

August 9, 2021

*Comments sent electronically via regulations.gov*

**Re: Food and Drug Administration (FDA) public workshop and request for comments: “Morphine Milligram Equivalents: Current Applications and Knowledge Gaps, Research Opportunities, and Future Directions.”**

We write this letter on behalf of the National Council on Independent Living (NCIL), the nation’s longest-running national cross-disability, grassroots organization run by and for people with disabilities. NCIL represents thousands of individuals with disabilities and organizations including Centers for Independent Living (CILs), Statewide Independent Living Councils (SILCs), and other organizations that advocate for the human and civil rights of people with disabilities throughout the US.

As an organization working to represent the 61 million people with disabilities across the country, many who live with chronic pain, NCIL works to protect the rights of people with chronic pain. Our work in this area began as efforts to address the opioid crisis ramped up in the US, and we saw people with chronic pain left out of these efforts and harmed as a result.

We thank the U.S. Food and Drug Administration for inviting comments on the science underlying the MME (morphine milligram equivalent) measure.

We are particularly concerned about the gaps and limitations in data surrounding morphine milligram equivalents (MMEs), including, but not limited to, the significant variability in how they are calculated and the variability in metabolism based on genetic or other factors. MMEs have become an increasingly important metric used frequently to change or deny treatment,

despite the American Medical Association stating that “no entity should use MME (morphine milligram equivalents) as anything more than guidance.”

At the June 7-8 meeting “Morphine Milligram Equivalents: Current Applications and Knowledge Gaps, Research Opportunities, and Future Directions,” the first discussion question summarized current uses of MME: as a tool for converting medication dosage, and as a risk predictor for broader populations.

We ask the FDA to emphasize the use of MME as a guide for clinicians treating individual patients, not as a population-wide risk predictor.

Given the consequences for patients, it is deeply problematic that the MME metric insufficiently accounts for variations in drug metabolization, both among medications and from genetic variability.[[1]](#footnote-1) [[2]](#footnote-2)

In addition, MMEs are calculated in the real world using flawed methods. As a result, recent research found that the same medication given at the same interval could be calculated as having an MME that falls below and above the 50-90 MME thresholds mentioned in the *CDC Guideline for Prescribing Opioids for Chronic Pain*.[[3]](#footnote-3)

Since the publication of the *CDC Guideline* in 2016, nearly every entity involved with opioid prescribing has equated dosage reduction with success, regardless of the health or functional status of the patients subjected to tapering.[[4]](#footnote-4) Recent observational studies paint a bleak picture of how opioid tapering is happening in the real world. Tapering often happens abruptly with negative health consequences, and may actually increase patients’ risk of overdose or suicide, in addition to destabilizing their lives.[[5]](#footnote-5) [[6]](#footnote-6) [[7]](#footnote-7) [[8]](#footnote-8) [[9]](#footnote-9) [[10]](#footnote-10) [[11]](#footnote-11) [[12]](#footnote-12)

National Committee on Quality Assurance (NCQA) quality metrics rate health plans by number of patients maintained on doses above 90 MME, “to align with CDC recommendations.”[[13]](#footnote-13) In 2020, this threshold was lowered to 90 MME from 120 MME, despite a letter from experts (including some involved in developing the *CDC Guideline*) protesting the use of dosage as a quality measure.[[14]](#footnote-14)

State Medicaid programs enforce dosage limits regardless of medical condition or disability. State legislatures, state agencies, pharmacies, pharmacy benefit managers, health systems, and insurance companies incentivize or require across-the-board dosage reduction, justified as “alignment with the Centers for Disease Control and Prevention’s (CDC) guidelines for opioid use.”[[15]](#footnote-15) [[16]](#footnote-16)

State and national metrics define “quality” as dosage reduction to 120, 90, or 50 MME,[[17]](#footnote-17) described as “full alignment to the CDC.” Individuals who were stable, functioning, and meeting life goals at higher dosage are “addressed” via nonconsensual taper. [[18]](#footnote-18)

As one pharmacy benefit manager announced: “the program has reduced prescriptions above the CDC recommended dose by 85%.... It has also decreased prescriptions for current chronic opioid users by 68%. Further, the average dose across all opioid prescriptions has been reduced by 14%.”[[19]](#footnote-19)

Whether the affected patients function better post-reduction – or even whether they are still alive – is rarely measured or even mentioned in such “quality improvement plans.”

