

# Global psychotropic medicine consumption in 65 countries and regions from 2008 to 2019

## Authors

Ruth Brauer, PhD<sup>1</sup>, Basmah Alfageh, MSc<sup>1,2</sup>, Joseph E Blais, BScPharm<sup>3</sup>, Esther W Chan, BPharm, PhD<sup>3,4</sup>, Celine SL Chui, PhD<sup>4-6</sup>, Joseph F Hayes MD, PhD<sup>7</sup>, Kenneth KC Man, PhD<sup>1,3,4</sup>, Wallis CY Lau, PhD<sup>1,3,4</sup>, Vincent KC Yan, BPharm<sup>3</sup>, Maedeh Y Beykloo, PhD<sup>1</sup>, Zixuan Wang, MSc<sup>1</sup>, Li Wei, MD, PhD<sup>1</sup>, Ian CK Wong, BPharm, PhD<sup>1,3,4</sup>

## Affiliations

<sup>1</sup> Research Department of Practice and Policy, UCL School of Pharmacy, London, UK

<sup>2</sup> College of Pharmacy, King Saud University, Riyadh, KSA

<sup>3</sup> Centre for Safe Medication Practice and Research, Department of Pharmacology and Pharmacy, LKS Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China

<sup>4</sup> Laboratory of Data Discovery for Health (D24H), Hong Kong Science Park, Hong Kong Special Administrative Region, China

<sup>5</sup> School of Public Health, LKS Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China

<sup>6</sup> School of Nursing, LKS Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China

<sup>7</sup> Division of Psychiatry, University College London, London, United Kingdom

## Correspondence

Ian CK Wong, Lo Shiu Kwan Kan Po Ling Endowed Professor in Pharmacy and Head  
wongick@hku.hk

T +852 3917 9441 | F +852 2817 0859 | web site: [www.pharma.hku.hk](http://www.pharma.hku.hk) 2/F, Laboratory Block,  
21 Sassoon Road, Pokfulam, Hong Kong

**Manuscript word count:** 4126

## **Research in context**

### **Evidence before this study**

We searched PubMed for studies written in English published from January 1, 1990, to January 19, 2021, with the following terms: (((((treatment) OR (medication)) AND (sales)) OR (MIDAS)) AND (trend)) AND (Mental health disorder). The search yielded 299 articles. We excluded articles deemed not to be relevant based on their titles. We reviewed abstracts of the remaining articles to identify potentially relevant articles and scanned reference lists of relevant articles. The primary criterion was that the study reported trends in psychotropic sales or consumption.

Most previous studies were from Europe, with a few studies comparing psychotropic medicine consumption of 27 countries. However, psychotropic medicine consumption in these multinational studies were often based on self-reported use or individual level prescription data. Most studies reported trends in the consumption of antidepressants, with only two studies comparing the consumption of tranquilisers in multiple countries. While a general increase in psychotropic medicine sales was observed in most studies, the consumption of hypnotics decreased.

### **Added value of this study**

This is the largest and most up-to-date assessment of consumption trends of all major classes of psychotropic medicines for 65 countries and regions from 2008 to 2019, grouped according to country income level: lower-middle-, upper-middle-, and high-income and geographic region. This comprehensive description of the epidemiology of psychotropic medicine consumption (1) identified countries with very low consumption of psychotropic medicines, (2) provided baseline consumption rates that can be used as a benchmark to measure and monitor future global, regional, and national use of psychotropic medicines, and (3) assessed the relationship between psychotropic medicine consumption and the prevalence of mental

disorders, life expectancy, and health expenditure at the country-level. We have identified 17 countries with very low consumption of psychotropic medicines in 2019. These countries are unlikely to provide sufficient access to psychotropic medicines for patients. The reasons for such low consumption are multifactorial, with both the direction and the strength of the association between psychotropic medicine consumption and the prevalence of mental disorders, life expectancy, and health expenditure varying according to country income level.

### **Implications of all the available evidence**

The consumption of antidepressants, mood stabilisers and antipsychotics, has increased from 2008 to 2019, suggesting improved overall access to these medicines, but consumption rates of individual countries varied substantially. Disparities in access to psychotropic medicines remain a challenge across most of the world, especially in middle-income countries. Strategies to improve access to psychotropic medicines that should be considered include: training healthcare workers who can prescribe cost-effective, essential, psychotropic medicines; public education; and involving community leaders to promote appropriate understanding of psychotropic medicine use. Our study findings can be used as a foundation to evaluate future interventions designed to improve appropriate use of psychotropic medicines.

**Abstract (367 words)**

**Background:** The Mental Health Action Plan 2013-2030 encourages routine collection and reporting of a set of essential mental health indicators including the availability of psychotropic medicines. The global monitoring of country-level psychotropic medicine consumption trends can provide information on the extent of the availability of psychotropic medicines. The primary objective of this study was to investigate global trends in psychotropic medicines consumption from 2008 to 2019 across 65 countries and regions according to country income level and geographic region.

**Methods:** This longitudinal trends study used pharmaceutical sales data from the IQVIA-Multinational Integrated Data Analysis System (IQVIA-MIDAS). We analysed monthly sales data of psychotropic medicines between January 2008 and December 2019. Total psychotropic medicine consumption included sales of antidepressants, antipsychotics, tranquilisers, sedatives/hypnotics, and mood stabilisers. Population estimates of each country/region (lower-middle-income countries [LMICs], n=8; upper-middle-income countries [UMICs], n=19; high-income countries [HICs], n=38) were based on the UN World Population Prospects 2019 report. Average annual sales trends of psychotropic medicines, expressed as defined-daily-dose/1000-inhabitants/day (DDD/TID), were estimated using a random effects model.

