Psychological Medicine

cambridge.org/psm

Antidepressant use in low- middle- and high-income countries: a World Mental Health Surveys report

Alan E. Kazdin[1], Chi-Shin Wu[2], Irving Hwang[3], Victor Puac-Polanco[3], Nancy A. Sampson[3], Ali Al-Hamzawi[4], Jordi Alonso[5,6,7], Laura Helena Andrade[8], Corina Benjet[9], José-Miguel Caldas-de-Almeida[10], Giovanni de Girolamo[11], Peter de Jonge[12,13], Silvia Florescu[14], Oye Gureje[15], Josep M. Haro[16], Meredith G. Harris[17,18], Elie G. Karam[19,20], Georges Karam[19,20], Viviane Kovess-Masfety[21], Sing Lee[22], John J. McGrath[18,23,24], Fernando Navarro-Mateu[25], Daisuke Nishi[26,27], Bibilola D. Oladeji[15], José Posada-Villa[28], Dan J. Stein[29,30], T. Bedirhan Üstün[31], Daniel V. Vigo[32,33], Zahari Zarkov[34], Alan M. Zaslavsky[3], Ronald C. Kessler[3] and the WHO World Mental Health Survey collaborators

Original Article

Cite this article: Kazdin AE *et al* (2023). Antidepressant use in low- middle- and high-income countries: a World Mental Health Surveys report. *Psychological Medicine* **53**, 1583–1591. https://doi.org/10.1017/S0033291721003160

Received: 24 June 2021
Revised: 15 July 2021
Accepted: 17 July 2021
First published online: 23 September 2021

Keywords:
Antidepressant medications; perceived effectiveness; reasons for use

Author for correspondence:
Ronald C. Kessler,
E-mail: kessler@hcp.med.harvard.edu

Abstract

Background. The most common treatment for major depressive disorder (MDD) is antidepressant medication (ADM). Results are reported on frequency of ADM use, reasons for use, and perceived effectiveness of use in general population surveys across 20 countries.

Methods. Face-to-face interviews with community samples totaling $n = 49\,919$ respondents in the World Health Organization (WHO) World Mental Health (WMH) Surveys asked about ADM use anytime in the prior 12 months in conjunction with validated fully structured diagnostic interviews. Treatment questions were administered independently of diagnoses and asked of all respondents.

Results. 3.1% of respondents reported ADM use within the past 12 months. In high-income countries (HICs), depression (49.2%) and anxiety (36.4%) were the most common reasons for use. In low- and middle-income countries (LMICs), depression (38.4%) and sleep problems (31.9%) were the most common reasons for use. Prevalence of use was 2–4 times as high in HICs as LMICs across all examined diagnoses. Newer ADMs were proportionally used more often in HICs than LMICs. Across all conditions, ADMs were reported as *very* effective by 58.8% of users and *somewhat* effective by an additional 28.3% of users, with both proportions higher in LMICs than HICs. Neither ADM class nor reason for use was a significant predictor of perceived effectiveness.

Conclusion. ADMs are in widespread use and for a variety of conditions including but going beyond depression and anxiety. In a general population sample from multiple LMICs and HICs, ADMs were widely perceived to be either very or somewhat effective by the people who use them.

Introduction

Major depressive disorder (MDD) is one of the most common psychiatric disorders, affecting an estimated 4.4% of the world's population each year (World Health Organization, 2017). MDD is associated with substantial distress (Goldstein et al., 2020), impairment (Cooper, 2018), and early mortality (Wang et al., 2020). The economic costs of MDD are enormous, including lost income and productivity, high utilization of health-care services, and high use of social services (Chisholm et al., 2016).

Several effective antidepressant treatments exist, including medications, psychological therapies, transcranial magnetic stimulation, electroconvulsive therapy, and others. Many of these treatments have been well studied (Barth et al., 2016; Cipriani et al., 2018) and shown to be cost-effective (Prukkanone, Vos, Bertram, & Lim, 2012; Wiles et al., 2016). Worldwide, antidepressant medication (ADM) is the most frequently used treatment for depression (Brody & Gu, 2020; Cipriani et al., 2018; Herrman et al., 2019) and is often used for anxiety disorders as well (Bandelow, Michaelis, & Wedekind, 2017). Among the reasons for use of ADMs is empirical support spanning years of research, low-cost relative to other treatments, and accessibility of medications in countries where access to psychological services is limited.

CAMBRIDGE UNIVERSITY PRESS

Prior research has evaluated the use of ADMs, often based on information from a single country (Fava et al., 2008; Olfson & Marcus, 2009; Wu et al., 2012) as well as surveys from small numbers of countries, most often in Asia or Europe (Abbing-Karahagopian et al., 2014; Rajaratnam et al., 2016; Souery et al., 2007). In addition, one large survey assessed ADM use among approximately 27 000 individuals across 27 European countries (Lewer, O'Reilly, Mojtabai, & Evans-Lacko, 2015). That study focused primarily on prevalence of ADM use, socio-demographic characteristics of users, country-level health care and attitudes toward mental health problems. Typically, studies have drawn on administrative data on prescriptions received rather than on patient reports of ADM use.

Fundamental questions remain about the use of ADMs, including the conditions for which they are used and how effective they are perceived to be. The present study builds on prior work in addressing these questions in several ways. First, we examine ADM use across 20 countries of varying income levels throughout the world. Second, we evaluate the diagnoses of the people who use ADMs with special attention to depression as well as anxiety. Third, we examine the reasons given by patients for ADM use. Finally, we examine how effective patients perceive their ADMs to be overall and as a function of reasons for use. The data come from the World Health Organization (WHO) World Mental Health (WMH) surveys, a large cross-national series of community epidemiological surveys on the prevalence and correlates of common mental disorders (https://www.hcp.med.harvard.edu/wmh/).

Methods

Sample

Data are included from 22 WMH surveys with adult respondents (18 years or older) in 20 countries. Nine surveys were carried out in low- or middle-income countries (LMICs; Brazil, Bulgaria, two surveys in Colombia, Iraq, Lebanon, Mexico, Nigeria, Peru, and Romania) and 11 in high-income countries (HICs; Argentina, Belgium, France, Germany, Israel, Italy, Japan, the Netherlands, Portugal, two surveys in Spain, and the United States). Thirteen of these surveys were based on nationally representative multistage clustered area probability household designs, two others on samples representative of all urbanized areas in the countries, and the remaining surveys on samples representative of selected regions or Metropolitan areas (online Supplementary Table S1). Average response rate weighted by sample size was 71.1%.

The interview schedule used in the WMH surveys was developed in English and translated into other languages using a standardized WHO translation, team translation, and harmonization protocol (Harkness et al., 2008). Interviews were administered face-to-face in respondents' homes after obtaining informed consent. At all survey sites, the local ethics or institutional review committees reviewed and approved the protocol to ensure protection of human subjects in line with appropriate international and local guidelines.

