pain

Arzana Mitra, Richard A. Rawlins, and Richard A. Rawlins

## Association Between Opioid Prescribing Patterns and Opioid Overdose-Related Deaths

Amy S. B. Bohnert, PhD  
Marcia Valenstein, MD  
Matthew J. Bair, MD  
Dara Ganoczy, MPH  
John F. McCarthy, PhD  
Mark A. Ilgen, PhD  
Frederic C. Blow, PhD

**Context** The rate of prescription opioid-related overdose death increased substantially in the United States from 2000 to 2014, particularly among patients prescribed high-dose opioids. **Objective** To examine the association between opioid prescribing patterns and the risk of overdose death among patients with chronic pain. **Design** Case-control study using data from the National Health and Medical Research Council's Australian General Practice Research Database, 2000-2014.

## Opiate reduction in chronic pain patients: a comparison of patient-controlled reduction and staff controlled cocktail methods

Judith A. Ralphs <sup>a,\*</sup>, Amanda C de C Williams <sup>a</sup>, Phil H. Richardson <sup>b</sup>, Charles E. Pither <sup>a</sup>, and Michael K. Nicholas <sup>a</sup>

<sup>a</sup>Department of Psychiatry, UMDS, St. Thomas Hospital, Lambeth Palace Road, SE1 7EH (UK)  
<sup>b</sup>Department of Psychology, University of Exeter, Exeter, UK  
3, accepted 13 August 1993)

## Trends in opioid use and dosing among socio-economically disadvantaged patients

TARA GOMES, DAVID N. JUURLINK, IRFAN A. DHALLA, ANGELA MAILIS-GAGNON, J. MICHAEL PATERSON, MUHAMMAD M. MAMDANI

## The Role of Opioid Prescription in Incident Opioid Abuse and Dependence Among Individuals with Chronic Non-Cancer Pain: The Role of Opioid Prescription

Mark J. Edlund<sup>1,7</sup>, Bradley C. Martin<sup>2</sup>, Braden<sup>3</sup>, and Mark D. Sullivan<sup>3</sup>

## High-Risk Use by Patients Prescribed Opioids for Pain and Its Role in Overdose Deaths

Jane A. Gwira Baumbatt, MD; Caleb Wiedeman, MPH; John R. Dunn, DVM, PhD; William Schaffner, MD; Leonard J. Paulozzi, MD, MPH; Timothy F. Jones, MD

## Risk Factors for Serious Opioid-Related Toxicity in Veterans Health Administration Prescription Opioid Dependence

## Assessing Risk for Drug Overdose in a National Cohort: Role for Both Daily and Total Opioid Dose?

Yuanyuan Liang<sup>†,‡,§</sup> and Barbara J. Turner<sup>†,‡,§</sup>

## Prescription Opioid Dependence

### Comparison of Two Methods

Forest S. Tennant, Jr, MD, Dr PH, Richard A. Rawlins

## Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study

## Drug Overdose in a Retrospective Cohort with Non-Cancer Pain Treated with Opioids, Antidepressants, and/or Sedative-Hypnotics: Interactions with Mental Health Disorders

Barbara J. Turner, M.D., M.S.Ed.<sup>1,2,3</sup> and Yuanyuan Liang, Ph.D.<sup>2,3,4</sup>

Dara Ganoczy,<sup>3</sup> Mark A Ilgen,<sup>3,4</sup> Amy S B Bohnert<sup>3,4</sup>

# Alan Kinlaw, University of North Carolina



*“Something that matters a lot to me is that equations can help a researcher identify the concept they want to measure, and then measure it.*

*And since each concept or formula has a very different relationship to the common 90 MME/day threshold, these equations clarify how we should be more nuanced with whether or how we set thresholds.”*

# The discrepancy is arithmetic. Equations make the differences explicit.



Full details at [go.unc.edu/mme](http://go.unc.edu/mme)

To complete all calculations and relate competing definitions of daily MME, notation is as follows:

- $q_{ij}$ , quantity (units) dispensed for prescription  $j$  for person  $i$
- $m_{ij}$ , strength per unit in milligrams for a given prescription  $j$  for person  $i$
- $c_{ij}$ , equianalgesic potency conversion factor for medication in prescription  $j$  for person  $i$
- $d_{ij}$ , days supply on a given prescription  $j$  for person  $i$
- $s_{ij}$ , start (dispensing) date of prescription  $j$  for person  $i$
- $w_i$ , start date of observation window for person  $i$
- $l_i$ , length (in days) of observation window for person  $i$
- $g_{ik}$ , date of follow-up day  $k$  during observation window for person  $i$

# D<sub>1</sub>: Total Days Supply

$$x_i = \frac{\sum_{j=1}^n a_{ij}}{\sum_{j=1}^n o_{ij}} = \frac{\sum_{j=1}^n (qmc f)_{ij}}{\sum_{j=1}^n o_{ij}} = \frac{\sum_{j=1}^n (qmc)_{ij} \left(\frac{o}{d}\right)_{ij}}{\sum_{j=1}^n o_{ij}}$$

$$\frac{2,805 \text{ MME}}{37 \text{ days supply}} = 75.8 \text{ daily MME}$$

Number of days can be longer than calendar time.

Underestimates daily MME when IR and ER opioids are used in combination.

## De Facto Long-term Opioid Therapy for Noncancer Pain

*Michael Von Korff, ScD,\* Kathleen Saunders, JD,\* Gary Thomas Ray, MBA,†  
Denise Boudreau, PhD,\* Cynthia Campbell, PhD,† Joseph Merrill, MD, MPH,§  
Mark D. Sullivan, MD, PhD,‡ Carolyn M. Rutter, PhD,\* Michael J. Silverberg, PhD, MPH,†  
Caleb Banta-Green, MSW, MPH,|| and Constance Weisner, Dr PH, MSW†¶*