**Outcomes:** Psychotropic medicine sales increased from 28.54 DDD/TID in 2008 to 34.77 DDD/TID in 2019, corresponding to a 4.08% (95% CI 2.96%-5.21%) average increase annually. The absolute annual increase was greater in HICs (3.31 DDD/TID, 95% CI 3.01-3.61) compared to UMICs (1.94 DDD/TID, 95% CI 1.45-2.44) and LMICs (0.88 DDD/TID, 95% CI 0.62-1.13). Trends by age or gender were not available. In 2019, the regional consumption of psychotropic medicines varied greatly, with the lowest sales of all psychotropic medicine classes reported in Asia. Seventeen countries had very low

consumption of psychotropic medicines in 2019, including HICs and countries with a high prevalence of mental disorders.

**Interpretation:** The consumption of psychotropic medicines has increased over a 12-year period whilst the absolute growth rate is highest in HICs, the relative growth is highest in MICs and especially UMICs. Disparities in psychotropic medicine consumption of countries can only partly be explained by geographic location and income. Greater efforts are needed to increase the availability of psychotropic medicines in countries with very low consumption, which is likely due to financial or cultural reasons as well as lack of trained health care professionals to prescribe psychotropic medicines.

**Funding:** None.

## **Introduction**

Globally, mental disorders such as depression and anxiety are among the top ten causes of years lived with disability in 10-49 year olds.<sup>1-3</sup> Pharmacological treatment of mental disorders is effective and often used as first-line treatment in countries where psychological interventions are difficult to access.<sup>3</sup> The World Health Organization (WHO) has recognised that the health systems of individual countries across the world have not yet adequately responded to the burden of mental disorders and that there is often a substantial gap between the need for mental health treatment and its availability, especially in low- and middle-income countries.<sup>4</sup> As part of the comprehensive Mental Health Action Plan 2013-2030, targets have been set to increase the output of global research on mental health and to encourage routine collection and reporting of a core set of mental health indicators.<sup>4,5</sup> Routine monitoring of the availability of psychotropic medicines in individual countries is specifically mentioned as a mental health indicator of health and social system actions.<sup>4</sup> The global monitoring of country-level psychotropic consumption trends can provide information on the extent of pharmacological interventions for mental disorders, and the availability of psychotropic medicines. Moreover, psychotropic medicine consumption data can be used to inform future policy evaluation, especially in middle-income countries where these data are lacking.<sup>4</sup> To our knowledge, there are no global surveillance studies to track and compare country-level use of psychotropic medicines. The few published international comparison studies on the consumption of psychotropic medicines are limited to one type of psychotropic drug only.<sup>6-8</sup>

To improve our understanding of global trends in medication treatment for mental health conditions in high-income, lower- and upper middle-income countries (HICs, LMICs and UMICs respectively), we described the consumption of psychotropic medicines in 65 countries and regions from 2008 to 2019. Additionally, we set out to capture any changes in consumption over time by geographic location and in relation to the prevalence of mental disorders, life

expectancy, and health expenditure. Lastly, we identified countries which have very low consumption of psychotropic medicines, which likely suggests poor access to psychotropic medicine therapy.

## **Methods**

Psychotropic medicine sales data (EphMRA [European Pharmaceutical Marketing Research Association] N5A, N5B, N5C and N6A, appendix pp 2) were obtained from the IQVIA Multinational Integrated Data Analysis System (IQVIA-MIDAS) database in September 2020. MIDAS captures global data on the volume of specific pharmaceutical products sold to retail and hospital pharmacies and enables comparisons of national-level sales audits by providing international standardisation of sales value and volumes and medical prescription data.<sup>9</sup> Data sources differ by country, and by data type, but are usually a combination of sales data from manufacturers (direct sales) and wholesalers; in some countries, sales data are also acquired from hospital and retail pharmacies (appendix pp 3-5). The average coverage has been shown to be 88%,<sup>10</sup> with adjustments made to estimate the total sales volume based on knowledge of market share of the contributing retail or hospital pharmacies and wholesalers.<sup>11</sup> Data from IQVIA-MIDAS have been internally validated from alternative sources of sales data and are used for evaluation of global medicine consumption patterns.<sup>12,13</sup> Consumption of both generic and brand products are included. The database does not contain patient-level data, thus no information on indications and patient demographics were available. Hence, institutional review board approval was not required.

### *Data inclusion and exclusion*

We categorised psychotropic medicines into five major medicine classes: antidepressants, mood stabilisers, antipsychotics, tranquilisers, and sedatives/hypnotics. We excluded attention deficit hyperactivity disorder (ADHD) medications as they are mainly used in children and



adolescents which make direct comparisons with other psychotropic medicines inappropriate. Antidepressants were subdivided, mainly according to mode of action into the following groups<sup>14</sup>: non-selective monoamine reuptake inhibitors (tricyclic), selective serotonin reuptake inhibitors (SSRIs), serotonin-noradrenaline re-uptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), and antidepressants not otherwise categorised (*other*, appendix pp 6). Antipsychotics were divided into typical (N5A9) and atypical (N5A1) agents.

### *Data analysis*

The sales data of selected medicine classes were stratified based on country income level (i.e., LMICs, UMICs and HICs) to investigate how consumption trends vary with country income level. We calculated both the standard units per person and the defined-daily-dose/1000-inhabitants/day (DDD/TID) for each year using the sales volume data and national population data.<sup>15</sup> Defined daily dose is the assumed average maintenance dose per day for a drug used for its main indication in adults and is only available for single molecule products. As such, combination products and herbal products were excluded from these analyses. Population estimates of each country were obtained from the UN World Population Prospects 2019 report.<sup>16</sup> Of the 65 countries/regions, 27 were classified as MICs (8 LMICs and 19 UMICs), and 38 as HICs. For each medicine class, we calculated the absolute changes in sales for each year throughout the study period using a random effects model adjusted for income level and region. Relative changes in the prevalence per year were assessed as percentage change for each medicine class.