Interviews were in two parts to reduce respondent burden. Part I was administered to all respondents and assessed core mental disorders. Part II was administered to all Part I respondents with any lifetime disorder and a probability subsample of other respondents. Part II data were weighted to adjust for the under-sampling of Part I non-cases, with the resulting Part II prevalence estimates being equivalent to Part I estimates (Heeringa et al., 2008). Of the $n = 49\,919$ Part II respondents, we focused analyses on the $n = 2\,448$ 12-month ADM users who did not meet criteria for lifetime bipolar spectrum disorder and did not report bipolar disorder as a reason for their ADM use. These exclusions were made because ADMs are not recommended for the treatment of bipolar depression (Yatham et al., 2018; Zhang et al., 2013). Seven of the surveys (Israel, Japan, Brazil, Bulgaria, Iraq, Lebanon, Nigeria) did not ask the detailed survey questions about reasons for use and perceived effectiveness that were included in the other surveys. These surveys were consequently dropped from the analyses that used these variables, reducing the sample to $n = 2377$. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Measures

Diagnoses

The survey instrument was the WHO Composite International Diagnostic Interview (CIDI) Version 3.0 (Kessler & Üstün, 2004), a fully structured interview generating diagnoses of lifetime and 12-month DSM-IV disorders. The disorders considered here are MDD and a series of anxiety disorders that include agoraphobia, generalized anxiety disorder, panic disorder, post-traumatic stress disorder, social phobia and specific phobia. Blinded clinical reappraisal interviews using as the gold standard diagnoses based on the Structured Clinical Interview for DSM-IV (SCID; First et al., 2002) blinded to diagnoses based on the CIDI found good concordance between the two diagnoses (Haro et al., 2006). We categorized respondents into four MDD categories: threshold 12-month prevalence (12 M MDD), lifetime but not 12-month prevalence (LT MDD), 12-month subthreshold MDD in the absence of LT MDD (Partial MDD), and none of the above. The same four categories were used to define anxiety disorders hierarchically (i.e. 12 M anxiety includes respondents who met full criteria for at least one anxiety disorder; LT anxiety includes other respondents who met lifetime criteria for at least one anxiety disorder; partial anxiety includes other respondents who met 12-month subthreshold criteria for at least one anxiety disorder, and other respondents had none of these disorders). We also created a four-category hierarchical variable that combined scores on the separate four-category MDD and anxiety variables.

Antidepressant medication use

ADM users were defined as those who took an ADM at any time in the past 12 months. Respondents who were prescribed but did not take an ADM were excluded. Information on use was captured by presenting respondents with a list of psychotropic medications using both generic and trade names and asking about use of these medications in the past 12 months for *problems with your emotions, nerves, mental health, substance use, energy, concentration, sleep, or ability to cope with stress.* The medication list included ADMs, anxiolytics, hypnotics, antipsychotics, mood stabilizers, and other psychotropic agents. Respondents were instructed to *include medicines even if you took them only once.* Because drug administration policies vary across countries, the medication list was modified for each country. We asked about a total of 41 ADMs (online Supplementary Table S2), which were categorized for analysis into SSRIs (selective serotonin reuptake inhibitors), other new-generation ADMs (those marketed after fluoxetine, 1986), TCAs (tricyclic ADMs), and other older ADMs (e.g. monoamine oxidase inhibitors, St. John's Wort, trazodone, and unspecified). Two clinical psychiatrists

https://doi.org/10.1017/S0033291721003160 Published online by Cambridge University Press

with expertise in public health (DV, CSW) independently reviewed responses about medications used in the past 12 months (which involved selecting from country-specific lists including generic and brand names) and classified ADMs into the four categories. Discrepancies were reconciled by consensus.

For each psychotropic medication used in the past 12 months, the type and duration of use were recorded. As noted above in the section on the sample, additional questions were asked in 15 of the 22 surveys. We focus on those surveys for analyses using these questions, which included two that we consider here. (1) *What problems did you take* (*NAME OF MEDICATION*) *for?* Both structured and open-ended responses were recorded and classified into the categories (i) depression (sadness/depression/crying or suicidal thoughts), (ii) anxiety (nerves/anxiety or panic), (iii) poor sleep, (iv) other physical problems (low energy, poor appetite or physical pain), and (v) other reasons, such as little or no sexual functioning, sexual problems, not getting along with others, poor work performance, alcohol or drug problems, poor concentration, and poor memory (online Supplementary Table S3). Respondents could report multiple reasons, which is important because some of the 'other' reasons are also symptoms of MDD and anxiety. (2) *Overall, how effective was* (*NAME OF MEDICATION*) *in doing the things you expected it to do – very, somewhat, not very, or not at all effective?* These medication-specific follow-up questions were asked separately for up to five psychotropic medications in six European countries (Belgium, France, Germany, Italy, Netherlands, Spain) and up to three in other countries. These numbers captured well over 90% of ADM uses in each survey.

Data analysis

Individual weights were applied within survey to adjust for differences in within-household probabilities of selection. Part II data were then weighted to adjust for differential probabilities of selection into Part II and deviations between the sample and population demographic–geographic distributions. All statistical analyses were carried out using the Taylor-series linearization method (Wolter, 1985), a design-based method implemented in SAS 9.4 program (SAS/STAT, 2016) that adjusts estimates of standard errors (SEs) for design effects. Logistic regression analysis was used to examine predictors of patient reports about the effectiveness of specific ADMs. In cases where the predictors were categorical (e.g. ADM classes), log-odds-ratios were normalized by centering them around a mean of zero on the log-odds scale rather than omitting a contrast category. Coefficients and ±2 of their design-based SEs were then exponentiated to create odds ratios (ORs) and 95% confidence intervals (CIs). The centered ORs for the individual predictor categories had a product of 1.0, which means that these individual ORs can be interpreted in comparisons to average odds across categories. Significance of OR sets defining a single categorical variable (e.g. the dummy variables defining ADM classes) was evaluated with Wald χ^2 tests based on design-corrected coefficient variance–covariance matrices. Statistical significance was evaluated consistently using two-sided design based 0.05-level tests.

Results

Prevalence and associations of ADM use with depression and anxiety disorders

After removing respondents with a history of bipolar spectrum disorder, 3.1% of the remaining $n = 48\,420$ Part-II WMH survey respondents reported using ADMs in the 12 months before the interview (Table 1, Part I). This prevalence was considerably higher in HICs than LMICs (4.7% *v.* 1.3%, $\chi^2_1 = 244.2$, $p < 0.001$). In addition, prevalence was highest in both HICs and LMICs among respondents with partial 12-month MDD (41.5% and 12.3%), lower among respondents with full 12-month MDD (24.4% and 9.6%), lower still among respondents with lifetime but no 12-month MDD (11.3% and 3.8%), and by far lowest among respondents with no history of MDD (1.7 and 0.6%). The higher prevalence among respondents with partial than full 12-month MDD was found in 10 of the 12 HIC surveys and 4 of the 10 LMIC surveys.