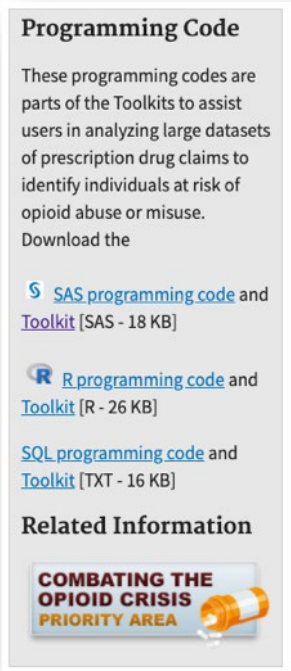
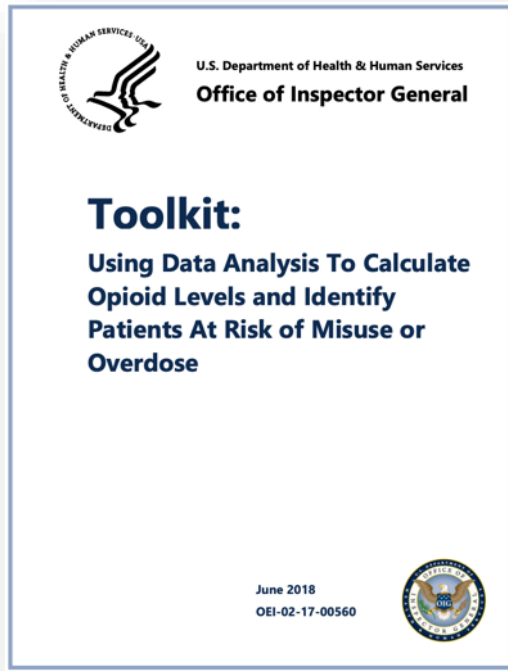
Total days supply is the sum of days supply for each opioid dispensed during an episode. Days supply may not represent the intended days supply of a particular prescription as it is usually calculated by pharmacists using the maximum dose and frequency permitted within the range specified by the prescribing provider. Therefore, total days supply tends to underestimate the actual days supply dispensed.

PMID: 18574361

# D2: On-therapy Days

$$x_i = \frac{\sum_{j=1}^n a_{ij}}{\sum_{k=1}^l u_{ik}} = \frac{\sum_{j=1}^n (qmcf)_{ij}}{\sum_{k=1}^l u_{ik}} = \frac{\sum_{j=1}^n (qmc)_{ij} \left(\frac{o}{d}\right)_{ij}}{\sum_{k=1}^l u_{ik}}$$

$$\frac{2,805 \text{ MME}}{30 \text{ days supply}} = 93.5 \text{ daily MME}$$



## Drug Overdose in a Retrospective Cohort with Non-Cancer Pain Treated with Opioids, Antidepressants, and/or Sedative-Hypnotics: Interactions with Mental Health Disorders

Barbara J. Turner, M.D., M.S.Ed.<sup>1,2,3</sup> and Yuanyuan Liang, Ph.D.<sup>2,3,4</sup>

The total MED was computed by summing the MEDs for all opioid prescriptions within a given 6-month interval. The mean daily MED in a 6-month interval was calculated by **dividing the total MED by days' supply for all prescriptions in that interval, excluding overlapping days.** We examined five categories for the mean daily MED (i.e., 0, 1–19, 20–49, 50–99, and  $\geq 100$  mg), similar to other studies.<sup>9,10</sup> For the first overdose, the mean daily MED was based on data from exactly 6 months before that event (Fig. 2).

PMID: 25650263

Accounts for overlapping prescriptions.  
Method provided by HHS OIG.

# D3: Defined Observation Window

$$x_i = \frac{\sum_{j=1}^n a_{ij}}{l_i} = \frac{\sum_{j=1}^n (qmc)_{ij} \left(\frac{o}{d}\right)_{ij}}{l_i}$$

$$\frac{2700 + 105}{90} = \frac{2,805 \text{ MME}}{90 \text{ days window}} = 31.2 \text{ daily MME}$$

Other studies used 120, 180, 365 days.

## Opioid Prescriptions for Chronic Pain and Overdose

### A Cohort Study

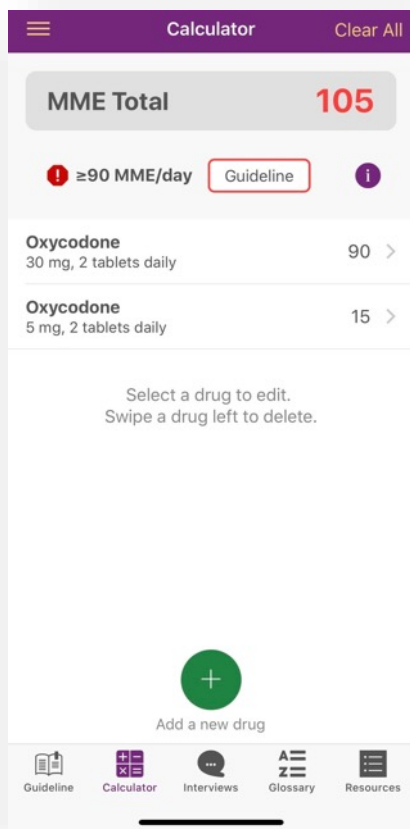
Kate M. Dunn, PhD; Kathleen W. Saunders, JD; Carolyn M. Rutter, PhD; Caleb J. Banta-Green, MSW, MPH, PhD; Joseph O. Merrill, MD, MPH; Mark D. Sullivan, MD, PhD; Constance M. Weisner, DrPH, MSW; Michael J. Silverberg, PhD, MPH; Cynthia I. Campbell, PhD; Bruce M. Psaty, MD, PhD; and Michael Von Korff, ScD

### Classification of Opioids

We obtained medication data from GHC automated pharmacy files. These data cover more than 90% of the prescription medications used by GHC enrollees (23). We calculated total morphine equivalents dispensed for each opioid prescription filled during follow-up, defined by the quantity of pills dispensed multiplied by their strength (in milligrams), multiplied by a conversion factor (22). We then calculated the average daily morphine equivalent dose dispensed for 90-day exposure windows (see Statistical Analysis) by adding the morphine equivalents for the prescriptions dispensed during the 90 days and then dividing by 90. For each 90-day exposure window and each person, we calculated the average daily opioid dose dispensed and divided these into 5 categories: none, 1 to 19 mg, 20 to 49 mg, 50 to 99 mg, and 100 mg or more.

# D4: Maximum Daily Dose

$$z_{ik} = \sum_{j=1}^n p_{ijk} \quad x_i = \max_i(z_{i,k=1}, \dots, z_{i,k=l})$$



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## A History of Being Prescribed Controlled Substances and Risk of Drug Overdose Death

Leonard J. Paulozzi, MD, MPH,\*  
Edwin M. Kilbourne, MD,† Nina G. Shah, MS,‡  
Kurt B. Nolte, MD,§ Hema A. Desai, MMS,¶  
Michael G. Landen, MD, MPH,‡ William Harvey,  
RPH,\*\* and Larry D. Loring, RPH\*\*

Critical revision of the manuscript for important intellectual content: Paulozzi, Kilbourne, Shah, Landen, Nolte, Harvey, Loring

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Presented: National Harold Rogers Prescription Drug Monitoring Program Meeting, Washington, DC, June 29, 2010.