Psychotropic medicine sales from 2019 were compared to the prevalence of mental disorders, and life expectancy, as reported in the Global Burden of Disease Study 2019,<sup>17</sup> and health expenditure using fixed-effects panel regression analysis. Income level and health expenditure estimates for each country were obtained from the World Bank.<sup>18,19</sup> Data from low-income countries were not available. Data from 2019 were tabulated per UN geographic region<sup>15</sup>

(Africa, Asia, Europe, Latin America and the Caribbean, Northern America, Oceania), and subregion (Western Asia [Middle East]). We also identified countries which had very low consumption of psychotropic medicines, defined as 25th percentile of DDD/TID in 2019. Data were analysed using Stata (version 16). There was no funding source for this study.

## **Results**

### *Global trends 2008-2019*

Detailed global trends of psychotropic medicine consumption between 2008 and 2019 are shown in Table 1. The total consumption of psychotropic medicines increased from 28.54 DDD/TID in 2008 to 34.77 DDD/TID in 2019, corresponding to an average increase of 2.61 DDD/TID (95% CI 2.37 to 2.85) annually. The greatest increase in DDD/TID over time was seen for antidepressants (1.33 DDD/TID, 95% CI 1.22-1.44), corresponding to a relative average increase per year of 3.5% (95% CI 3.23%-3.76%, Table 2). Consumption of SSRIs was 8.79 DDD/TID in 2008 and remained high during the study period, with an average annual increase of 0.26 DDD/TID. A further upward trend was observed for SNRIs (0.09 DDD/TID); for antidepressants not otherwise categorised (0.10 DDD/TID); and antipsychotics (0.22 DDD/TID or a relative annual increase of 2.49%, 95% CI 2.22%-2.75% [Table 2]).

### *Global trends 2008-2019 by income level*

In 2019, the total consumption of psychotropic medicines was 123.61 DDD/TID in HICs, 13.52 DDD/TID in UMICs and 6.77 DDD/TID in LMICs. The greatest absolute increase in sales from 2008 to 2019 was reported in HICs (3.31 DDD/TID, 95% CI 3.01-3.61). The average annual change in sales was statistically different between HICs, UMICs (1.94 DDD/TID, 95% CI 1.45-2.44) and LMICs (0.88 DDD/TID, 95% CI 0.62-1.13;  $p < 0.01$ , Table 1). In contrast, the relative average annual increase in psychotropic medicine sales from 2008 until 2019 was greater in UMICs (7.88%, 95% CI 6.99%-8.77%) compared to LMICs (2.90%, 95% CI 2.40%-3.39%) and HICs (1.02%, 95% CI 0.80%-1.24%, appendix pp 7).

The average percentage change per year, measured as standard units per person per year, was greatest in LMICs (1·99%, 95% CI 1·67%- 2·30%, appendix pp 7). In LMICs, there was an upward trend for sales of all psychotropic medicine classes, except for tranquilisers. The sales of tricyclic antidepressants, typical antipsychotics, tranquilisers and sedatives/hypnotics decreased in HICs. Trends in antidepressants consumption in UMICs largely followed those of HICs, with steeper growth in HICs for SSRIs, SNRIs, and antidepressants not otherwise defined. In contrast to HICs and LMICs, the sales of tranquilisers (0·14 DDD/TID, 95% CI 0·04-0·24) and sedatives (0·04 DDD/TID, 95% CI 0·02-0·06) increased in UMICs.

*Psychotropic medicine sales and prevalence of mental disorders, life expectancy and health expenditure by country income level*

Whilst we found a positive association between changes in the psychotropic medicine consumption of a country and the prevalence of mental disorders ( $p < 0\cdot05$ , Figure 1), and the average life expectancy of the people of a country ( $p < 0\cdot01$ ; Figure 2), these associations were largely driven by UMICs. For HICs and LMICS only, the relationship between changes in psychotropic medicine consumption and prevalence of mental illness was weaker ( $p = 0\cdot083$  and  $p = 0\cdot152$ , respectively). LMIC countries like Morocco and India have a relatively low consumption of psychotropic medicines, but a high prevalence of mental disorders. The association between changes in consumption of psychotropic medication and life expectancy was strong for countries of all income levels ( $p < 0\cdot01$ , appendix pp 10). For LMICs and UMICs, there was an association between changes in psychotropic medicine consumption and health expenditures (% GDP) and (LMICs:  $p = 0\cdot041$  and UMICs:  $p = 0\cdot038$ , Figure 3).

*Sales of psychotropic medicines by region in 2019*

After adjusting for income, overall psychotropic sales were highest in Northern America (167·54 DDD/TID), but higher levels of consumption were found in some individual European countries (Appendix, pp8-9). The lowest levels of consumption were found in Asia (5·59

DDD/TID). In 2019, the country with the highest psychotropic sales volume was Portugal (249·1 DDD/TID), followed by Belgium (200·4 DDD/TID), Spain (198·5 DDD/TID), Sweden (170·8 DDD/TID) and the US and Canada (167·5 DDD/TID) (Figure 4). Despite the overall global increase in psychotropic consumption, countries such as Finland, Norway, Luxembourg and France, with the highest volume of psychotropic sales in 2008, reduced their psychotropic consumption over the study period. Countries with the lowest consumption in 2019 were the Philippines (0·93 DDD/TID), Venezuela (3·69 DDD/TID), UAE (3·97 DDD/TID), Kuwait (4·34 DDD/TID), China (4·57 DDD/TID) and Kazakhstan (4·84 DDD/TID). Except for Venezuela, the same countries also had the lowest psychotropic medicine consumption in 2008. For antidepressants and antipsychotic agents, regional trends were similar to those of psychotropic agents overall. Greece had the highest level of antipsychotic consumption among all the included countries/regions (26·0 DDD/TID), whilst the consumption of sedatives/hypnotics was highest in Belgium (46·9 DDD/TID) (Figure 4 and appendix pp 8-9). The sales of tranquilisers ranged from 2·2 DDD/TID in Asia to 14·92 DDD/TID in Europe. Within Europe, the consumption of tranquilisers was highest in Serbia (94·5 DDD/TID), followed by Portugal (90·9 DDD/TID). Most countries reported low sales of mood stabilisers (<0·05 DDD/TID). The highest consumption was recorded in Belgium (0·7 DDD/TID), followed by the Netherlands (0·4 DDD/TID) and Luxembourg (0·4 DDD/TID).