We also looked at ADM use by anxiety. Prevalence of ADM use was higher in both HICs and LMICs among respondents with full 12-month anxiety disorders (15.5 and 4.8%) than either lifetime anxiety disorders (11.2 and 3.2%) or partial 12-month anxiety disorders (12.2 and 3.1%) and was by far lowest among respondents with no history of any anxiety disorder (1.7 and 0.6%). (Table 1, Part II). Although statistically significant, the elevated prevalence estimates associated with 12-month full and partial anxiety disorders were much lower than the comparable elevations among respondents with 12-month full and partial MDD. For example, the prevalence ratios of ADM use among respondents with full 12-month MDD *v.* non-cases were 14.3 (i.e. 24.4 *v.* 1.7%) in HICs and 16.0 (9.6 *v.* 0.6%) in LMICs, whereas the comparable prevalence ratios for anxiety disorders were 9.1–8.0. Discrepancies between MDD and anxiety disorders were even more pronounced among patients with partial 12-month MDD *v.* partial 12-month anxiety disorders relative to non-cases (24.4–20.5 *v.* 7.2–5.2). Country-specific results are presented in online Supplementary Table S4.

Given the prevalence estimates of MDD and anxiety disorders in the surveys in conjunction with the above differences in proportions using ADMs across those disorders, only a minority of the patients using ADMs met full 12-month criteria for either MDD (27.9%), anxiety disorder (31.6%), or either (44.1%) (Table 2). One-third (32.3%) of ADM users had neither full nor partial MDD and 28.5% of users had neither full nor partial anxiety disorder. However, it was rare for an ADM user not to have either MDD or an anxiety disorder (12.7%), although the latter pattern was twice as common in LMICs as HICs (21.2% *v.* 10.5%, $\chi^2_1 = 11.1$, $p = 0.001$). Other notable differences were a consistently higher proportion of ADM users with lifetime but not 12-month disorders in HICs than LMICs ($\chi^2_1 = 4.6–13.4$, $p = 0.032–<0.000$) and a consistently higher proportion of ADM users meeting criteria for none of the 12-month or lifetime disorders in LMICs than HICs ($\chi^2_1 = 6.2–11.1$, $p = 0.013–0.001$).

Use of antidepressants by type

SSRIs were the ADM class used most commonly across surveys (62.4%), followed by other newer ADMs (25.3%), TCAs (14.4%), and other older ADMs (10.0%) (Table 3). These percentages sum to more than 100% because 11.3% of respondents used two or more ADM classes in the past year. Use of SSRIs and other newer ADMs was proportionally higher in HICs than LMICs ($\chi^2_1 = 14.5–30.4$, $p < 0.001$), whereas use of TCAs and other older ADMs was proportionally higher in LMICS than HICs ($\chi^2_1 = 4.6–35.7$, $p = < 0.001–0.033$). Use of two or more ADMs in the last year was similar in countries of different income levels ($\chi^2_1 = 0.09$, $p = 0.77$). Country-specific results are presented in online Supplementary Table S5.

https://doi.org/10.1017/S0033291721003160 Published online by Cambridge University Press

Table 1. Prevalence of ADM use by MDD and anxiety disorder histories within and across country income groups ($n = 48\,420$)

	Total		High-Income		Low- and Middle-Income		
	%	(S.E.)	%	(S.E.)	%	(S.E.)	χ^2_1 HIC *v.* LMIC
MDD							
12-month	18.3	(0.8)	24.4	(1.1)	9.6	(1.0)	74.7*
Lifetime[a]	8.8	(0.4)	11.3	(0.6)	3.8	(0.6)	45.7*
Partial[b]	29.8	(1.5)	41.5	(1.9)	12.3	(1.6)	91.8*
None[c]	1.2	(0.1)	1.7	(0.1)	0.6	(0.1)	47.2*
Total	3.1	(0.1)	4.7	(0.2)	1.3	(0.1)	244.2*
Anxiety							
12-month	10.7	(0.4)	15.5	(0.7)	4.8	(0.5)	127.7*
Lifetime	8.4	(0.7)	11.2	(0.9)	3.2	(0.7)	33.4*
Partial	8.0	(0.4)	12.2	(0.7)	3.1	(0.4)	114.9*
None	1.2	(0.1)	1.7	(0.1)	0.6	(0.1)	38.3*
Total	3.1	(0.1)	4.7	(0.2)	1.3	(0.1)	244.2*

Significant at the 0.05 level, two-sided test.
ADM, anti-depressant medication; MDD, major depressive disorder; HIC: high-income countries; LMIC: low- and middle-income countries.
[a]Lifetime: Meet full criteria for lifetime MDD/anxiety, excluding 12-month MDD or anxiety.
[b]Partial: Did not meet full criteria but has 12-month symptoms or selected depression or anxiety as reason for medication use.
[c]No diagnosis: Did not meet criteria for 12-month, lifetime, or partial MDD or anxiety.

Reasons for antidepressants use

ADM users reported depression (49.2%) and anxiety (36.4%) as their most common reasons for use followed by poor sleep (16.2%), other physical reasons (11.2%), problems with cognition (3.4%), impairments in role functioning (2.2%), alcohol/drug problems (0.4%), and unspecified 'other' reasons (8.2%) (Table 4). These percentages sum to more than 100% because respondents were allowed to report as many reasons as they wanted. Depression and anxiety were more commonly reported proportionally in HICs than LMICS (51.1–38.7% *v.* 38.4–23.3%, $\chi^2_1 = 11.1$–21.6, $p < 0.001$), whereas poor sleep and the residual category of 'other' problems were more commonly reported proportionally in LMICs than HICs (31.9–11.9% *v.* 13.4–7.5%, $\chi^2_1 = 22.7$–4.0, $p < 0.001$–0.045). Country-specific results are presented in online Supplementary Table S6.

Distributions of all major reported reasons for ADM use (i.e. depression, anxiety, poor sleep) differed significantly by ADM class ($\chi^2_3 = 32.7$–100.4, $p < 0.001$), MDD ($\chi^2_3 = 25.2$–70.9, $p < 0.001$), and in some cases anxiety ($\chi^2_3 = 14.6$–43.9, $p = <0.001$–0.001). With regard to ADM class, newer ADMs (SSRIs and other newer ADMs) were much more likely than older ADMs (TCAs and other older ADMs) to be used for depression (55.6–64.4% *v.* 33.0–25.3%) and much less likely than older ADMs to be used for poor sleep (8.0–12.6% *v.* 26.1–48.4%). In the case of clinical diagnoses, the majority of respondents with full or partial MDD reported using ADMs for depression (56.6–86.4%), whereas none of the $n = 137$ ADM users without a history of MDD reported using for depression. Respondents with depression were also less likely than others to report using ADMs for either anxiety (24.3–36.9 *v.* 48.5%) or poor sleep (8.7–15.8 *v.* 24.1%).

Patterns and predictors of perceived treatment effectiveness

Treatment was reported to be *very* effective by 58.8% of patients and *somewhat* effective by an additional 28.3% of patients. ADMs were not differentially effective as a function of depression or anxiety, as the basis for taking the medications. Those who used medication for depression rated treatment as very effective or somewhat effective (57.5 and 30.2%, respectively); those who used ADMs for anxiety rated treatment as very effective or somewhat effective (54.8 and 33.2%, respectively). There were no differences in this pattern for the overall sample or between LMICs and HICs.