\*Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, Centers for Disease Control and Prevention, Atlanta, Georgia;

†Martin, Blanck, & Associates, Falls Church, Virginia;

dosage of opioid prescribed in MME per day [27] in three different ways. The single peak dosage was the highest amount per day in any single opioid prescription. **The total peak dosage was the highest dosage per day at any time during the exposure period** after summing dosages from all overlapping opioid prescriptions. The average dosage was the average daily opioid dosage during the entire study period from all opioid prescriptions combined. For regression analysis, we categorized each measure of daily dosage into 0–40, >40–120, and >120 MME/day.

PMID: 22026451

Ignores date, days supply, and previous opioid use.



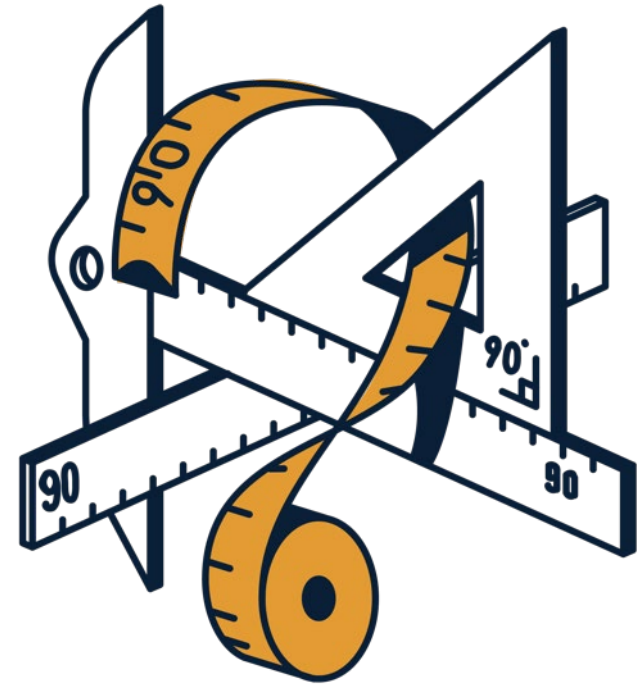
# Yanning Wang, University of Florida



*“Lack of consistency in calculating patient-level daily MME has always been a headache for me as an analyst and epidemiologist.”*

*To ease the computational complexity, software vendors prefer ‘straightforward’ calculations but may not provide enough details behind the measure for the clinicians.”*

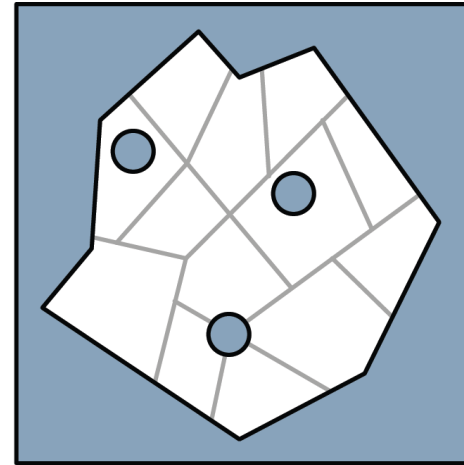
How much difference can these definitions actually make in real world studies?



# A Controlled Experiment

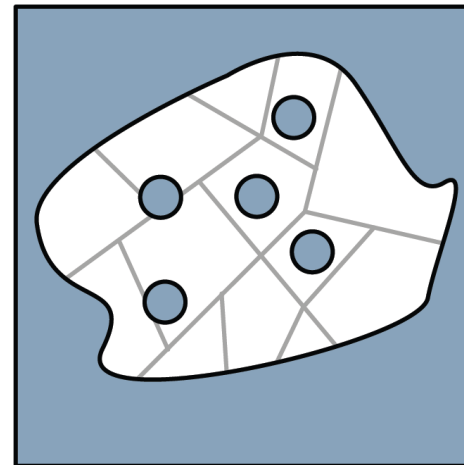
We may want to compare how many “high dose” patients are in one state versus another.

We used a meta-analysis technique developed by FDA to determine if 4 studies using the same data have statistically consistent results.

