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## **EDITORIALS**



## Rethinking "long term" opioid therapy

Definitions are heterogeneous, arbitrary, and potentially harmful

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Long term opioid therapy for non-cancer pain has been much debated because of concerns that the harms may outweigh benefits. What has received less attention is how long term should be defined and whether the label has any value for patients, doctors, or researchers.

Although long term opioid therapy seems a simple concept, definitions vary widely. Most studies define long term as  $\geq$ 90 days of opioid use, but the threshold ranges from one week to one year.<sup>12</sup> Definitions also vary in terms of frequency of use (consistent daily dosing versus intermittent use) and if use is self-reported or based on dispensing records. Other definitions consider the dose as well as duration. Variations in terminology (such as chronic opioid therapy) add further confusion.

The variation in definitions has important consequences. Although the scientific community agrees there is an opioid crisis, without a consistent definition we cannot characterise the crisis or measure the success of interventions to tackle it. It is impossible to get consistent and reproducible measurements of the prevalence of long term therapy or to assess risk factors, comorbidities, harms, economic costs, and the effects of interventions to prevent unnecessary continuation of treatment. The lack of a consistent definition also limits the generalisability of research findings or guideline recommendations.

In clinical practice, strict definitions such as "more than six months of use"<sup>3</sup> may result in missed opportunities to identify people at risk of harm earlier, when stopping opioids may be simpler and more effective. Conversely, lax definitions such as "at least three opioid prescriptions in the last year"<sup>4</sup> may flag up people who are taking opioids intermittently for occasional exacerbations (of osteoarthritis or endometriosis, for example) and are at low risk of opioid related harm.

## Reducing harm

It is important to consider what we are trying to achieve with the label long term opioid therapy. It may seem appealing to use three months as the standard definition since this is the most commonly used, but this threshold is arbitrary. If the aim is to reduce harm from overuse of opioids, it may be more appropriate to select a duration grounded in evidence and linked to meaningful clinical outcomes, such as a threshold after which risk of persistent use at one year substantially increases.

Recent evidence suggests that the first month after starting opioids is critical: the risk of persistent use at one year is roughly 24% after 12 days' use of an opioid analgesic, roughly 35% after 21 days' use, and roughly 43% after 31 days' use.<sup>56</sup> Furthermore, a cumulative dose of more than 120 morphine mg equivalents in the first month roughly doubles risk of persistent use at one year.<sup>5-7</sup> Duration of use and dose in the first month are both key determinants of persistent use.

Another possibility is to abandon aspects of the dose regimen (duration and dose) and instead define long term opioid therapy according to the presence or absence of features of opioid use disorder,<sup>8</sup> including physical harm (such as overdose) and behaviours that may indicate tolerance (such as frequent requests for increases in dose or quantity). This option would identify patients at risk of harm and may trigger a conversation about deprescribing, but the dose regimen that led to this point in care would vary from person to person.

Recent evidence also suggests that multiple factors help predict risk of harm when prescribing opioids for pain, including social and economic factors, medical history, and opioid formulation.<sup>910</sup> A history of substance use disorder, personality disorder, or other mental health conditions and concomitant prescription of psychiatric drugs are indicators of higher risk of addiction to prescription opioids.<sup>9</sup> Furthermore, overdose events are six times more likely among patients prescribed a long acting opioid than those given a short acting opioid.<sup>10</sup> Clinicians must consider all these factors with patients when considering opioid treatment, in line with patient centred, biopsychosocial management of chronic pain.

The consequences of heterogeneous and arbitrary definitions of long term opioid therapy are borne by people living with

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chronic pain. But a common definition based on opioid regimen is not ideal, as harms may occur sooner than a defined cumulative dose or duration. It may be better to consider the manifestations of opioid related harm instead when deciding whether opioid therapy has continued for too long. Research is needed to investigate how best to decide when opioid therapy has continued for too long and, importantly, what should be done to avoid harm when this point in care is reached.

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