ADM users from LMICs evaluated medication as very effective at a higher rate than those from HICs (74.1 *v.* 56.4%, $\chi^2_1 = 45.1$, $p < 0.001$). One reason that might explain this difference is slightly different use of ADMs. The use of ADMs for sleep problems was more common in LMICs and perhaps the effectiveness of ADMs with those problems explains the difference in perceived effectiveness. However, further analysis showed that differences in effectiveness ratings between LMICs and HICs did not vary as a function of whether sleep problems were among the reasons for use.

There was substantial cross-national variation in these reports ($\chi^2_{14} = 114.1$, $p < 0.001$ for very effective; $\chi^2_{13} = 36.8$, $p < 0.001$ for either very or somewhat effective, the reduction in degrees of freedom due to 100% of patients in Romania reporting treatment being at least somewhat effective) (online Supplementary Table S7). This was due to a small number of very high normalized ORs in a few surveys (Spain, Murcia region and Peru for very effective; Argentina for very or somewhat effective) and a general pattern for these ORs to be higher in LMICs than HICs. The latter can be seen most clearly in the model for very effective treatment, where four of the five highest ORs were in LMICs (Table 5). Recency and severity of depression and anxiety were also significant predictors of reported treatment effectiveness in both models ($\chi^2_3 = 25.2$–13.1, $p < 0.001$–0.004 for depression; $\chi^2_3 = 8.7$–11.2, $p = 0.033$–0.011 for anxiety). The highest normalized ORs in both models were among patients with a history of lifetime depression not active in the 12 months before interview, presumably representing maintenance treatment, whereas the lowest ORs were among patients with

https://doi.org/10.1017/S0033291721003160 Published online by Cambridge University Press

Table 2. The distributions of depression and anxiety among ADM users ($n = 2448$)

	Total		High-Income		Low- and Middle-Income		
	%	(S.E.)	%	(S.E.)	%	(S.E.)	χ^2_1 HIC *v.* LMIC
MDD							
12-month	27.9	(1.1)	27.4	(1.1)	29.7	(3.0)	0.5
Lifetime	17.8	(0.9)	19.2	(1.0)	12.3	(2.0)	7.5*
Partial	22.1	(1.1)	23.0	(1.3)	18.3	(2.3)	2.8
None	32.3	(1.4)	30.4	(1.5)	39.7	(3.6)	6.2*
Anxiety							
12-month	31.6	(1.2)	31.7	(1.3)	31.4	(2.7)	0.0
Lifetime	12.6	(1.0)	13.6	(1.1)	8.6	(1.7)	4.6*
Partial	27.3	(1.1)	28.2	(1.3)	23.6	(2.5)	2.4
None	28.5	(1.4)	26.5	(1.4)	36.4	(3.7)	6.9*
MDD or Anxiety							
12-month	44.1	(1.3)	43.7	(1.3)	45.6	(3.4)	0.3
Lifetime	18.8	(1.0)	20.7	(1.1)	11.4	(1.8)	13.4*
Partial	24.4	(1.2)	25.1	(1.3)	21.8	(2.6)	1.2
None	12.7	(1.2)	10.5	(1.1)	21.2	(3.7)	11.1*

*Significant at the 0.05 level, two-sided test.
MDD, major depressive disorder; HIC: high-income countries; LMIC: low- and middle-income countries.

Table 3. Among ADM users, distribution of antidepressant classes by country income group ($n = 2448$)[a]

	Total		High-income		Low- and middle-income		
	%	(S.E.)	%	(S.E.)	%	(S.E.)	χ^2_1 HIC *v.* LMIC
SSRI	62.4	(1.3)	65.1	(1.4)	51.8	(3.3)	14.5*
Other newer ADMs	14.4	(0.9)	16.9	(1.0)	4.6	(1.1)	30.4*
TCA	25.3	(1.2)	21.5	(1.2)	40.6	(3.3)	35.7*
Other older ADMs	10.0	(1.1)	8.6	(0.9)	15.3	(3.6)	4.6*
Used 2 + ADMs in the past year	11.3	(0.8)	11.1	(0.9)	11.7	(1.9)	0.1

*Significant at the 0.05 level, two-sided test.
SSRI, selective serotonin reuptake inhibitor; ADM, antidepressant medication; TCA, tricyclic antidepressants; HIC: high-income countries; LMIC: low- and middle-income countries.
[a]See Appendix Table 2 for classifications for types of antidepressants.

12-month threshold depression (significant only in the model for very effective treatment) and anxiety. Neither medication class ($\chi^2_3 = 4.2$–1.5, $p = 0.24$–0.69) nor self-reported reasons for ADM use ($\chi^2_5 = 6.2$–9.6, $p = 0.29$–0.09) was a significant predictor of reporting ADM use to be either very effective or at least somewhat effective. We also failed to find evidence for significant interactions of several sorts, including between depression and anxiety, country income level and the other predictors, clinical diagnoses and reasons for ADM use, and between clinical diagnoses and ADM class (online Supplementary Table S8).

An intriguing finding was that although having a 12-month anxiety disorder was associated with significantly *reduced* odds of reporting treatment to be at least somewhat effective, reporting that anxiety was a reason for ADM use was associated with significantly *elevated* odds of the same outcome. As opposite-sign patterns of this sort can sometimes be caused by multicollinearity, we investigated this possibility by examining the cross-classification of 12-month anxiety with reported use of ADMs for anxiety in predicting perceived ADM effectiveness. Results showed that respondents with 12-month anxiety disorder who did not say anxiety was among their reasons for ADM use had a significantly reduced odds of reporting that ADMs were either very effective (OR = 0.77, 95% CI = 0.60–0.98) or at least somewhat effective (OR = 0.52, 95% CI = 0.36–0.74). None of the ORs of other combinations of 12-month anxiety disorder with anxiety as a reason for ADM use was significant in either model (online Supplementary Table S9).

Discussion

The study provides information about ADM use across 20 countries. 3.1% of respondents reported ADM use in the 12 months

https://doi.org/10.1017/S0033291721003160 Published online by Cambridge University Press

Table 4. Reasons for ADM use ($n = 2342$)[a]

	Total		High-income		Low- and middle-income		
	%	(S.E.)	%	(S.E.)	%	(S.E.)	χ^2_1 HIC *v.* LMIC
Depression	49.2	(1.3)	51.1	(1.4)	38.4	(3.5)	11.1*
Anxiety	36.4	(1.2)	38.7	(1.3)	23.3	(2.6)	21.6*
Poor sleep	16.2	(1.3)	13.4	(1.2)	31.9	(4.5)	22.7*
Other physical reasons	11.2	(1.0)	10.9	(1.1)	12.9	(3.1)	0.4
Alcohol/Drug use	0.4	(0.2)	0.5	(0.2)	0.0	(0.0)	839.8*
Cognitive	3.4	(0.4)	3.8	(0.4)	1.1	(0.8)	3.3
Role	2.2	(0.3)	2.5	(0.4)	0.2	(0.0)	285.0*
Other reason	8.2	(0.8)	7.5	(0.8)	11.9	(2.3)	4.0*

*Significant at the 0.05 level, two-sided test.