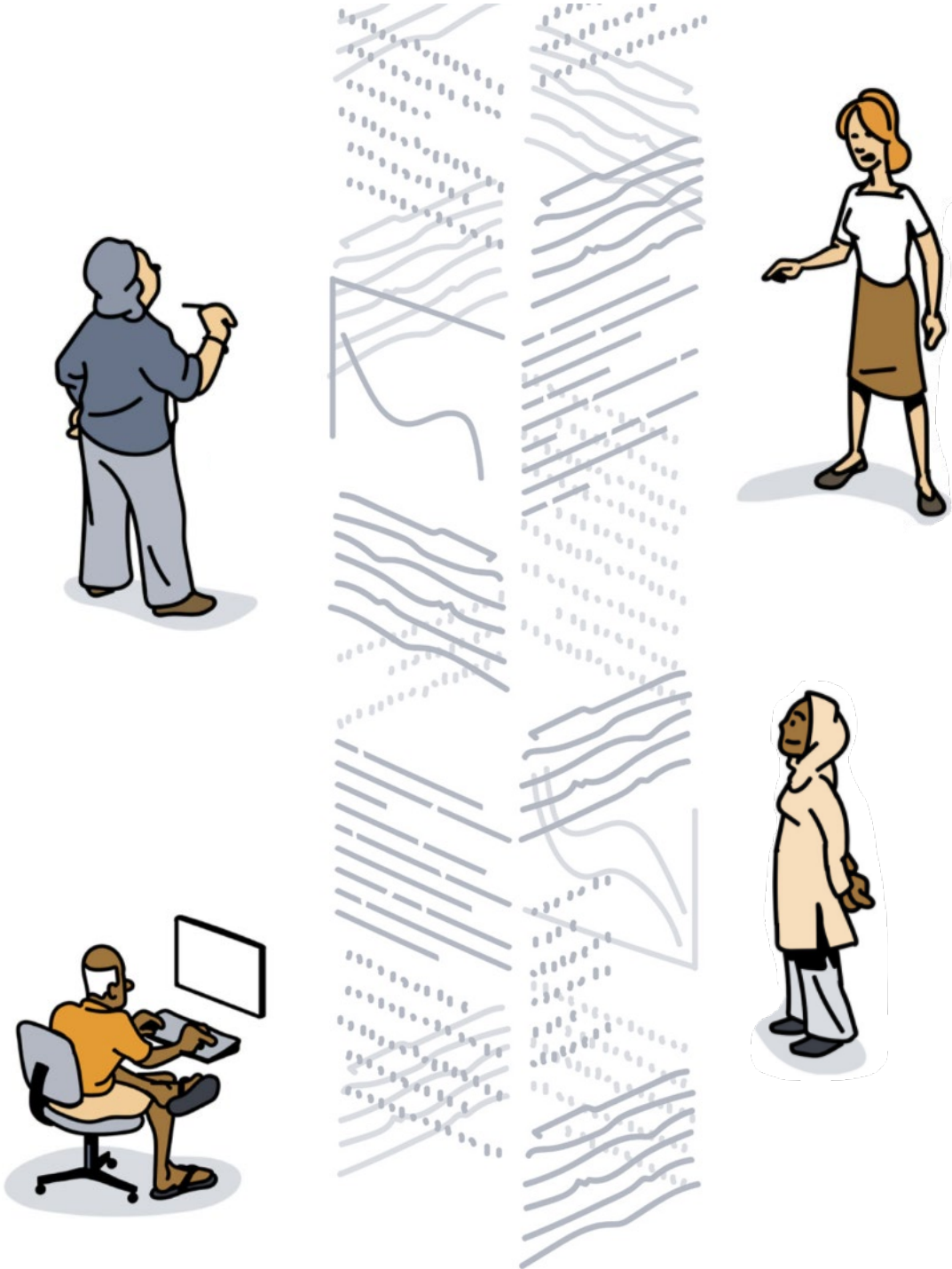


7.9  
per 100  
adult residents

*Total opioid analgesic  
3-month dispensing rate*



8.7  
per 100  
adult residents



The only source of variation comes from the 4 definitions of daily MME

# Methods



## Study Setting

- PDMP data from California and Florida
- All adult residents
- July through September 2018

## Drugs

- Outpatient prescriptions for solid oral opioid analgesics
- Excludes buprenorphine
- “High dose” defined as greater than >90 daily MME
- Uniform conversion factors (CDC)

## Main Analysis

- 1: Number of “high dose” patients compared between CA and FL
- 2: mg difference by patient between CA and FL
- 3: Meta-analysis with fixed-effects (no sampling variation) inverse variance model using Higgins and Thompson’s  $I^2$  and  $X^2$

# Sample Size

9,436,640 opioid analgesic prescriptions

- California n=5,677,277
- Florida n=3,759,363

3,916,461 unique adult residents

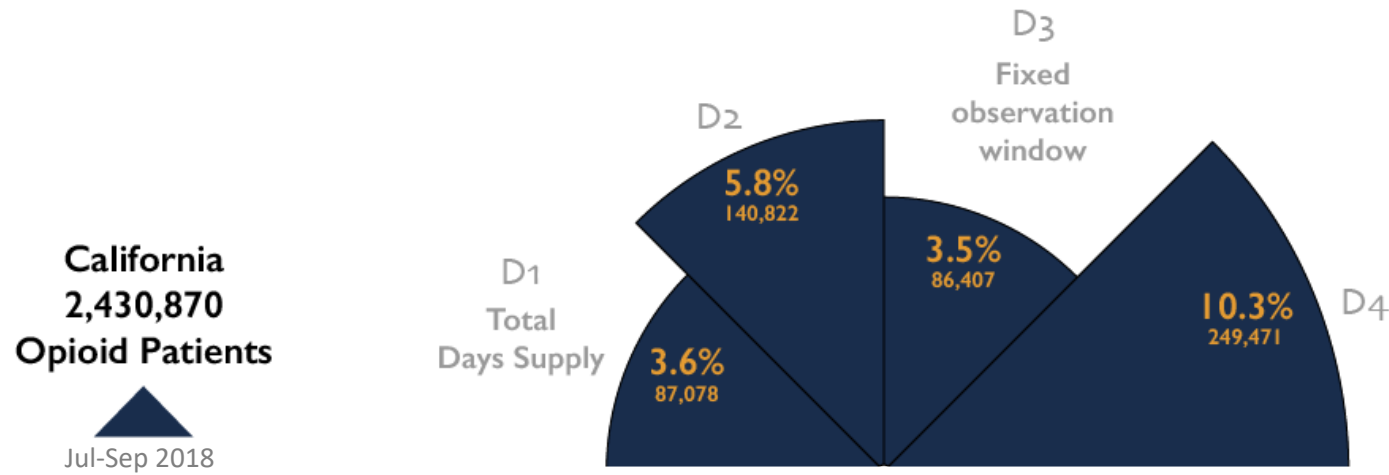
- California n=2,430,870
- Florida n=1,485,591

**7.9**  
per 100  
adult California residents

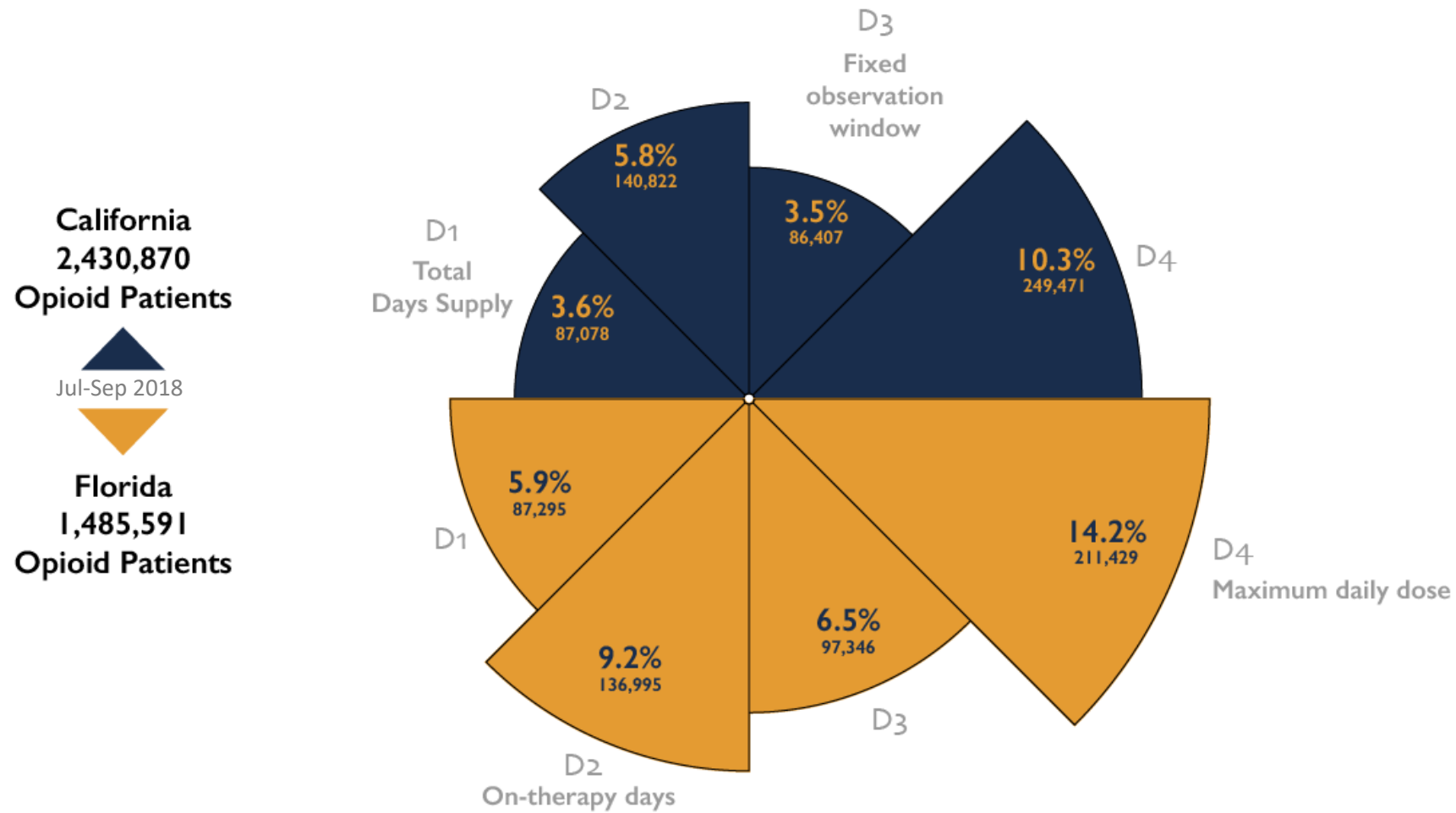
*Total opioid analgesic  
3-month dispensing rate*