#### *Countries with very low consumption of psychotropic medicines in 2019*

There were 17 countries in the 25<sup>th</sup> percentile of consumption as measured by DDD/TID in 2019. Beside the above mentioned six countries with the lowest DDD/TID (the Philippines, Venezuela, UAE, Kuwait, China and Kazakhstan), Jordan, Colombia, India, Mexico, Saudi Arabia, Peru, Ecuador, Russia, Pakistan, Egypt and Morocco had consumption ranging from 4·97 to 13·07 DDD/TID (Appendix, pp 8-9).

## **Discussion**

This study reported the consumption of psychotropic medicines in 65 countries and regions disaggregated by country income level and geographic region and serves two important purposes: (1) to identify countries and regions with relatively low consumption of psychotropic medicines, and (2) to serve as the baseline to monitor future improvement. We compared global trends of psychotropic medicine sales data and found that the consumption of psychotropic medicines has increased with a relative average annual increase of 4% over a 12-year period. The global increase in the use of psychotropic medicine has been linked to more awareness of mental health as a pivotal part of overall health,<sup>20</sup> behavioural changes leading to a greater willingness to seek treatment,<sup>21</sup> and drug treatment lasting longer.<sup>22</sup> In addition, polypharmacy with psychotropic medicines is now more prevalent.<sup>23,24</sup> The growth of psychotropic medicine consumption is not uniform. Notably, HICs such as Luxembourg, Norway, Finland and France as well as Venezuela (a LMIC) have seen a decrease in the consumption of psychotropic medicine. Our study suggests that the increase in sales of psychotropic medicines in UMICs can partly be explained by the country level burden of mental illness, life expectancy and health expenditure.

Throughout the study period, the consumption of psychotropic medicines in LMICs and UMICs was lower than in HICs, but the average annual increase in sales of psychotropic medicine from 2008 to 2019 was 7.9 % in UMICs compared to 1.02% in HICs. According to the Global Burden of Disease study, prevalence rates of mental health disorders in UMICs and LMICs did not rise to the same extent and have remained stable at 13%.<sup>17</sup> Although a high prevalence of mental health disorders, such as schizophrenia, is reported in Southeast and East Asia,<sup>25</sup> most Asian countries in our study had very low rates of antipsychotics consumption. The Philippines (0.93 DDD/TID), China (4.57 DDD/TID), and India (4.98 DDD/TID) were among the countries with the lowest consumption of psychotropics in 2019. Our results support

WHO findings that between 76% and 85% of people with severe mental health disorders receive no treatment with medicines for their disorder in MICs.<sup>4</sup>

In addition to country income level, we found geographical differences in the consumption of psychotropic medicines. In 2019, the total consumption of psychotropic medicines, controlled for income, in Asia (5.59 DDD/TID) was ~3% of that of North American countries (167.54 DDD/TID). Within regions, not all drug classes have high consumption rates despite having a high level of total psychotropic medicine consumption. For instance, certain HICs appear to preferentially consume either sedatives/hypnotics or tranquilisers, and only a few countries have high consumption rates of both. In 2019, consumption rates of antidepressant and antipsychotic medicines in the US and Canada were similar, but the consumption of tranquilisers in the US was higher than in Canada, where the consumption of sedatives was lower. In some instances, countries that are similar in terms of geographic location, for example, the neighbouring countries of Sweden, Norway, and Finland, have different patterns of psychotropic consumption rates. These differences may be explained by variations in healthcare policy.<sup>26,27</sup> Similar observations also occur in the UK and France and different Asian regions such as Taiwan and China. Overall, regional differences in medicine consumption are likely due to multiple factors. Previous research has suggested variations in the role of health technology assessment, service organisation and delivery, and medicine reimbursement policies. Each of these factors likely play a role in explaining international variation in medicines use, but their relative importance will vary depending on the disease area in question and the system context.<sup>28</sup>

Results for analyses by psychotropic medicine class show that the overall consumption of antidepressants is rising in all 65 countries/regions, with the relative rate of increase higher in LMICs and UMICs compared to HICs. The increase in the consumption of antidepressants in

this study is in line with a rising trend shown in a previous study on antidepressants consumption in 25 HICs.<sup>29</sup> There is substantial overlap in the HICs included in both studies and when we compared the results from 2008-2013, the results were, unsurprisingly, very similar, which supports the validity of our results. Our study shows that the increase in consumption of antidepressants in HICs continues after 2013. More importantly, our study shows that the relative increase in antidepressant sales is even more pronounced in LMICs and UMICs. Despite the rise in overall sales of antidepressants, recent WHO studies suggest there is considerable evidence of undertreatment.<sup>30</sup> In 2019, the global sales of SSRIs were twice as high as the consumption of all other antidepressants combined. Few studies from individual countries have reported trends of antidepressants as well as other psychotropic medicine use that are similar to the findings of this study.<sup>31,32</sup> This trend aligns with the main clinical practice guidelines in children and adults which recommend that people with moderate to severe depression receive medication treatment.<sup>33</sup> SSRIs are recommended as a first-line antidepressant and have replaced benzodiazepines as first line treatment of generalised anxiety disorders, panic attacks and post-traumatic stress disorder due to their favourable risk-benefit ratio.<sup>34</sup> In all countries, SSRIs, SNRIs and other antidepressants are being favoured over tricyclic antidepressants and MAOIs, but in LMICs, the consumption of older, and potentially more affordable, antidepressants is still growing. Tricyclic antidepressants are prescribed for indications other than depression or anxiety, particularly in chronic pain and sleeping disorders. Our study found a decreasing trend in the sales of typical antipsychotics, largely driven by HICs. The sales of both typical and atypical antipsychotic medicines are rising in UMICs. The broad use of antipsychotics can be linked to expanded regulatory approval for indications outside of psychosis, and an increase in their off-label use, notably their more common use for mood disorders.<sup>35</sup> A previous cross-sectional electronic health record study on the consumption of antipsychotics in Australia, New Zealand and 14 European, American and Asian countries

