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Re: eCQM460 "Potential Opioid Overuse"

Under a CMS Contract "Electronic Clinical Quality Measures Development and Maintenance for Eligible Professionals", the Lewin Group proposes a quality metric defined as, "Percentage of patients aged 18 years or older who receive opioid therapy for 90 days or longer and are prescribed an average daily dosage of 90 milligram morphine equivalents or greater."

We write to register our opposition to this binary high-stakes metric on three distinct grounds. They are as follows:

1. Reliance on a simple binary dose metric is an extremely poor method to identify persons at-risk for adverse events while receiving opioids, as it is both extremely insensitive and non-specific.

2. A high stakes binary dose metric of this nature incentivizes medical practices that are not based on evidence and that have proven dangerous, both in our observation and in the emerging literature on opioid dose reduction.

3. High stakes binary numeric metrics for care quality have a robust history of incentivizing harmful medical practices. Tragic outcomes are even more likely in the context of parallel initiatives from governmental and non-governmental agencies mandating or incentivizing opioid dose reduction without reference to patient safety.

We first underscore our clinical and research expertise to comment on this issue. All three signatories are general internal medicine physicians with deep experience in opioid safety, addiction care, and primary care. All three of us are board-certified in addiction medicine. **Dr. Stefan G. Kertesz** is Professor of Medicine at the University of Alabama at Birmingham School of Medicine and Birmingham VA Medical Center, serving on the Opioid Safety Initiative and Opioid Advice Team for the Birmingham VA Medical Center. He has published over 60 articles on addiction and primary care of homeless populations. **Dr. Adam J. Gordon** is Professor of Medicine and Psychiatry at the University of Utah and the Chief of Addiction Medicine at the

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All three of us have direct experience and extensive observational contact with tragic harms to patients that result from physicians who have acted under regulatory inducements to curtail opioid doses, slowly or quickly. Having regularly observed suicides, medical deteriorations, and overdoses resulting from such pressures, we have re-evaluated the available data on dose thresholds as a method to enforce opioid safety. We present below our scientific and clinical concerns about a quality measure that will further incentivize a harmful and non-evidenced based alteration to care.

1. **Reliance on a simple binary dose metric is an extremely poor method for identifying persons at risk for adverse events while receiving opioids. It is insensitive and non-specific.**

Based on our research and primary care experience, we fully appreciate the observed correlation between opioid dose and risk of adverse outcome among persons who have received a prescription for opioids at some time in the prior year (2). This may suggest that on whole, a lower dose ought to be safer than a higher dose, all things being equal. However, the effort to stratify dangerous or high-risk patients from low-risk patients based on dose will not succeed, because the 90 MME threshold misses the overwhelming number of persons who suffer overdose events, and it reflects a fundamental misconception of the event we term "overdose".

Among overdose events in persons who have received a prescription, the dose is typically low or nonexistent at the time of the lethal event, as the published data makes very clear. In a case-control study from the Veterans Administration, the median dose for an overdose patient was 60 MME (3). In publicly reported Veterans Administration-wide data for Fiscal Year 2013, 86% of overdose/suicide events occurred at <90 MME, and VA has approved submission of a manuscript showing that these percentages are similar when overdose and suicide are tabulated separately. Similarly, in published analyses of 1452 opioid overdose events in Washington state citizens who had received opioid prescriptions, only 21% occurred at a time when the patient received opioid doses exceeding 90 MME (4). Fully 42.6% occurred at a time when the Medicaid recipient had no prescription whatsoever on hand, while 27.8% occurred while receiving a dose under 50 MME. Were it the case that dose could be used as a method of identifying prescription recipients who would die from overdose, the proposed 90 MME threshold would ignore and fail to protect roughly 70-90% of persons at risk, suggesting that this is at the very least an insensitive measure.

The correlation between dose prescribed and overdose event is a real finding (2). However, high prescription dose appears in large part to serve as a marker for multiple psychological and social vulnerabilities (5-7). This does not mean that every person receiving high doses has such vulnerabilities. However, it does suggest such vulnerabilities are likely to play a counfounding role in the prediction of overdose events in large correlational data analyses.

in contemporary studies that more sensitively measure other characteristics of persons who suffer overdose, opioid dose turns out to be either a weak predictor of overdose (8), or it loses its predictive power altogether (9). One study, published this year, looked at 42,828 chronic opioid recipients in the Kaiser system, where access to care is high and where diagnoses for mental illness are more likely to be applied in a timely fashion (9). In appropriately adjusted models, mental health diagnoses, tobacco dependence, substance abuse/dependence diagnoses and long-acting agents **were independent** predictors of overdose. Dose, however, did **not independently predict overdose at all.**

The VA Stratification Tool for Opioid Risk Mitigation (STORM) system was used to assess VA-wide risk of overdose or suicidal events (prior models demonstrated that the same variables predicted both overdose and suicide) (8). A report from STORM **did** find a statistically **independent** association between opioid dose and risk. However, the augmentation of risk related to dose was weaker than cardinal determinants of risk such as mental illness (including PTSD), substance use disorder (in remission or active), and the co-administration of other sedating medicines. For example, a man with post-traumatic stress disorder and a dose of 20 MME would be a higher risk than a man with no similar risk but a dose of 200 MME.

Historic heroin overdose literature helps to explain why dose itself is so poor at predicting an adverse event. In that literature, most events we call “overdose” transpire at low doses, even with heroin (10). Death occurred when heroin was combined with other substances and the patient took the heroin outside of normal circumstances. Put another way, opioid users develop tolerance over time, if opioid dose is regular and consistent and not combined with other substances in dangerous ways.