**8.7**  
per 100  
adult Florida residents

# Results – Definition choice places thousands more patients in the “high dose” category.



# Results – Definition choice places thousands more patients in the “high dose” category.





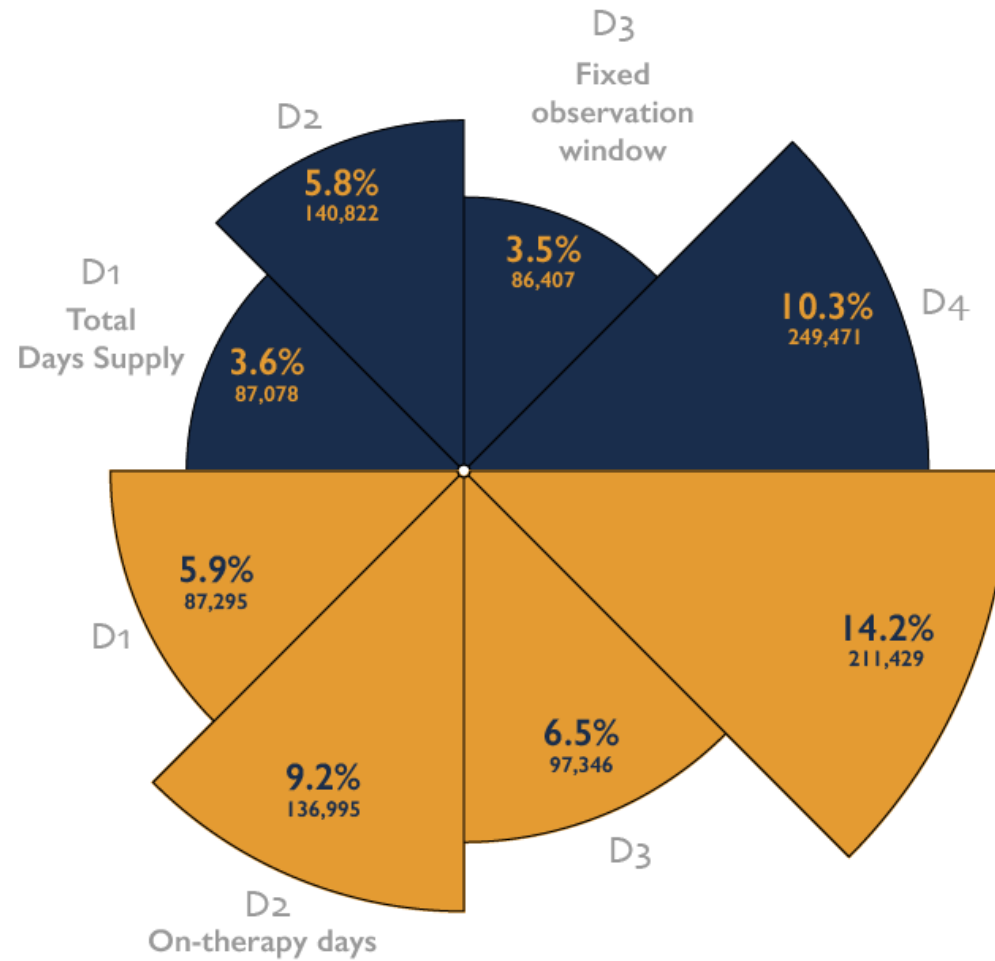
# Results – Definition choice places thousands more patients in the “high dose” category.

**California**  
2,430,870  
Opioid Patients



Jul-Sep 2018

**Florida**  
1,485,591  
Opioid Patients



**Texas, Jan-Mar 2020**  
*preliminary analysis*

Rx: 3,258,619

Patients: 1,608,250

D1: 2.4%

D2: 3.7%

D3: 1.6%

D4: 7.4%

# Results – The definitions do not agree how much many more “high dose” patients were in FL.

	% more “high dose” patients in FL vs. CA	95% CI
1. Total days supply	64.0%	62.5%, 65.5%
2. On-therapy days	59.2%	58.0%, 60.3%
3. Fixed observation window	84.3%	82.7%, 86.0%
4. Maximum daily dose	38.7%	37.9%, 39.4%
Tests for heterogeneity		
I <sup>2</sup> = 99.9%		
H <sup>2</sup> = 1086		
X <sup>2</sup> = 3257, 3 df, p<0.0001		