showed that the use of atypical antipsychotics from 2005-2014 was growing in all 16 countries.<sup>7</sup> In our study, for the same 16 countries, this growth continued after 2014 until our last recorded data point in December 2019.

Over the study period, there was a modest decrease in the average annual change of tranquiliser and sedative/hypnotic consumption in HICs, which may partly be explained by the increasing prescriber and patient awareness of the addictive nature, dependence, and withdrawal symptoms of drugs like benzodiazepines and z-drugs.<sup>36,37</sup> To our knowledge, only two studies have compared the consumption of tranquilisers in multiple countries.<sup>11</sup> Both studies found higher rates of consumption in France, Spain and the US compared to Germany and the UK. Individual European country studies on the use of anxiolytics confirm a North/South divide, with Southern European countries reporting an increase in the use of anxiolytics from 2006 onwards,<sup>38</sup> whereas Northern European countries have reported a decrease, particularly in younger age groups.<sup>39,40</sup> Our study found high rates of consumption of tranquilisers in Serbia (94.5 DDD/TID) and Croatia (80.3 DDD/TID) which was comparable to rates reported by Marković et al. (2018) who reported on the impact of socioeconomic instability on benzodiazepine exposure in three Balkan countries.<sup>41</sup> Whilst socioeconomic instability may explain the difference seen between three Eastern European countries in the study by Marković et al., our results suggest that, on a global level, socioeconomic unrest can only partly explain the variation in the consumption of tranquilisers. For instance, Algeria and Egypt, countries which have experienced considerable political and economic disruption in the past decade, have relatively low rates of consumption of tranquilisers (5.5 and 1.0 DDD/TID, respectively). We found a study which described and compared the change in consumption of sedatives and hypnotics, based on pharmacy dispensing data, in Spain, Italy, France and Portugal between 2003 and 2010.<sup>42</sup> Whilst our study covered a different period, we also found a decrease in the consumption of sedatives in Italy and France, and an increase in Spain, but not in Portugal. For



countries like Italy and France, this may be because of the social attitudes, governmental initiatives, and concerns about stimulant misuse, leading to a decrease in their consumption.<sup>43</sup>

The decrease of overall psychotropic consumption in HICs, such as Luxembourg, France, and Finland was largely driven by a steep decrease in sedative/hypnotic consumption. Further studies from individual countries confirm the decreasing trend in the consumption of sedatives.<sup>31,44</sup> Of note is the high level of sedative sales found in Belgium (46.9 DDD/TID) and Japan (44.5 DDD/TID) in 2019. According to the United Nations (UN) International Narcotics Control Board, Japan and Belgium ranked 2<sup>nd</sup> and 3<sup>rd</sup> for Sedative-Hypnotic consumption worldwide in 2015.<sup>45</sup> The high levels of sedatives/hypnotics in Japan and Belgium may be related to the high use of these medicines as a treatment for insomnia.<sup>46</sup>

Among the 17 countries with the lowest consumption in 2019, Philippines and Morocco are the lowest (0.93 DDD/TID) and highest (13.07 DDD/TID). Such low DDD/TID means that on average, the consumption of psychotropic medicine is only sufficient for one and 13 patients per 1000 inhabitants in Philippines and Morocco respectively assuming there is no polypharmacy. Clearly this is well below our current understanding of the epidemiology of mental health disorders. Urgent improvement in the access to psychotropic medication for patients is needed. Fourteen of these countries are MICs in which financial factors may contribute to such low consumption. However, three countries, namely Kuwait, UAE, Saudi Arabia, are HICs and thus a country's economic status does not fully explain the low consumption. Previous studies reported mental health patients in Arab countries tend to express their psychological problems in terms of physical symptoms, thereby avoiding the stigma attached to mental illness.<sup>47</sup> Furthermore, reliance upon a deity and religious leaders as a means of coping with mental health issues is another prevalent theme in the Arab world.<sup>47</sup> All these factors may partly explain the low consumption in these countries.

China has one of the lowest consumptions of psychotropic medications (one of the bottom five) in contrast to Taiwan, which has a consumption around ten times that of China (4.57 DDD/TID for China vs 46.04 DDD/TID for Taiwan). Previous studies also suggest that the Taiwanese population had higher endorsement of psychotropic medications than other Chinese communities, especially for antidepressants and tranquillisers.<sup>48</sup> Moreover, studies suggest the Taiwanese population also have a better recognition of depression when compared to other Chinese communities.<sup>48</sup> Despite the similar Chinese ethnicity, religion, and cultural traditions between China and Taiwan, this suggests that other social factors may still have an important role in affecting psychotropic medication consumption.

