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## Reply to Chang et al.

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### Letter to the Editor:

We appreciate the letter by Chang et al. related to our study, which examined patterns and variation in daily opioid dosage among patients newly initiated on long-term opioid therapy using IQVIA Longitudinal Prescription (LRx) all-payer pharmacy data.<sup>7</sup> As Chang et al. note, our study only included individuals with retail pharmacy-dispensed prescriptions, which we describe as a limitation in our article. Although IQVIA collects data across retail, mail order, and long-term care pharmacy channels, the longitudinal data used for this study were only available for retail pharmacy-dispensed prescriptions. According to our analysis of the IQVIA National Prescription Audit database, among opioid prescriptions dispensed in 2019, 90.3% (154 million) were by means of retail pharmacies vs 9.2% (15.6 million) from long-term care, and <1% (1 million) from mail-order pharmacies. Furthermore, the amount of opioids dispensed directly by physicians decreased substantially after 2010 in most states.<sup>6</sup> Given that approximately 90% of opioid prescriptions were dispensed by retail pharmacies during the study period, the IQVIA LRx database was well suited for a longitudinal study of patterns and variation in daily opioid dosage among patients.

Chang et al. note an additional limitation described in our study, which was the lack of clinical information in the IQVIA LRx database, such as diagnoses, patient history, or adverse events such as nonfatal or fatal overdose, hospitalizations, or death from other causes. Due to the lack of clinical information in this database, we cannot infer why long-term opioid therapy has been prescribed or comment on changes in dosage that may be initiated due to adverse events. Despite these limitations, the IQVIA LRx database is a national all-payer pharmaceutical database, which captures more than 92% of all retail prescriptions dispensed in the United States regardless of payer, including prescriptions paid with cash. Future research that builds on our study through the inclusion of clinical

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Conflict of interest statement

The authors have no conflicts of interest to declare.

information would be an important contribution to the literature on patterns in prescribing for long-term opioid therapy.

Finally, Chang et al. advise that future research could include a longer follow-up period than was used in our study. Our study used a 90-day baseline period to define the study cohort of patients newly initiated on long-term opioid therapy, which is consistent with previous studies of long-term opioid therapy.<sup>2,5,8</sup> We followed patients in the study cohort for an additional 9 months after their baseline period, for a total of 12 months of longitudinal prescription data. A longer follow-up period, which results in more longitudinal data for each individual, would substantially increase the computational complexity of time series cluster analysis, which may be computationally intractable or require a smaller, less representative patient cohort. The focus of our analysis was on variations in average daily opioid dosage and outcomes such as tapering and discontinuation of opioids. Previous studies of long-term opioid therapy that have included longer follow-up periods considered longer-term clinical outcomes, such as fatal and nonfatal overdose, mental health crises, and hospitalizations.<sup>1,4</sup> As such, the follow-up period used in our study was appropriate for the research question and methods applied.

Our study was the first, to our knowledge, to conduct cluster analysis of opioid dosage trajectories for patients prescribed long-term opioid therapy and provides a unique visual representation and characterization of patterns in prescribed opioid dosage. The results of this study identified several clusters of patients with daily dosages of >50 morphine milligram equivalent who experienced frequent discontinuation or rapid tapering of opioid dosages. These findings highlight opportunities for clinician training pertaining to guideline-concordant opioid prescribing, including the risks of high-dosage opioid prescribing and the importance of shared decision making with patients when initiating changes in opioid dosage.<sup>3,9</sup>

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