This does not mean opioids are risk-free at any dose. They are a deeply problematic drug treatment with real risk at any dose, most notably the reality of dependence, which can take less or more devastating forms. But to the extent that the goal is to prevent overdose, a single dose threshold is simply at odds with the literature as we know it.

Even worse, the proposed metric is also at odds with the CDC Guideline on Prescribing Opioids for Chronic Pain (11), at least in one way. The CDC Guideline drew a crucial distinction between initial dose escalation and the care of legacy patients, a distinction that the proposed measure ignores.

The Guideline's recommendations 1-5 focus on caution in initiation and escalation of dose. Even those recommendations do not **prohibit** a dose above 50 or 90 MME. Rather, they call upon clinicians to carefully consider risk and benefit before dose escalation.

For patients already on opioids, recommendation 7 applies. It sets no dose target whatsoever. It demands an individualized decision based on the patient's current benefit and harm. This was an intentional decision of the CDC's experts, and reflected a conspicuous lack of data to support dose reduction in such patients, save when they are voluntarily seeking dose reduction and are properly supported (12).

We are distressed that the proposed metric ignores such a central component of the CDC Guideline. By taking numeric thresholds and ignoring key evidence considerations that went into that Guideline, the proposed measure undermines the Guideline itself. In this, we want to note that fully 80 experts in addiction and pain, including four who assisted the CDC Guideline's development, formally protested when the National Committee for Quality Assurance sought to advance a similar metric (13).

2. **A high stakes binary dose metric of this nature incentivizes medical practices that are not based on evidence, and that have, sadly, proven harmful to patients, both in our observation and in the emerging literature on opioid dose reduction.**

The inevitable result of a binary numeric metric of 90 MME is that it will contribute to the many pressures already operating on clinicians to force doses downward, even when doing so is both dangerous and unproven as medical practice.

Today's physicians are under mandates from other quality metric agencies, state regulators, medical boards, and threat of investigation to **force** doses downward in currently stable patients. For them to protect their patients despite such pressure, already entails professional risk (14).

We question the outcomes achieved through the intense focus on dose control. High dose prescriptions have fallen by 48% since 6 years ago (15). The decline does not appear to have reduced overdose events of any kind, either those involving illicit or licit opioids (16). The period of late 2016 through 2017 featured many reports of pain patients subject to opioid termination who committed suicide, attacked physicians, died in withdrawal, suffered medical decline, or overdosed on illicit opioids (17-21).

Indeed, preliminary data from the US Department of Veterans Affairs, reported publicly on the website for the 2018 National Rx Drug Abuse and Heroin Summit (for presentation on April 4, 2018) show that opioid discontinuation (between one fiscal year and the following one) was not associated with any reduction in overdose, but was associated with a rise in suicide. We recognize that this analysis does not assess "taper to lower dose" per se, but it should signal an additional warning beyond the many anecdotes.

It is tempting, but incorrect, to assert that such events simply reflect tapering "too quickly". We have personally observed and publicly reviewed many cases of slow tapers that produced the same outcomes. One, written about in The Hill (22), and later presented at a scientific meeting, involved a patient who lost capacity to take renal transplant protection medications after a taper over a year. The reason for deterioration is *dependence*. The opioids' utility for pain, for some, is intimately bound up with their effect on reward/affect in the brain. Slow taper in a person with dependence does not routinely resolve the long-term brain changes that have occurred.

3. **High stakes binary numeric metrics for care quality have a robust history of incentivizing harmful medical practices. Tragic outcomes are even more likely in the context of other parallel initiatives from governmental and non-governmental agencies.**

Finally, we caution that history depicts the harms that result from embracing simple numeric indicators of quality care when there is a conspicuous lack of properly-conducted trial data to show that such quality metrics protect patients.

On this matter, the trial data to support forced dose reductions that will be incentivized by the proposed metric do not exist. In the most exhaustive review of opioid dose tapers ever published, Frank et al cautioned that they identified "no prospective studies" of involuntary dose reduction, and that there were serious risks of overdose, suicidality, and resurgent mental health symptoms if mandates of this nature were applied (12).

The embrace of a simplistic numeric indicator of quality care, based on observational data alone, finds ominous precedent in the application of the 7% hemoglobin A1c metric for care of diabetes. While helpful to some patients, subsequent randomized controlled trials found that the efforts to minimize glucose to "ace the metric" caused death for a number patients (23, 24). The later trial data made clear that lives had been lost as a result of well-intentioned efforts to improve performance using all-or-nothing binary performance targets based on alluring numbers (25). Indeed, today's problems of opioid over-prescription are similarly attributable to a scientifically unsound, clinically inappropriate, dangerous and yet well-intentioned effort to optimize precisely one number, the pain score (26), in the absence of sufficient trial data.

We fully appreciate the constructive intent that lies behind current efforts to reconfigure opioid prescribing. We regard the run-up in prescribing from 1999 to 2011 as **tragic**, as we believe that the distribution and redistribution of those pills contributed to market of new patients with addiction. Similarly, we have certainly seen pain patients sedated to death, typically with multiple psychoactive substances (rather than just a carefully titrated opioid). And we have seen many patients where the institution of opioid therapy was clearly harmful.

At the same time, we take note of the profound, relentless harms to patients that result from the untested, unscientific, and nonpatient-centered dose reductions that many simultaneous

initiatives have caused to take place (25). This quality metric will accelerate that harm. It is not carefully rooted in the science of overdose. It does an injustice to the CDC Guideline.

We heartily credit the good intentions that lie behind such a metric, but we must strongly urge its rejection as both insensitive, nonspecific, and likely to cause harms we will later come to regret.

Please note that views presented here are solely those of the authors, and do not represent positions of the US Department of Veterans Affairs, any other agency of the US Federal Government, or any of our employing universities.

Signed,

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