### *Strengths and limitations*

The use of international pharmaceutical sales data enables a unique global comparison of trends in psychotropic medicine consumption despite differences in health care systems. However, there were some limitations to this study. Our data only reflect the country level supply side of psychotropic medication. Factors such as costs, access, and quality assurance have a profound effect on the demand side. Pharmaceutical sales data do not reflect individual-level treatment for mental health conditions. For this reason, we could not measure trends by age, gender, and indications or appropriateness of prescribing. Individual level data are needed to inform us about potential overuse, underuse, misuse, unnecessarily expensive use and access to psychotropic medicine.<sup>49</sup> Particularly in some of the LMICs included in our study, current regulatory capacity and enforcement may not be sufficient to ensure affordable access to quality medication for people living in those countries.<sup>50</sup> International studies of medicine use usually present data in DDDs in order to allow comparisons between population groups. However, DDD is not a measure of therapeutic use; hence our study cannot address quality of prescribing. We did not measure societal differences and attitudes towards mental health. Studies have suggested that higher country spending on healthcare and positive cultural

attitudes towards mental illness are associated with regular use of psychotropic medicines.<sup>21</sup> Psychosocial interventions are effective in treating some mental disorders with or without concurrent pharmacological treatment, such as depression or anxiety.<sup>51,52</sup> However, in other conditions, such as schizophrenia and bipolar disorder, psychosocial interventions are commonly considered adjunctive to medication. We were unable to investigate the availability of these other interventions, however there is evidence to suggest the access to psychosocial interventions in many LMICs is lower than psychotropic medication access.<sup>53</sup> Lastly, as our study included data from 65 countries/regions, the findings are only applicable to these countries/regions. In order to provide a full picture, data from the most vulnerable countries are urgently needed to further our understanding of how to improve our global mental health.

#### *Implications and recommendations*

Each cultural and geo-political region presents its own set of factors that influence treatment referral and prescribing behaviours. We have identified 17 countries with very low consumption on psychotropic medicines. Countries with low consumption rates for psychotropic medicines are unlikely to provide sufficient access to psychotropic drugs and the reasons for this should be identified.<sup>4</sup> Poor access to health care in general, and affordability may prevent many individuals who might benefit from psychotropic medication from receiving treatment, especially in these MICs where the use of psychotropic medicines is further restricted because of the lack of qualified health workers with the appropriate authority to prescribe medications.<sup>49,54</sup> These governments should focus on training healthcare workers who can prescribe cost-effective psychotropic medicines in the WHO model list of essential medicines.<sup>55</sup> However, countries like Saudi Arabia, UAE and Kuwait, which are HICs, have low consumption rates of psychotropic medicine; hence the barriers to access were not fully due to economic reasons. There is some evidence that stigma and cultural considerations contribute to low consumption of psychotropics.<sup>21</sup> Therefore, it is important for governments

to address this with public education and consider involving community and religious leaders to promote appropriate understanding of psychotropic medicine use. Our study findings can be used as the baseline to evaluate future interventions to improve access.

## **Conclusion**

The consumption of psychotropic medicines has increased over a 12-year period and whilst the absolute growth rate is highest in HICs, the relative growth is highest in LMICs and UMICs. Disparities in psychotropic medicine consumption of countries can only partly be explained by geographic location and income. Efforts need to be made to improve the availability of psychotropic medicines in countries with a low consumption of psychotropic medicines, but high prevalence of mental disorders.

## **Data sharing**

The underlying MIDAS data were provided by IQVIA under license. The terms of our agreement do not permit disclosure, sublicensing, or sharing of IQVIA MIDAS data. IQVIA will honour legitimate requests for MIDAS data from qualified researchers. Please contact IQVIA to seek approval for data access; a license fee may be applied.

## **Acknowledgements**

We thank IQVIA for their assistance and information regarding the use of IQVIA-MIDAS data.

## **Author Contributions**

Prof Ian Wong and Prof Li Wei have accessed and verified the underlying data.

Conceptualization and design: Brauer, Blais, Chan, Yan & Wong.

Acquisition of data: Alfageh, Brauer, Chan, Wei & Wong.

Statistical analysis: Brauer, Wei, Man & Lau.

Interpretation of data: All authors.

Literature review: Wang & Beykloo.

Drafting of the manuscript: Brauer & Wei.

Figures: Brauer & Chui

Critical revision of the manuscript for important intellectual content: All authors.

### **Conflict of Interest Disclosures**

JEB is supported by the Hong Kong Research Grants Council as a recipient of the Hong Kong PhD Fellowship Scheme. JFH is supported by the Wellcome Trust (211085/Z/18/Z), the University College London Hospitals NIHR Biomedical Research Centre and the NIHR North Thames Applied Research Collaboration. KKCM is the recipient of the CW Maplethorpe Fellowship; and report grants from the National Institute for Health Research, UK; the Research Grant Council, Hong Kong; personal fees from IQVIA Ltd., unrelated to the submitted work. EWC has received honorarium from the Hospital Authority, research grants from Research Grants Council (RGC, HKSAR), Research Fund Secretariat of the Food and Health Bureau (HMRF, HKSAR), National Natural Science Fund of China, National Health and Medical Research Council NHMRC, Australia, Wellcome Trust, Bayer, Bristol-Myers Squibb, Pfizer, Janssen, Amgen, Takeda, and Narcotics Division of the Security Bureau of HKSAR, outside the submitted work. CSLC has received grants from the Food and Health Bureau of the Hong Kong Government, Hong Kong Research Grant Council, Hong Kong Innovation and Technology Commission, Pfizer, IQVIA, and Amgen; personal fee from Primevigilance Ltd.; outside the submitted work. ICKW reports research funding outside the submitted work from Amgen, Bristol-Myers Squibb, Pfizer, Janssen, Bayer, GSK, Novartis, the Hong Kong RGC, and the Hong Kong Health and Medical Research Fund, National Institute for Health Research in England, European Commission, National Health and Medical Research Council in Australia, and also received expert testimony payment from Hong Kong Appeal court and speaker fees from Janssen and Medice in the previous 3 years.