ADM, antidepressant medication; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressants; MDD, major depressive disorder; HIC: high-income countries; LMIC: low- and middle-income.

[a]See Appendix Table 7 for distributions in specific surveys. As noted in the text, seven of the surveys (in Israel, Japan, Brazil, Bulgaria, Iraq, Lebanon, and Nigeria) did not ask about reasons for use or effectiveness. These surveys were dropped from the analyses that used these variables, reducing the sample to $n = 2377$. An additional 35 records were dropped because of missing responses on the questions asking about reason for medication, further reducing the n value to 2342. See online Supplementary Table S3 for classifications for reasons for medication.

before the interview, but with considerably higher prevalence in HICs than LMICs. Several reasons may be driving this difference, three of which are especially noteworthy. First, lower relative personal income and higher health related out-of-pocket costs can be assumed for respondents in LMICS *v.* HICs, which would inevitably result in lower use of psychopharmacology. Second, there may be significant rural and urban differences among LMICs and HICs and that could contribute to delivery and use. Finally, adherence to evidence-based prescription practices may vary with country-income level, which may compound the financial constraints, although this would not explain why use of ADMs for MDD was over twofold in HICs *v.* LMICs but over threefold for anxiety disorders. In HICs, depression and anxiety were the most common reasons for ADM use, whereas in LMICs depression and sleep problems were the most common reasons. Much higher ADM use was found inboth sets of countries among respondents who met diagnostic criteria for 12-month full or partial MDD or anxiety disorders than others.

Most users reported ADMs to be very effective and most others reported ADMs to be at least somewhat effective, although these proportions were higher in LMICs than HICs. It is important to reiterate that these evaluations were across all indications for which ADMs were used. Within-country analyses found that neither ADM class nor reasons for use predicted perceived effectiveness. An intriguing exception was the interaction between meeting criteria for an anxiety disorder but not reporting anxiety as a reason for ADM use in predicting significantly reduced odds of perceived effectiveness. This might be explained in part by type of diagnostic overshadowing in which the main diagnosis or lead reason for ADM use by the clinician or respondent precludes or overshadows the focus on other conditions (Shefer, Henderson, Howard, Murray, & Thornicroft, 2014).

The high proportion of individuals reporting ADMs to be effective is noteworthy and promising. The proportion cannot be directly compared with the findings from controlled trials (Cipriani et al., 2018). We sampled from the general population and evaluated the manifold conditions for which ADMs are be used. The findings provide an important complement to controlled trials by reporting on perceived effectiveness outside of the context and restrictions of cases included in controlled trials.

Limitations

The study has several limitations worth noting. First, data came from an overall global self-report of treatment effectiveness rather than corroboration of treatment response from clinical evaluations. A global overall evaluation of effectiveness may be a useful complement because it allows for the evaluation to take into account patient views about the benefits they experience from treatment in everyday life on the dimensions that matter most to them (Harris et al., 2020; Zimmerman et al., 2006).

Second, information of key characteristics about the use of ADMs were not assessed. Thus, we did not assess the dose of ADM or the duration over the 12-month period in which the medications were used. In addition, we did not evaluate the timeline in relation to taking ADMs and the occurrence of symptoms. It is possible that evaluations of effectiveness would be influenced by when the medications were taken in relation to symptoms and variation of symptoms and medication use over the course of the 12-month period.

Third, although we made comparisons across different classes of ADMs, it is important to recognize that respondents were not randomly assigned to ADM class. Many factors (e.g. diagnosis, severity of dysfunction, geographical local) influence type of medication received. Consequently, the study is not able to comment on differential effectiveness of ADM classes.

Conclusions

Despite these limitations, we were able to document across 20 countries that the great majority of users perceive ADMs to be at least somewhat effective and that the majority perceive ADMs to be very effective. We also documented comparable perceptions of effectiveness across ADM classes and found that this comparability was similar in HICs and LMICs, a finding broadly consistent with meta-analyses of clinical trials (Maslej et al., 2021). Overall, in a general population sample from multiple

https://doi.org/10.1017/S0033291721003160 Published online by Cambridge University Press

Table 5. Predictors of perceived treatment effectiveness ($n = 2235$)[a]

	Very effective		Very/somewhat effective	
	OR	(95% CI)	OR	(95% CI)
I. Depression				
12-month MDD	0.8*	(0.6–0.9)	0.8	(0.7–1.0)
LT without 12-month MDD	1.6*	(1.3–1.9)	1.6*	(1.2–2.1)
12-month subthreshold MDD[b]	1.0	(0.8–1.2)	0.9	(0.7–1.2)
Others	0.8	(0.7–1.1)	0.9	(0.6–1.2)
χ^2_3	25.2*		13.1*	
II. Anxiety				
12-month anxiety	0.8	(0.7–1.0)	0.7*	(0.6–0.9)
LT without 12-month anxiety	1.2	(0.9–1.6)	1.2	(0.8–1.7)
12-month subthreshold anxiety[b]	0.8	(0.7–1.0)	0.9	(0.6–1.2)
Others	1.2	(1.0–1.5)	1.4	(1.0–2.0)
χ^2_3	8.7*		11.2*	
III. Antidepressant classes				
SSRI	1.1	(0.9–1.3)	1.0	(0.8–1.2)
Other new	0.8	(0.7–1.1)	0.9	(0.6–1.3)
TCA	1.1	(0.9–1.4)	1.2	(0.9–1.6)
The others	0.9	(0.7–1.3)	1.0	(0.7–1.5)
χ^2_3	4.2		1.5	
IV. Reasons for taking ADMs				
Depression	0.8	(0.6–1.1)	1.4	(1.0–2.0)
Anxiety	1.0	(0.8–1.3)	1.7*	(1.1–2.6)
Physical reasons	0.9	(0.6–1.4)	1.4	(0.8–2.2)
Poor sleep	1.3	(1.0–1.9)	1.3	(0.8–2.0)
Alcohol/Drug, cognitive, role, or other reasons	1.2	(0.8–1.6)	1.1	(0.7–1.7)
χ^2_5	6.2		9.6*	

*Significant at the 0.05 level, two-sided test.
Abbreviations: ADM, anti-depressant medication; LT, lifetime; MDD, major depressive disorder; HIC: high-income countries; LMIC: Low- and Middle-income.
[a]Controlling for survey. See Appendix Table 7 for ORs associated with surveys. As noted in the text, seven of the surveys (in Israel, Japan, Brazil, Bulgaria, Iraq, Lebanon, and Nigeria) did not ask about reasons for use or assess the detailed survey items exploring details about medication use (e.g. current use or stop; reason for medication use; perceived effectiveness). These surveys were dropped from the analyses that used these variables, reducing the sample to $n = 2377$. Another 142 records were dropped due to missing values for the questions asking about reasons for treatment and effectiveness, further reducing the sample to 2235. In addition, Romania was dropped from the model predicting Very/somewhat Effective because all $n = 39$ ADM uses in Romania were reported to be either very or somewhat effective, reducing the sample size for that model to $n = 2196$.
[b]Without a lifetime history of the threshold disorder.

countries, ADMs are widely perceived to be very or somewhat effective by the majority of people who use them in both LMICs and HICs.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291721003160.