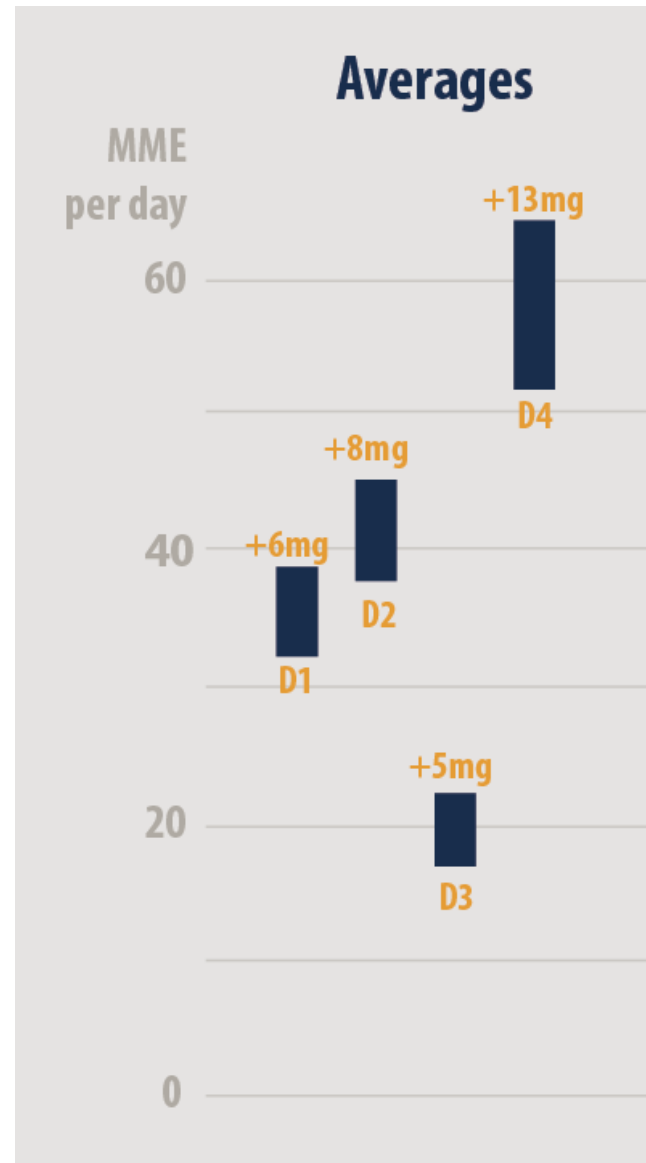
Results – The definitions do not agree if the average ER-only opioid patient is receiving a “high dose.”

Average daily MME	California n=40,038	Florida N=26,039
1. Total days supply	90 mg	87 mg
2. On-therapy days	104 mg	97 mg
3. Fixed observation window	73 mg	67 mg
4. Maximum daily dose	154 mg	143 mg

# Results – Without standardizing definitions, it would be impossible to conclude how much more mg were given to patients in FL.

D4 exaggerated the differences between states.

By not taking overlapping prescriptions into account (D1 vs. D2), MME differences are underestimated by 33%.

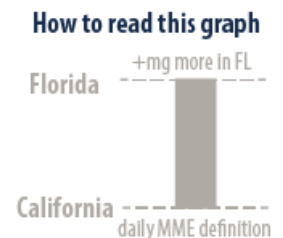


D1: Total Days Supply  
D2: On-therapy Days  
D3: Fixed Observation Window  
D4: Maximum Daily Dose

July-September 2018

n=9,436,640 opioid Rx  
n=3,916,461 patients

Only source of variation comes from choice of definition and metrics for daily MME

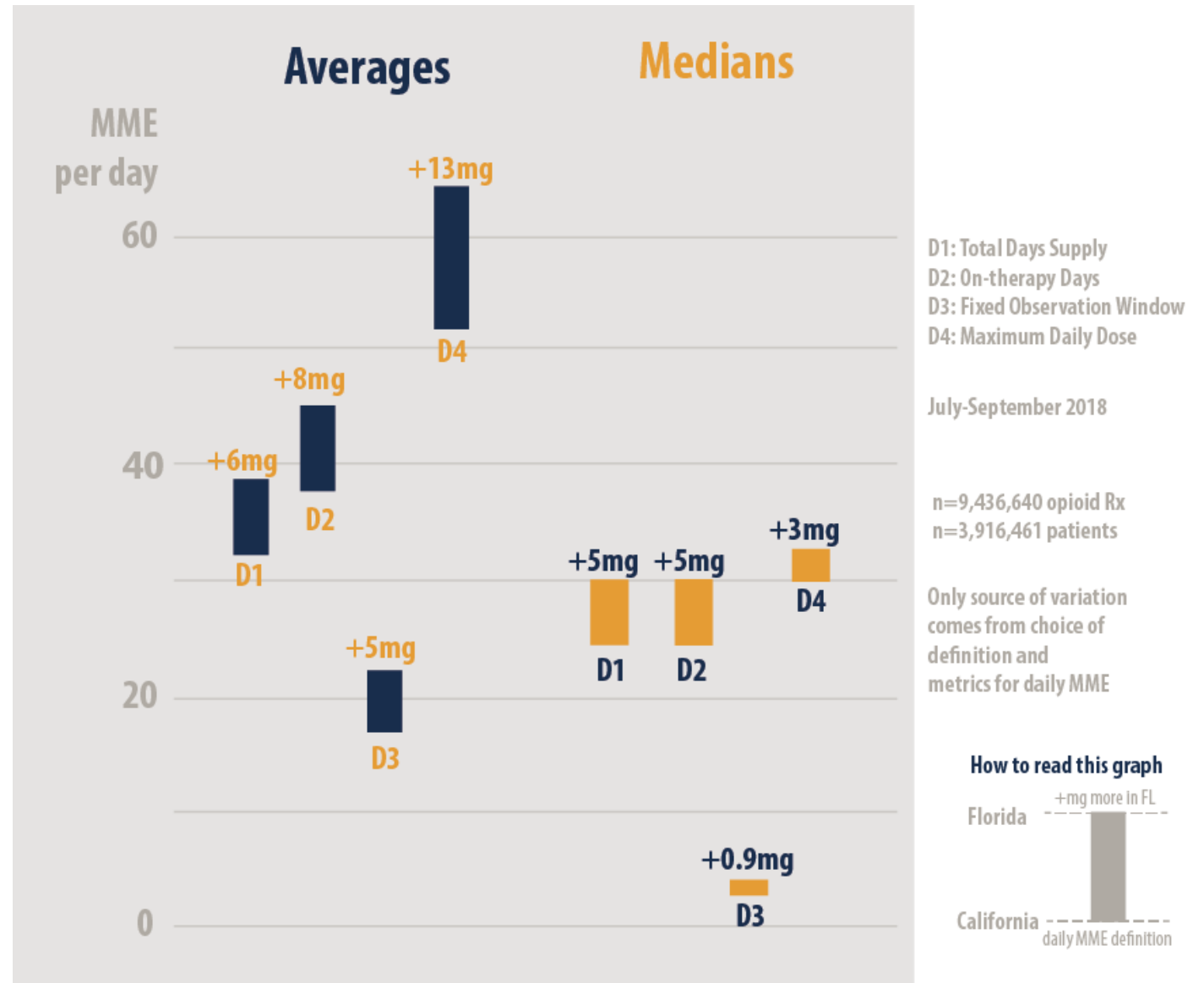


# Results – The definitions even provide differing results for means versus medians.

A policy analysis could legitimately conclude that Florida had anywhere from 0.9mg to 13mg more daily MME.