## References

1. Whiteford HA, Degenhardt L, Rehm J, et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet* 2013; **382**(9904): 1575-86.
2. Diseases GBD, Injuries C. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020; **396**(10258): 1204-22.
3. Cipriani A, Furukawa TA, Salanti G, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. *Lancet* 2018; **391**(10128): 1357-66.
4. World Health Organization. Mental health action plan 2013–2020. 2013. [http://apps.who.int/iris/bitstream/10665/89966/1/9789241506021\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/89966/1/9789241506021_eng.pdf) (accessed May 12, 2020).
5. Organization WH. Mental health action plan 2013–2020 (extended to 2030). 2019. <http://www.emro.who.int/mnh/mental-health-action-plan/index.html> (accessed 9 July 2021).
6. M Chalabi for the Guardian. Antidepressants: global trends. 2013. Available from: <https://www.theguardian.com/news/2013/nov/20/mental-health-antidepressants-global-trends> (accessed May 12, 2020).
7. Halfdanarson O, Zoega H, Aagaard L, et al. International trends in antipsychotic use: A study in 16 countries, 2005-2014. *Eur Neuropsychopharmacol* 2017; **27**(10): 1064-76.
8. Raman SR, Man KKC, Bahmanyar S, et al. Trends in attention-deficit hyperactivity disorder medication use: a retrospective observational study using population-based databases. *Lancet Psychiatry* 2018; **5**(10): 824-35.
9. Cook MN. Estimating national drug consumption using data at different points in the pharmaceutical supply chain. *Pharmacoepidemiol Drug Saf* 2006; **15**(10): 754-7.
10. Van Boeckel TP, Gandra S, Ashok A, et al. Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. *Lancet Infect Dis* 2014; **14**(8): 742-50.
11. Khong TP, de Vries F, Goldenberg JS, et al. Potential impact of benzodiazepine use on the rate of hip fractures in five large European countries and the United States. *Calcif Tissue Int* 2012; **91**(1): 24-31.
12. IQVIA. ACTS: IQVIA quality assurance. 2018. <https://www.iqvia.com/landing/acts> (accessed Feb 1, 2020).
13. Hsia Y, Sharland M, Jackson C, Wong ICK, Magrini N, Bielicki JA. Consumption of oral antibiotic formulations for young children according to the WHO Access, Watch, Reserve (AWaRe) antibiotic groups: an analysis of sales data from 70 middle-income and high-income countries. *Lancet Infect Dis* 2019; **19**(1): 67-75.
14. World Health Organization. ATC/DDD index. Nervous system. 2019. [https://www.whocc.no/atc\\_ddd\\_index/?code=N06A](https://www.whocc.no/atc_ddd_index/?code=N06A) (accessed May 12, 2020).
15. World Health Organization Collaborating Centre for Drug Statistics Methodology. ATC/DDD Index 2019. . 2019. [https://www.whocc.no/atc\\_ddd\\_index/](https://www.whocc.no/atc_ddd_index/) (accessed April 20, 2020).
16. United Nations. World population prospects 2019. 2019. . <https://population.un.org/wpp/> (accessed April 20, 2020).
17. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2017 (GBD 2017) results. 2018. <http://ghdx.healthdata.org/gbd-results-tool> (accessed 12-05-2020).
18. The World Bank. World bank open data. 2019. <https://data.worldbank.org/> (accessed May 12, 2020).
19. The World Bank. World Health Organization Global Health Expenditure database. 2020. [apps.who.int/nha/database](http://apps.who.int/nha/database) (accessed June 1, 2020).
20. Prince M, Patel V, Saxena S, et al. No health without mental health. *Lancet* 2007; **370**(9590): 859-77.