Financial support. The World Health Organization World Mental Health (WMH) Survey Initiative is supported by the United States National Institute of Mental Health (NIMH; R01 MH070884), the John D. and Catherine T. MacArthur Foundation, the Pfizer Foundation, the United States Public Health Service (R13-MH066849, R01-MH069864, and R01 DA016558), the Fogarty International Center (FIRCA R03-TW006481), the Pan American Health Organization, Eli Lilly and Company, Ortho-McNeil Pharmaceutical Inc., GlaxoSmithKline, and Bristol-Myers Squibb. We thank the staff of the WMH Data Collection and Data Analysis Coordination Centres for assistance with instrumentation, fieldwork, and consultation on data analysis. None of the funders had any role in the design, analysis, interpretation of results, or preparation of this paper. The views and opinions expressed in this report are those of the authors and should not be construed to represent the views of the World Health Organization, other sponsoring organizations, agencies, or governments.

The Argentina survey – Estudio Argentino de Epidemiología en Salud Mental (EASM) – was supported by a grant from the Argentinian Ministry of Health (Ministerio de Salud de la Nación) – (Grant Number 2002-17270/13-5). The São Paulo Megacity Mental Health Survey is supported by the State of São Paulo Research Foundation (FAPESP) Thematic Project Grant 03/00204-3. The Bulgarian Epidemiological Study of common mental disorders EPIBUL is supported by the Ministry of Health and the National Center for Public Health Protection. The Colombian National Study of Mental Health (NSMH) is supported by the Ministry of Social Protection. The Mental Health Study Medellín – Colombia was carried out and supported jointly by the Center for Excellence on Research in Mental Health (CES University) and the Secretary of Health of Medellín. The ESEMeD project is

funded by the European Commission (Contracts QLG5-1999-01042; SANCO 2004123, and EAHC 20081308), the Piedmont Region (Italy), Fondo de Investigación Sanitaria, Instituto de Salud Carlos III, Spain (FIS 00/0028), Ministerio de Ciencia y Tecnología, Spain (SAF 2000-158-CE), Generalitat de Catalunya (2017 SGR 452; 2014 SGR 748), Instituto de Salud Carlos III (CIBER CB06/02/0046, RETICS RD06/0011 REM-TAP), and other local agencies and by an unrestricted educational grant from GlaxoSmithKline. Implementation of the Iraq Mental Health Survey (IMHS) and data entry were carried out by the staff of the Iraqi MOH and MOP with direct support from the Iraqi IMHS team with funding from both the Japanese and European Funds through United Nations Development Group Iraq Trust Fund (UNDG ITF). The Israel National Health Survey is funded by the Ministry of Health with support from the Israel National Institute for Health Policy and Health Services Research and the National Insurance Institute of Israel. The World Mental Health Japan (WMHJ) Survey is supported by the Grant for Research on Psychiatric and Neurological Diseases and Mental Health (H13-SHOGAI-023, H14-TOKUBETSU-026, H16-KOKORO-013, H25-SEISHIN-IPPAN-006) from the Japan Ministry of Health, Labour and Welfare. The Lebanese Evaluation of the Burden of Ailments and Needs of the Nation (L.E.B.A.N.O.N.) is supported by the Lebanese Ministry of Public Health, the WHO (Lebanon), National Institute of Health / Fogarty International Center (R03 TW006481-01), anonymous private donations to IDRAAC, Lebanon, and unrestricted grants from, Algorithm, AstraZeneca, Benta, Bella Pharma, Eli Lilly, Glaxo Smith Kline, Lundbeck, Novartis, OmniPharma, Pfizer, Phenicia, Servier, and UPO. The Mexican National Comorbidity Survey (MNCS) is supported by The National Institute of Psychiatry Ramon de la Fuente (INPRFMDIES 4280) and by the National Council on Science and Technology (CONACyT-G30544-H), with supplemental support from the Pan American Health Organization (PAHO). The Nigerian Survey of Mental Health and Wellbeing (NSMHW) is supported by the WHO (Geneva), the WHO (Nigeria), and the Federal Ministry of Health, Abuja, Nigeria. The Peruvian World Mental Health Study was funded by the National Institute of Health of the Ministry of Health of Peru. The Portuguese Mental Health Study was carried out by the Department of Mental Health, Faculty of Medical Sciences, NOVA University of Lisbon, with collaboration of the Portuguese Catholic University, and was funded by Champalimaud Foundation, Gulbenkian Foundation, Foundation for Science and Technology (FCT) and Ministry of Health. The Romania WMH study projects 'Policies in Mental Health Area' and 'National Study regarding Mental Health and Services Use' were carried out by National School of Public Health & Health Services Management (former National Institute for Research & Development in Health), with technical support of Metro Media Transilvania, the National Institute of Statistics-National Centre for Training in Statistics, SC Cheyenne Services SRL, Statistics Netherlands and were funded by Ministry of Public Health (former Ministry of Health) with supplemental support of Eli Lilly Romania SRL. The Psychiatric Enquiry to General Population in Southeast Spain – Murcia (PEGASUS-Murcia) Project has been financed by the Regional Health Authorities of Murcia (Servicio Murciano de Salud and Consejería de Sanidad y Política Social) and Fundación para la Formación e Investigación Sanitarias (FFIS) of Murcia. US National Comorbidity Survey Replication (NCS-R) is supported by the National Institute of Mental Health (NIMH; U01-MH60220) with supplemental support from the National Institute of Drug Abuse (NIDA), the Substance Abuse and Mental Health Services Administration (SAMHSA), the Robert Wood Johnson Foundation (RWJF; Grant 044708), and the John W. Alden Trust. Dr Laura Helena Andrade is supported by the Brazilian Council for Scientific and Technological Development (CNPq Grant # 307933/2019-9). A complete list of all within-country and cross-national WMH publications can be found at http://www.hcp.med.harvard.edu/wmh/.

Conflict of interest. In the past 3 years, Dr Kessler was a consultant for Datastat, Inc., Holmusk, RallyPoint Networks, Inc., and Sage Therapeutics. He has stock options in Mirah, PYM, and Roga Sciences. Dr Navarro-Mateu reports non-financial support from Otsuka outside the submitted work. In the past 3 years, Dr Stein has received research grants and/or consultancy honoraria from Johnson & Johnson, Lundbeck, Servier, Takeda and Vistagen. All other authors have no conflicts of interest to declare.