When means and medians diverge, both should be reported. Medians are less prone to influence by outliers.

Zheng doi: 10.1080/03610926.2015.1081948



# How does interpretation change based on metric?

D3: Fixed Observation Window  
Median

+0.9mg  
higher in FL

84%  
more "high dose"  
patients in FL

*Doses are similar, but many more "high dose" patients in FL.*

---

D4: Maximum Daily Dose  
Mean

+13mg  
higher in FL

39%  
more "high dose"  
patients in FL

*Doses much higher in FL, and somewhat more "high dose" patients.*

# Comparing ER and IR, the impact of definition choice is differential.

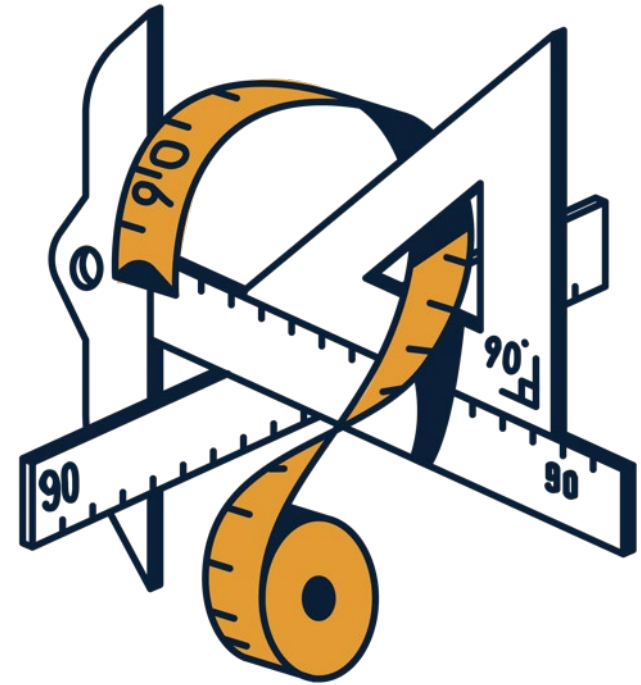
Meta-analysis of 4 studies using the *same data* would suggest that the studies are not measuring the same construct.

If we had selected patients who only received ER opioids, we would have concluded that California had higher opioid prescribing instead.

## Mean difference in daily MME in Florida (vs. California)

	Difference in MME (95% CI)
<b>Immediate-release only (n=3,611,856)</b>	
1. Total days supply	3.7 mg (3.3, 4.1)
2. On-therapy days	3.5 mg (3.1, 3.9)
3. Fixed observation window	2.2 mg (2.2, 2.3)
4. Maximum daily dose	5.1 mg (4.6, 5.6)
$I^2 = 98.63\%$	
Test of heterogeneity $X^2 = 219, 3 \text{ df}, p < 0.0001$	
<b>Extended-release only (n=66,077)</b>	
1. Total days supply	-3.3 mg (-1.8, -4.8)
2. On-therapy days	-6.8 mg (-4.9, -8.7)
3. Fixed observation window	-5.9 mg (-4.4, -7.4)
4. Maximum daily dose	-10.6 mg (-7.7, -13.6)
$I^2 = 86.38\%$	
Test of heterogeneity: $X^2 = 22, 3 \text{ df}, p = 0.0001$	
<b>Both extended-release and immediate-release (n=238,528)</b>	
1. Total days supply	8.8 mg (8.3, 9.3)
2. On-therapy days	16.7 mg (15.0, 17.3)
3. Fixed observation window	10.4 mg (9.2, 11.5)
4. Maximum daily dose	17.2 mg (15.1, 19.3)
$I^2 = 98.34\%$	
Test of heterogeneity: $X^2 = 181, 3 \text{ df}, p < 0.0001$	

Why is this happening?





Overlapping prescriptions dictate definition performance. Chronic pain patients have more overlapping scripts, so definition choice impacts them more strongly.



42%  
prescriptions

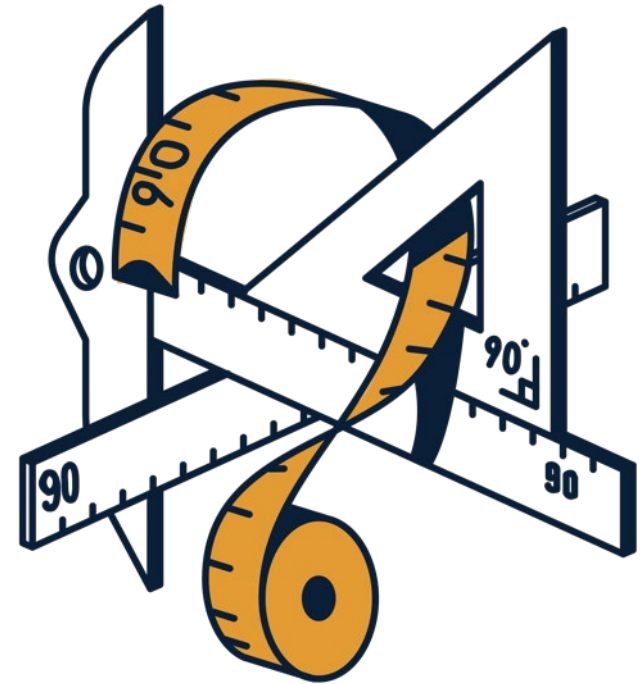
*Overlapping days supply  
within 3 months*

*n=9,436,640 Rx  
n=3,916,461 patients*

25%  
patients

90.0 versus 90.9

How much influence  
is exerted at the  
threshold boundary?



Patients are unnaturally clustered at the boundary threshold of 90 MME/day.



15.4%

more patients would be considered “high dose” if the threshold were shifted down from 90.9 to 90.0 mg.

