## AN INTERNATIONAL SYSTEMATIC REVIEW OF METHADONE AND BUPRENORPHINE DOSES USED IN THE TREATMENT OF OPIOID USE DISORDER

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**Background:** Opioid agonist treatment (OAT; i.e. methadone and buprenorphine for the treatment of opioid use disorder) reduces hepatitis C incidence, overdose deaths, and other opioid-related harms. Treatment effectiveness is in part determined by the dose of methadone or buprenorphine that is prescribed. Minimum doses recommended by the World Health Organization (WHO) to achieve clinical benefit are 60mg for methadone and 8mg for buprenorphine. We undertook a systematic review of literature that documented the delivery of OAT in routine clinical care.

**Methods:** We searched PubMed and Embase for papers reporting relevant data, including only papers reporting data relevant to clinical practice from 2010 onwards. Clinical guidelines were excluded from the review as these may not reflect actual practice. We extracted dose data (mean/median dose and proportion of clients receiving greater than the WHO minimum recommended doses of >60mg methadone/>8mg buprenorphine). Data were synthesized for each country.

**Results:** We identified 101 reports from 34 countries with data on methadone or buprenorphine dosing in routine clinical care. Mean/median dose of methadone was <60mg in 27 of 75 studies from 31 countries reporting this metric. Fourteen countries (45%) had data indicating inadequate methadone doses, including China, France, Georgia, Tanzania, and the United Kingdom. There were 31 studies from 14 countries presenting data on buprenorphine dosing; of these, mean/median buprenorphine dose was <8mg in 24 studies. Seven countries (50%) had data indicating inadequate buprenorphine doses, including Germany, Iran, Malaysia, and Nepal.

**Conclusion:** Our findings suggest that many people prescribed OAT receive insufficient doses of methadone or buprenorphine. Examples of under-dosing were found in low-, middle-, and high-income countries. The full clinical and population health benefits of OAT will not be realized unless greater attention is given to ensuring adequate doses or methadone and buprenorphine are prescribed.

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