Collaborators:. The WHO WMH Survey collaborators are: Lukoye Atwoli, Department of Mental Health and Behavioural Sciences, Moi University School of Medicine, Eldoret, Kenya Brain and Mind Institute and Medical College East Africa, the Aga Khan University, Nairobi, Kenya; Yasmin Altwaijri, Epidemiology Section, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia; Guilherme Borges, Maria Elena Medina-Mora, National Institute of Psychiatry Ramón de la Fuente Muñiz, Mexico City, Mexico; Evelyn J. Bromet, Department of Psychiatry, Stony Brook University School of Medicine, Stony Brook, New York, USA; Brendan Bunting, School of Psychology, Ulster University, Londonderry, United Kingdom; Andrzej Kiejna, University of Lower Silesia, Wroclaw, Poland; Kate M. Scott, Department of Psychological Medicine, University of Otago, Dunedin, Otago, New Zealand; Margreet ten Have, Trimbos-Instituut, Netherlands Institute of Mental Health and Addiction, Utrecht, Netherlands

Disclaimer. None of the funders had any role in the design, analysis, interpretation of results, or preparation of this paper. The views and opinions expressed in this report are those of the authors and should not be construed to represent the views of the World Health Organization, other sponsoring organizations, agencies, or governments.

[1]Department of Psychology, Yale University, New Haven, CT, USA; [2]Department of Psychiatry, National Taiwan University Hospital & College of Medicine, Taipei, Taiwan; [3]Department of Health Care Policy, Harvard Medical School, Boston, MA, USA; [4]College of Medicine, Al-Qadisiya University, Diwaniya governorate, Al Diwaniyah, Iraq; [5]Health Services Research Unit, IMIM-Hospital del Mar Medical Research Institute, Barcelona, Spain; [6]Pompeu Fabra University (UPF), Barcelona, Spain; [7]CIBER en Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain; [8]Núcleo de Epidemiologia Psiquiátrica - LIM 23, Instituto de Psiquiatria Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, Brazil; [9]Department of Epidemiologic and Psychosocial Research, National Institute of Psychiatry Ramón de la Fuente Muñiz, Mexico City, Mexico; [10]Lisbon Institute of Global Mental Health and Chronic Diseases Research Center (CEDOC), NOVA Medical School | Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Lisbon, Portugal; [11]IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy; [12]Department of Developmental Psychology, University of Groningen, Groningen, The Netherlands; [13]Interdisciplinary Center Psychopathology and Emotion Regulation, University Medical Center Groningen, Groningen, The Netherlands; [14]National School of Public Health, Management and Development, Bucharest, Romania; [15]Department of Psychiatry, University College Hospital, Ibadan, Nigeria; [16]Parc Sanitari Sant Joan de Déu, CIBERSAM, Universitat de Barcelona, Sant Boi de Llobregat, Barcelona, Spain; [17]School of Public Health, The University of Queensland, Herston, QLD 4006, Australia; [18]Queensland Centre for Mental Health Research, The Park Centre for Mental Health, Wacol QLD 4072, Australia; [19]Faculty of Medicine, Department of Psychiatry and Clinical Psychology, St George Hospital University Medical Center, Balamand University, Beirut, Lebanon; [20]Institute for Development, Research, Advocacy and Applied Care (IDRAAC), Beirut, Lebanon; [21]Ecole des Hautes Etudes en Santé Publique (EHESP), EA 4057, Paris Descartes University, Paris, France; [22]Department of Psychiatry, Chinese University of Hong Kong, Tai Po, Hong Kong; [23]Queensland Brain Institute, The University of Queensland, St Lucia QLD 4065, Australia; [24]National Centre for Register-based Research, Aarhus University, Aarhus V 8000, Denmark; [25]UDIF-SM, Servicio Murciano de Salud; IMIB-Arrixaca; CIBERESP-Murcia, Región de Murcia, Spain; [26]Department of Mental Health, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; [27]National Center of Neurology and Psychiatry, Tokyo, Japan; [28]Colegio Mayor de Cundinamarca University, Faculty of Social Sciences, Bogota, Colombia; [29]Department of Psychiatry & Mental Health and South African Medical Council Research Unit on Risk and Resilience in Mental Disorders, University of Cape Town, Cape Town, South Africa; [30]Groote Schuur Hospital, Cape Town, South Africa; [31]Department of Psychiatry, Koç University, Istanbul, Turkey; [32]Department of Psychiatry, University of British Columbia, Vancouver, BC, Canada; [33]Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA, USA and [34]Department of Mental Health, National Center of Public Health and Analyses, Sofia, Bulgaria

https://doi.org/10.1017/S0033291721003160 Published online by Cambridge University Press

References

Abbing-Karahagopian, V., Huerta, C., Souverein, P., De Abajo, F., Leufkens, H., Slattery, J., … Oliva, B. (2014). Antidepressant prescribing in five European countries: Application of common definitions to assess the prevalence, clinical observations, and methodological implications. *European Journal of Clinical Pharmacology*, *70*, 849–857. doi: 10.1007/s00228-014-1676-z

Bandelow, B., Michaelis, S., & Wedekind, D. (2017). Treatment of anxiety disorders. *Dialogues in Clinical Neuroscience*, *19*, 93–107. doi: 10.31887/DCNS.2017.19.2/bbandelow

Barth, J., Munder, T., Gerger, H., Nüesch, E., Trelle, S., Znoj, H., … Cuijpers, P. (2016). Comparative efficacy of seven psychotherapeutic interventions for patients with depression: A network meta-analysis. *Focus*, *14*, 229–243. doi: 10.1176/appi.focus.140201

Brody, D. J., & Gu, Q. (2020). Antidepressant use among adults: United States, 2015–2018. Retrieved from https://www.cdc.gov/nchs/products/databriefs/db377.htm.

Chisholm, D., Sweeny, K., Sheehan, P., Rasmussen, B., Smit, F., Cuijpers, P., & Saxena, S. (2016). Scaling-up treatment of depression and anxiety: A global return on investment analysis. *The Lancet Psychiatry*, *3*, 415–424. doi: 10.1016/S2215-0366(16)30024-4

Cipriani, A., Furukawa, T. A., Salanti, G., Chaimani, A., Atkinson, L. Z., Ogawa, Y., … Geddes, J. R. (2018). 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. *The Lancet Psychiatry*, *391*, 1357–1366. doi: 10.1016/s0140-6736(17)32802-7

Cooper, C. (2018). Global, regional, and national Disability-Adjusted Life-Years (DALY) for 359 diseases and injuries and Health Life Expectancy (HALE) for 195 countries and territories, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. *The Lancet Psychiatry*, *392*, 1859–1922. doi: 10.1016/S0140-6736(18)32335-3

Fava, M., Rush, A. J., Alpert, J. E., Balasubramani, G., Wisniewski, S. R., Carmin, C. N., … Howland, R. (2008). Difference in treatment outcome in outpatients with anxious versus nonanxious depression: A STAR* D report. *American Journal of Psychiatry*, *165*, 342–351. doi: 10.1176/appi.ajp.2007.06111868

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (2002). *Structured clinical interview for DSM-IV-TR axis I disorders, research version, Non-patient edition.* (*SCID-I/NP*). New York: Biometrics Research, New York State Psychiatric Institute.