21. Lewer D, O'Reilly C, Mojtabai R, Evans-Lacko S. Antidepressant use in 27 European countries: associations with sociodemographic, cultural and economic factors. *Br J Psychiatry* 2015; **207**(3): 221-6.
22. World Health Organization. Duration of antidepressant treatment. 2012. [https://www.who.int/mental\\_health/mhgap/evidence/resource/depression\\_q2.pdf?ua=1](https://www.who.int/mental_health/mhgap/evidence/resource/depression_q2.pdf?ua=1) (accessed June, 19, 2020).
23. Brett J, Daniels B, Karanges EA, et al. Psychotropic polypharmacy in Australia, 2006 to 2015: a descriptive cohort study. *Br J Clin Pharmacol* 2017; **83**(11): 2581-8.
24. Loggia G, Attah-Mensah E, Pothier K, et al. Psychotropic Polypharmacy in Adults 55 Years or Older: A Risk for Impaired Global Cognition, Executive Function, and Mobility. *Front Pharmacol* 2019; **10**: 1659.
25. Naveed S, Waqas A, Chaudhary AMD, et al. Prevalence of common mental disorders in South Asia: a systematic review and meta-regression analysis. *Frontiers in psychiatry* 2020; **11**: 899.
26. Vallgarda S. Addressing individual behaviours and living conditions: four Nordic public health policies. *Scand J Public Health* 2011; **39**(6 Suppl): 6-10.
27. Vilhelmsson A. Depression and antidepressants: a nordic perspective. *Front Public Health* 2013; **1**: 30.
28. Nolte E, Corbett J. International Variation in Drug Usage: An Exploratory Analysis of the "Causes" of Variation. *Rand Health Q* 2015; **4**(4): 1.
29. Chalabi M. Antidepressants: global trends. 2013. Available from: <https://www.theguardian.com/news/2013/nov/20/mental-health-antidepressants-global-trends> (accessed May 12, 2020).
30. Thornicroft G, Chatterji S, Evans-Lacko S, et al. Undertreatment of people with major depressive disorder in 21 countries. *Br J Psychiatry* 2017; **210**(2): 119-24.
31. Stephenson CP, Karanges E, McGregor IS. Trends in the utilisation of psychotropic medications in Australia from 2000 to 2011. *Aust N Z J Psychiatry* 2013; **47**(1): 74-87.
32. Wu CS, Shau WY, Chan HY, Lee YC, Lai YJ, Lai MS. Utilization of antidepressants in Taiwan: a nationwide population-based survey from 2000 to 2009. *Pharmacoepidemiol Drug Saf* 2012; **21**(9): 980-8.
33. American Psychological Association. Guideline Development Panel for the Treatment of Depressive Disorders. Clinical Practice Guideline for the Treatment of Depression Across Three Age Cohorts. Feb. 16, 2019. <https://www.apa.org/depression-guideline/guideline.pdf> (accessed 12-05- 2020).
34. National institute for Health and Care Excellence (NICE). Depression in adults: treatment and management. NICE guideline: short version (update NICE guideline CG90). May 2018 <https://www.nice.org.uk/guidance/GID-CGWAVE0725/documents/short-version-of-draft-guideline> (accessed 12-05-2020).
35. Alexander GC, Gallagher SA, Mascola A, Moloney RM, Stafford RS. Increasing off-label use of antipsychotic medications in the United States, 1995-2008. *Pharmacoepidemiol Drug Saf* 2011; **20**(2): 177-84.
36. Ilyas S, Moncrieff J. Trends in prescriptions and costs of drugs for mental disorders in England, 1998-2010. *Br J Psychiatry* 2012; **200**(5): 393-8.
37. Lader M, Tylee A, Donoghue J. Withdrawing benzodiazepines in primary care. *CNS Drugs* 2009; **23**(1): 19-34.
38. Carrasco-Garrido P, Hernandez-Barrera V, Jimenez-Trujillo I, et al. Time Trend in Psychotropic Medication Use in Spain: A Nationwide Population-Based Study. *Int J Environ Res Public Health* 2016; **13**(12).
39. Kurko T, Saastamoinen LK, Tuulio-Henriksson A, et al. Trends in the long-term use of benzodiazepine anxiolytics and hypnotics: A national register study for 2006 to 2014. *Pharmacoepidemiol Drug Saf* 2018; **27**(6): 674-82.
40. Tahkapaa SM, Saastamoinen L, Airaksinen M, Tuulio-Henriksson A, Aalto-Setälä T, Kurko T. Decreasing Trend in the Use and Long-Term Use of Benzodiazepines Among Young Adults. *J Child Adolesc Psychopharmacol* 2018; **28**(4): 279-84.

41. Markovic SZ, Dimitrijevic Jovanovic NI, Sedic B, et al. Impact of Differences in Economic Development and Socioeconomic Stability on Benzodiazepine Exposure between the Three Balkans Countries. *Psychiatr Danub* 2019; **31**(Suppl 5): 750-60.
42. Vicente Sanchez MP, Macias Saint-Gerons D, de la Fuente Honrubia C, Gonzalez Bermejo D, Montero Corominas D, Catala-Lopez F. [Trends of use of anxiolytics and hypnotics in Spain from 2000 to 2011]. *Rev Esp Salud Publica* 2013; **87**(3): 247-55.
43. Zito JM, Safer DJ, de Jong-van den Berg LT, et al. A three-country comparison of psychotropic medication prevalence in youth. *Child Adolesc Psychiatry Ment Health* 2008; **2**(1): 26.
44. Barczyk ZA, Rucklidge JJ, Eggleston M, Mulder RT. Psychotropic Medication Prescription Rates and Trends for New Zealand Children and Adolescents 2008-2016. *J Child Adolesc Psychopharmacol* 2020; **30**(2): 87-96.
45. International Narcotics Control Board. Psychotropic Substances. Statistics for 2015. April 2020 2016. [https://www.incb.org/documents/Psychotropics/technical-publications/2016/Technical\\_Publication\\_2016.pdf](https://www.incb.org/documents/Psychotropics/technical-publications/2016/Technical_Publication_2016.pdf).
46. Doi Y, Minowa M, Okawa M, Uchiyama M. Prevalence of sleep disturbance and hypnotic medication use in relation to sociodemographic factors in the general Japanese adult population. *J Epidemiol* 2000; **10**(2): 79-86.
47. Al-Krenawi A. Mental health practice in Arab countries. *Current Opinion in Psychiatry* 2005; **18**(5): 560-4.
48. Wong DFK, Cheng C-W, Zhuang XY, et al. Comparing the mental health literacy of Chinese people in Australia, China, Hong Kong and Taiwan: Implications for mental health promotion. *Psychiatry research* 2017; **256**: 258-66.
49. Wirtz VJ, Hogerzeil HV, Gray AL, et al. Essential medicines for universal health coverage. *Lancet* 2017; **389**(10067): 403-76.
50. WHO. Improving access to and appropriate use of medicines for mental disorders. 2017. <https://apps.who.int/iris/bitstream/handle/10665/254794/9789241511421-eng.pdf> (accessed 22 June 2021).
51. NICE. Depression in adults: recognition and management. 2009. <https://www.nice.org.uk/guidance/cg90/chapter/Context> (accessed 09 July 2021).
52. NICE. Anxiety disorders, Quality statement 2: Psychological interventions. 2014. <https://www.nice.org.uk/guidance/qs53/chapter/quality-statement-2-psychological-interventions> (accessed 09 July 2021).
53. Rathod S, Pinninti N, Irfan M, et al. Mental health service provision in low-and middle-income countries. *Health services insights* 2017; **10**: 1178632917694350.
54. Henderson C, Evans-Lacko S, Thornicroft G. Mental illness stigma, help seeking, and public health programs. *Am J Public Health* 2013; **103**(5): 777-80.
55. WHO. WHO Model Lists of Essential Medicines. 2019. <https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/essential-medicines-lists> (accessed 22 June 2021).