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Too much or not enough? A comment on discrepancies in published estimates of opioid use in Australia

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Dear Editor,

Thank you for the request to comment on the methodology and different estimates reported in the paper by Islam and colleagues entitled *Prescription opioid analgesics for pain management in Australia: 20 years of dispensing*[1] and our recently published manuscript in the *British Journal of Clinical Pharmacology*.[2]

The majority of the estimates of opioid use presented by Islam *et al* were obtained using the database maintained by the Drug Utilisation Sub-Committee (DUSC); this data source was also used in our study. We note marked discrepancies between the results presented in the online accepted version of the Islam *et al* manuscript[3] and those presented in our paper and another publically-available source[4]. Specifically, we note a 10-fold inflation of prescription volume in Table 2 and overestimation of use according to DDD/1000 persons/day in Table 2 and Figure 3. The authors have acknowledged this in their corrigendum, and many of the errors appear to have been corrected in the published paper in this issue of the journal.

Hereafter, we discuss only the estimates presented in the corrected, published version of the Islam *et al* paper. Islam and his colleagues do not detail the medicines included in their analysis in the methods section of their paper, making verification of their results challenging. However, based on the medicines listed in Table 1 of Islam *et al*, we would expect good concordance between estimates of opioid use in their analysis and ours. We note that the yearly prescription volumes detailed in Islam's Table 2 are relatively consistent with those derived from our dataset (data not presented in our paper; see Table 1 for comparisons). However, their data on total opioid use by year according to DDD/1000 persons/day are lower than our estimates, which is unexpected given the comparability of prescription volume estimates. Notably, in 2011, we estimate total opioid use at

17.96 DDD/1000 pop/day, which exceeds the 14.46 DDD/1000 people/day in Islam *et al*'s Table 2 by almost a quarter.

Moreover, the DDD/1000 persons/day estimates reported in Figure 3 of Islam *et al* overestimate dextropropoxyphene use by 35% and underestimate codeine use by approximately 40%. For example, in 2011, codeine utilisation is reported as 4.4 DDD/1000 persons/day in the *Islam et al* paper compared to 7.4 DDD/1000 pop/day in our paper. We acknowledge that there appear to be small differences in the codeine preparations included in our respective analyses (based on the footnote to Figure 3 and the medicines listed in Table 1 of Islam *et al*), hence we would not expect our estimates to perfectly align. However, given the similarity in our estimates of codeine (and dextropropoxyphene) prescription volumes, we would expect closer concordance between our respective estimates of DDD/1000 persons/day.

The DDD/1000 pop/day metric can be used to obtain an approximate estimate of the proportion and size of the population treated *daily* with opioids. Extrapolating from our 2011 estimate of total opioid use (17.96 DDD/1000 pop/day), 1.8% of the Australian population (approximately 402,000 people) were treated with opioids daily that year. This exceeds the corresponding estimate from Islam *et al* by 0.35% of the population or 78,000 people. Similarly, our study suggests that approximately 165,000 Australians were treated daily with prescription codeine in 2011 (extrapolated from 7.4 DDD/1000 pop/day) compared to 98,000 from Islam *et al*, a discrepancy of 67,000 people. However, there are some important considerations when using DDD/1000 pop/day to extrapolate to population estimates. As noted in our manuscript and the Islam *at al* paper, the DDDs for many strong opioids were assigned when the medicines were initially listed for use in cancer pain, while the DDD of codeine was based on the lower doses used in cough suppression.[4] As such, absolute population estimates derived from DDD/1000 pop/day are likely to underestimate

the true utilisation of strong opioids, particularly morphine, buprenorphine and fentanyl, and overestimate the true utilisation of codeine. Limitations of the metric notwithstanding, the relative differences in our estimates and those of Islam *et al* still hold.

We did not undertake an analysis of opioid use by State/Territory in our paper and, given our uncertainty about the medicines and item codes included in the *Islam et al* paper, we did not attempt to verify the DDD/1000 people/day estimates presented in Figures 5 and 6. However, we question their accuracy in light of the previously-mentioned discrepancies between our papers on other DDD/1000 people/day estimates.

There are other considerations worth noting when interpreting the results of the State/Territory analysis. The paper uses two distinct data sources: that maintained by DUSC, described in detail in the methods, and publically available Medicare Australia PBS item reports[5]. The latter is used for the State/Territory analysis. Unlike the DUSC database, which records dispensing based on the date the medicine is *supplied* to the patient by the pharmacy, the PBS item reports record dispensing based on the date that the dispensing pharmacy's claim for reimbursement is processed by the Department of Human Services. Data based on date of processing are less likely to reflect medicine access patterns at particular time points, as delays in the processing of claims followed by periods of bulk processing can produce troughs and peaks in estimates[6]. The State/Territory analysis is also affected by changes in medicine reimbursement across different States and Territories due to the Public Hospital Pharmaceutical Reforms. The Reforms, which allow public hospitals to provide PBS-subsidised medicines to outpatients and discharging inpatients, were introduced gradually across most States and Territories of Australia from 2001[6]. It is unlikely that the Reforms account for all the differences in opioid use between the States and Territories but they should be acknowledged when comparing use by jurisdiction.

For the reasons stated above we suggest that the findings of the Islam *et al* paper are used with caution.

References

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