MME metrics are also used by law enforcement as a basis for surveillance of physician prescribing practices, often without any consideration of the patient population a physician treats.[[20]](#footnote-20)

As the HHS Pain Management Best Practices Inter-Agency Task Force report points out, although risks increase with higher dosage, given the variability in underlying conditions and in how patients metabolize opioids, there is no clear cut off point. Nor is there evidence for 50 MME, 90 MME, or 120 MME as a particular inflection point for increased risk.[[21]](#footnote-21) Recent data from CMS (Centers for Medicare and Medicaid Services) shows that dosage-based safety measures fail to capture the majority of patients at risk for overdose, and wrongly flag patients who are not at risk.[[22]](#footnote-22) These results suggest that high dose itself does not directly cause overdose, but rather correlates with underlying factors that, if correctly identified, might inform a more useful safety measure.[[23]](#footnote-23)

. Reliance on the MME metric – Originally intended to ensure patient safety, reliance on the MME metric has proven detrimental to patients with multiple chronic conditions, patients with disabilities, and to patient-centered and individualized care. In light of these serious concerns about the scientific integrity, viability, and overall usefulness of the MME metric, we urge the FDA to remove this metric.

Thank you very much for your consideration of these concerns of the disability community.

Any questions or comments may be directed to Lindsay Baran at lindsay@ncil.org or Kate Nicholson at kate@katemnicholson.com, Co-Chairs of the Chronic Pain/Opioids Task Force for NCIL.