Goldstein, B. I., Baune, B. T., Bond, D. J., Chen, P. H., Eyler, L., Fagiolini, A., … McElroy, S. L. (2020). Call to action regarding the vascular-bipolar link: A report from the Vascular Task Force of the International Society for Bipolar Disorders. *Bipolar Disorders*, *22*, 440–460. doi: 10.1111/bdi.12921

Harkness, J., Pennell, B., Villar, A., Gebler, N., Aguilar-Gaxiola, S., & Bilgen, I. (2008). Translation procedures and translation assessment in the world mental health survey initiative. In R. Kessler & T. Üstün (Eds.), *The WHO world mental health surveys: Global perspectives on the epidemiology of mental disorders* (pp. 91–113). New York, NY: Cambridge University Press.

Haro, J. M., Arbabzadeh-Bouchez, S., Brugha, T. S., De Girolamo, G., Guyer, M. E., Jin, R., … Vilagut, G. (2006). Concordance of the Composite International Diagnostic Interview version 3.0 (CIDI 3.0) with standardized clinical assessments in the WHO World Mental Health surveys. *International Journal of Methods in Psychiatric Research*, *15*, 167–180. doi: 10.1002/mpr.196

Harris, M. G., Kazdin, A. E., Chiu, W. T., Sampson, N. A., Aguilar-Gaxiola, S., Al-Hamzawi, A., … Kessler, R. C. (2020). Findings from World Mental Health Surveys of the perceived helpfulness of treatment for patients with major depressive disorder. *JAMA Psychiatry*, *77*, 830–841. doi: 10.1001/jamapsychiatry.2020.1107

Heeringa, S., Wells, J., Hubbard, F., Mneimneh, Z., Chiu, W., Sampson, N., & Berglund, P. (2008). *Sample designs and sampling procedures*. New York, NY: Cambridge University Press.

Herrman, H., Kieling, C., McGorry, P., Horton, R., Sargent, J., & Patel, V. (2019). Reducing the global burden of depression: A Lancet–World Psychiatric Association commission. *The Lancet Psychiatry*, *393*, e42–e43. doi: 10.1016/S0140-6736(18)32408-5

Kessler, R. C., & Üstün, T. B. (2004). The World Mental Health (WMH) survey initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *International Journal of Methods in Psychiatric Research*, *13*, 93–121. doi: 10.1002/mpr.168

Lewer, D., O'Reilly, C., Mojtabai, R., & Evans-Lacko, S. (2015). Antidepressant use in 27 European countries: Associations with sociodemographic, cultural and economic factors. *The British Journal of Psychiatry*, *207*, 221–226. doi: 10.1192/bjp.bp.114.156786

Maslej, M. M., Furukawa, T. A., Cipriani, A., Andrews, P. W., Sanches, M., Tomlinson, A., … Mulsant, B. H. (2021). Individual differences in response to antidepressants: A meta-analysis of placebo-controlled randomized clinical trials. *JAMA Psychiatry*, *78*, 490–497. doi: 10.1001/jamapsychiatry.2020.4564

Olfson, M., & Marcus, S. C. (2009). National patterns in antidepressant medication treatment. *Archives of General Psychiatry*, *66*(8), 848–856. doi: 10.1001/archgenpsychiatry.2009.81

Prukkanone, B., Vos, T., Bertram, M., & Lim, S. (2012). Cost-effectiveness analysis for antidepressants and cognitive behavioral therapy for major depression in Thailand. *Value in Health*, *15*, S3–S8. doi: 10.1016/j.jval.2011.11.009

Rajaratnam, K., Xiang, Y.-T., Tripathi, A., Chiu, H. F. K., Si, T.-M., Chee, K.-Y., … Kuga, H. (2016). Factors associated with antidepressant dosing in Asia: Findings from the research on Asian psychotropic prescription study. *Journal of Clinical Psychopharmacology*, *36*, 716–719. doi: 10.1097/JCP.0000000000000591

SAS Institute Inc. (2016). SAS Software Version 9.4.

Shefer, G., Henderson, C., Howard, L. M., Murray, J., & Thornicroft, G. (2014). Diagnostic overshadowing and other challenges involved in the diagnostic process of patients with mental illness who present in emergency departments with physical symptoms – a qualitative study. *PLoS One*, *9*, e111682. doi: 10.1371/journal.pone.0111682

Souery, D., Oswald, P., Massat, I., Bailer, U., Bollen, J., Demyttenaere, K., … Serretti, A. (2007). Clinical factors associated with treatment resistance in major depressive disorder: Results from a European multicenter study. *Journal of Clinical Psychiatry*, *68*, 1062–1070. doi: 10.4088/jcp.v68n0713

Wang, Y.-H., Li, J.-Q., Shi, J.-F., Que, J.-Y., Liu, J.-J., Lappin, J. M., … Qiao, Y.-L. (2020). Depression and anxiety in relation to cancer incidence and mortality: A systematic review and meta-analysis of cohort studies. *Molecular Psychiatry*, *25*, 1487–1499. doi: 10.1038/s41380-019-0595-x

Wiles, N. J., Thomas, L., Turner, N., Garfield, K., Kounali, D., Campbell, J., … Morrison, J. (2016). Long-term effectiveness and cost-effectiveness of cognitive behavioural therapy as an adjunct to pharmacotherapy for treatment-resistant depression in primary care: Follow-up of the CoBalT randomised controlled trial. *The Lancet Psychiatry*, *3*, 137–144. doi: 10.1016/S2215-0366(15)00495-2

Wolter, K. M. (1985). *Introduction to variance estimation*. New York, NY: Springer-Verlag. doi: 10.1007/978-0-387-35099-8

World Health Organization (2017). Depression and other common mental disorders: global health estimates. Retrieved from https://apps.who.int/iris/handle/10665/254610.

Wu, C.-S., Shau, W.-Y., Chan, H.-Y., Lee, Y.-C., Lai, Y.-J., & Lai, M.-S. (2012). Utilization of antidepressants in Taiwan: A nationwide population-based survey from 2000 to 2009. *Pharmacoepidemiology and Drug Safety*, *21*, 980–988. doi: 10.1002/pds.3255

Yatham, L. N., Kennedy, S. H., Parikh, S. V., Schaffer, A., Bond, D. J., Frey, B. N., … Berk, M. (2018). Canadian Network for mood and anxiety treatments (CANMAT) and international society for bipolar disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. *Bipolar Disorders*, *20*, 97–170. doi: 10.1111/bdi.12609

Zhang, Y., Yang, H., Yang, S., Liang, W., Dai, P., Wang, C., & Zhang, Y. (2013). Antidepressants for bipolar disorder: A meta-analysis of randomized, double-blind, controlled trials. *Neural Regeneration Research*, *8*, 2962. doi: 10.3969/j.issn.1673-5374.2013.31.009

Zimmerman, M., McGlinchey, J. B., Posternak, M. A., Friedman, M., Attiullah, N., & Boerescu, D. (2006). How should remission from depression be defined? The depressed patient's perspective. *American Journal of Psychiatry*, *163*, 148–150. doi: 10.1176/appi.ajp.163.1.148

https://doi.org/10.1017/S0033291721003160 Published online by Cambridge University Press