95% CI: 15.2%, 15.7%

across 4 definitions  
and 2 states

# June Bae, University of Kentucky



*“The difference between including 90 MME and excluding the category boundary ( $\geq 90$  vs.  $> 90$  mg) was unexpectedly huge.*”

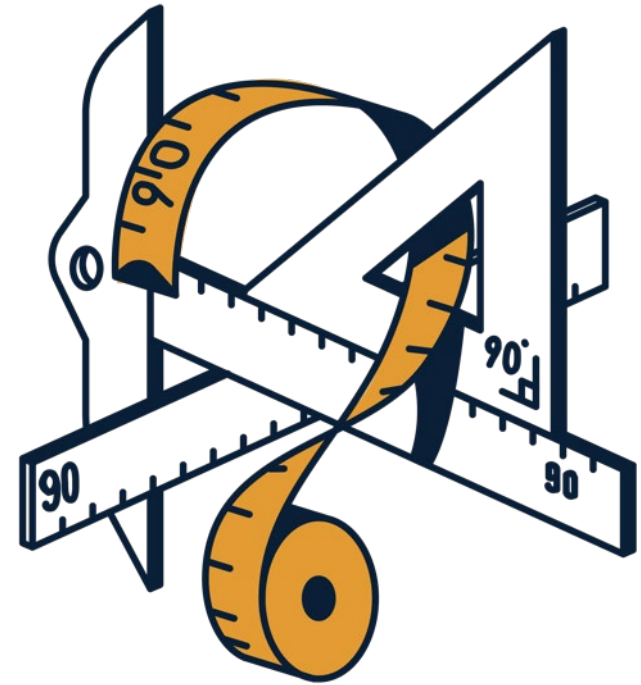
*The inclusion of the 90 daily MME cut point could potentially introduce misclassification especially when studies use the two different thresholds interchangeably.”*



# Limitations

- Assumed all medications taken as described
- Did not consider other sources, pharmaceutical or unregulated
- Did not differentiate cancer from non-cancer pain
- Did not consider atypical mu-opioid receptor agonism for respiratory depression (e.g., tapentadol)
- Did not consider pharmacist-based days supply variation
- Did not consider social and structural determinants

So, which definition should I use?



# Toska Cooper, University of North Carolina



*“There's no one size fits all approach here. It's not practical to have a universal MME formula when many factors go into patient care.”*

*“But what we can do is make all the calculations and code visible. Regardless of the audience, from clinical practice to legislation, it all should be seen.”*



## D1. Total Days Supply

- + Computationally simple
- Underestimates MME
- Single Rx scenarios



## D2. On-therapy Days

- + Strongest scientific and clinical precedent
- + Can be modified to account for gaps and unused medication
- Computationally complex
- Most research studies
- Clearest clinical interpretation



## D3. Fixed Observation Window

- + Most robust to misclassification bias
- + Most commonly used in evidence base
- Less clinical relevance
- Long-term studies
- Gaps between episodes



## D4. Maximum Daily Dose

- + Used in CDC mobile app
- +/- Ignores days supply
- Inaccuracy grows with long-term use
- Opioid naïve patients where toxicology is a concern



# A tool to compare definitions. We are looking for beta testers.



[go.unc.edu/mme](http://go.unc.edu/mme)

## MME Dosage Calculator

Start date

Days supply

Quantity

Form  ▾

Ingredient  ▾

Strength

Start date

Days supply

Quantity

Form  ▾

Ingredient  ▾

Strength

## Results

### Definition 1

76

### Definition 2

94

### Definition 3

32

### Definition 4

105

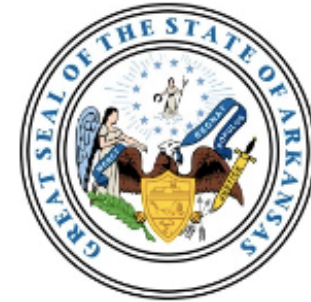
Do doctors and patients think these definition choices matter?






**Division of Medical Services  
Pharmacy Program**

P.O. Box 1437, Slot S415 · Little Rock, AR 72203-1437  
Phone: 501-683-4120 · Fax: 1-800-424-5851



**MEMORANDUM**

TO: Arkansas Medicaid Enrolled Prescribing Providers and Pharmacy Providers  
FROM: Jason Derden, Pharm.D. Division of Medical Services Pharmacy Program   
DATE: May 30, 2017

**REMINDERS:**

- 1) **The Maximum Daily Morphine Milligram Equivalent (MME) Dose DECREASED MAY 9, 2017 to  $\leq 250$  MME/day for non-cancer chronic pain beneficiaries. Incoming opioid claims that will cause the total MME/day to exceed 250 MME/day ( $>250$  MME/day) will reject at point of sale whether from same prescriber or different prescribers.**

*The Medicaid Pharmacy Program will continue reducing the maximum allowed Morphine Milligram Equivalent (MME) daily dose for chronic pain non-cancer patients by 50 MME approximately every 6 months to reduce the overdose risk and other risks associated with opioid use. The ultimate Medicaid goal is to reduce the TOTAL MME PER DAY for chronic non-cancer pain patients to meet the CDC recommendations.*

# Brooke Chidgey, University of North Carolina

Division Chief & Medical Director of UNC Hospitals Pain Management Center



*“Payors and lawmakers have grasped on to MME to guide policy decisions. While payors insist they are not dictating care because the patient can still pay out-of-pocket for the medication (I have many who do), for most patients this is not financially feasible.*

*As scientists, we often feel uncomfortable without objective data. While pain scores and MME give us numbers by which judgements are being made, they do not begin to tell the full story of the patient's pain condition. Because of this, the management of pain truly typifies the art of medicine.”*

# Liz Joniak-Grant, University of North Carolina

Chronic Pain Patient Representative and Sociologist



*“It is disheartening, but unfortunately not surprising.*

*Far too often, we are victims of the good intentions of those wanting to ‘do something’ about the opioid overdose epidemic, but the something that is done oversimplifies the problem and pushes cookbook medicine upon those of us with complicated medical situations.*

*And while everyone debates whether the MME limit was the right thing to do, we are forced to live by it, because medical personnel and others treat guidelines as mandates.*

*So we wait. And we suffer. And we hope it will all get sorted so we can get the care we need.”*

# Chris Delcher, University of Kentucky



*“It is clear that some patient experiences with prescription drug monitoring programs are negative.*

*This work is an example of how we can put PDMP data to work positively for an issue so critical to patient care.*

*Because our study was conducted in partnership with state PDMPs, we had an opportunity to educate them on the impact of these important measures.”*

Thanks for your attention.  
Thanks to the patients  
represented in the data.  
Thanks to PDMP administrators.

**Nabarun Dasgupta**

Yanning Wang, Jungjun Bae, Alan Kinlaw,

Brooke Chidgey, Toska Cooper, Chirs Delcher

Thanks to our project administrators LaMonda Sykes and Yana Biblin

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**go.unc.edu/mme**

**OpioidData.org**

June 7-8, 2021

FDA Workshop