1. Deepti Agarwal, Mercy A. Udoji, and Andrea Trescot. “Genetic Testing for Opioid Pain Management.” Pain Ther. 2017 Jun; 6(1): 93–105. [↑](#footnote-ref-1)
2. Renae A Lloyd, Elizabeth Hotham, Catherine Hall, Marie Williams, Vijayaprakash Suppiah, Pharmacogenomics and Patient Treatment Parameters to Opioid Treatment in Chronic Pain: A Focus on Morphine, Oxycodone, Tramadol, and Fentanyl, Pain Medicine, Volume 18, Issue 12, December 2017, Pages 2369–2387, https://doi.org/10.1093/pm/pnw317 [↑](#footnote-ref-2)
3. Dasgupta, Nabarun PhD; Wang, Yanning MS; Bae, Jungjun BS; Kinlaw, Alan C. PhD; Chidgey, Brooke A. MD; Cooper, Toska MPH; Delcher, Chris PhD. Inches, Centimeters, and Yards, The Clinical Journal of Pain: August 2021 - Volume 37 - Issue 8 - p 565-574 doi: 10.1097/AJP.0000000000000948 [↑](#footnote-ref-3)
4. Stefan G. Kertesz, et al. (2019) Opioid discontinuation as an institutional mandate: Questions and answers on why we wrote to the Centers for Disease Control and Prevention, Substance Abuse, DOI: 10.1080/08897077.2019.1613830 [↑](#footnote-ref-4)
5. Mark, T.L., Parish, W., Opioid Medication Discontinuation and Risk of Adverse Opioid-Related Health Care Events, 103 J. Subst. Abuse Treat. 58-63 (2019). <https://doi.org/10.1016/j.jsat.2019.05.001> [↑](#footnote-ref-5)
6. Oliva Elizabeth M, Bowe Thomas, Manhapra Ajay, Kertesz Stefan, Hah Jennifer M, Henderson Patricia et al. Associations between stopping prescriptions for opioids, length of opioid treatment, and overdose or suicide deaths in US veterans: observational evaluation BMJ 2020; 368 :m283 doi: <https://doi.org/10.1136/bmj.m283> [↑](#footnote-ref-6)
7. James, J.R., Scott, J.M., Klein, J.W. et al. Mortality after discontinuation of primary care-based chronic opioid therapy for pain: a retrospective cohort study. J GEN INTERN MED (2019) 34: 2749. <https://doi.org/10.1007/s11606-019-05301-2> [↑](#footnote-ref-7)
8. Glanz JM, Binswanger IA, Shetterly SM, Narwaney KJ, Xu S. Association Between Opioid Dose Variability and Opioid Overdose Among Adults Prescribed Long-term Opioid Therapy. JAMA Netw Open.2019;2(4):e192613. [doi:10.1001/jamanetworkopen.2019.2613](file:///C:\doi\10.1001:jamanetworkopen.2019.2613) [↑](#footnote-ref-8)
9. Perez, H., M. Buonora, C., Cunningham, M. et al., *Opioid Taper Is Associated with Subsequent Termination of Care: A Retrospective Cohort Study*, J Gen Intern Med (Aug 19 2019). <https://doi.org/10.1007/s11606-019-05227-9> [↑](#footnote-ref-9)
10. Demidenko MI, et al. Suicidal ideation and suicidal self-directed violence following clinician-initiated prescription opioid discontinuation among long-term opioid users, Gen Hosp Psychiatry. 2017 Jul;47:29-35. [doi:10.1016/j.genhosppsych.2017.04.011](file:///C:\doi\10.1016:j.genhosppsych.2017.04.011) Epub 2017 Apr 27. [↑](#footnote-ref-10)
11. Fenton, J., Agnoli, A., Xing, G., et al., Trends and Rapidity of Dose Tapering among Patients Prescribed Long-Term Opioid Therapy, 2008-2017. JAMA Netw Open.2019;2(11):e1916271. <https://doi.org/10.1001/jamanetworkopen.2019.16271> [↑](#footnote-ref-11)
12. Neprash, H.T., Gaye, M. & Barnett, M.L. Abrupt Discontinuation of Long-term Opioid Therapy Among Medicare Beneficiaries, 2012–2017. *J GEN INTERN MED* (2021). <https://doi.org/10.1007/s11606-020-06402-z> [↑](#footnote-ref-12)
13. National Committee on Quality Assurance, NCQA Seeks Feedback on New and Revised Measures. https://www.ncqa.org/news/ncqa-seeks-feedback-on-new-and-revised-measures/ [↑](#footnote-ref-13)
14. Stefan G. Kertesz, et al. (2017) An opioid quality metric based on dose alone? 80 professionals respond to NCQA. https://medium.com/@StefanKertesz/an-opioid-quality-metric-based-on-dose-alone-80-professionals-respond-to-ncqa-6f9fbaa2338 [↑](#footnote-ref-14)
15. Walmart Corporate Newsroom, “Walmart introduces additional measures to help curb opioid abuse and misuse,” May 7, 2018. https://corporate.walmart.com/newsroom/2018/05/07/walmart-introduces-additional-measures-to-help-curb-opioid-abuse-and-misuse [↑](#footnote-ref-15)
16. Letter from Lidgerwood Medical Clinic, Kaiser Permanente, Spokane, WA. https://twitter.com/CanadaPain/status/1189482268924022785 [↑](#footnote-ref-16)
17. NCQA HEDIS measures 2019, https://www.ncqa.org/hedis/measures/use-of-opioids-at-high-dosage/ [↑](#footnote-ref-17)
18. Medicaid Innovation Accelerator Program Webinar, August 29, 2019. https://www.medicaid.gov/state-resource-center/innovation-accelerator-program/iap-downloads/reducing-substance-use-disorders/alt-pain-treatment-transcript.pdf [↑](#footnote-ref-18)
19. “OptumRX Significantly Reduces Opioid Prescribing with Management Program,” First Report Managed Care, August 25, 2017. https://www.managedhealthcareconnect.com/content/optumrx-significantly-reduces-opioid-prescribing-management-program [↑](#footnote-ref-19)
20. OIG, “Opioids in Medicare Part D: Concerns about Extreme Use and Questionable Prescribing,” OEI-02-17-00250, July 2017. <https://oig.hhs.gov/oei/reports/oei-02-17-00250.pdf> [↑](#footnote-ref-20)
21. Nabarun Dasgupta, Michele Jonsson Funk, Scott Proescholdbell, Annie Hirsch, Kurt M. Ribisl, Steve Marshall, Cohort Study of the Impact of High-Dose Opioid Analgesics on Overdose Mortality, Pain Medicine**,** Volume 17, Issue 1, January 2016, Pages 85–98, https://doi.org/10.1111/pme.12907 [↑](#footnote-ref-21)
22. Yu-Jung JennyWei, PhD, Cheng Chen, BSPharm, Amir Sarayani, PharmD, Almut G.Winterstein, PhD , “Performance of the Centers for Medicare & Medicaid Services’ Opioid Overutilization Criteria for Classifying Opioid Use Disorder or Overdose” JAMA February 12, 2019 Volume 321, Number 6. [↑](#footnote-ref-22)
23. Oliva EM, Bowe T, Tavakoli S, Martins S, Lewis ET, Paik M, Wiechers I, Henderson P, Harvey M, Avoundjian T, Medhanie A, Trafton JA. Development and applications of the Veterans Health Administration's Stratification Tool for Opioid Risk Mitigation (STORM) to improve opioid safety and prevent overdose and suicide. Psychol Serv. 2017 Feb;14(1):34-49. doi: 10.1037/ser0000099. [↑](#footnote-ref-23)