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# Anxiolytic Medication Use in Low- Middle- and High-Income Countries: A World Mental Health Surveys Report

Dan J. Stein[1] | Alan E. Kazdin[2] | David S. Baldwin[3] | Meredith G. Harris[4,5] | Irving Hwang[6] | Julia R. Pozuelo[6,7] | Nancy A. Sampson[6] | Peter Woodruff[8] | Maria Carmen Viana[9] | Sergio Aguilar-Gaxiola[10] | Ali Al-Hamzawi[11] | Jordi Alonso[12,13,14] | Laura Helena Andrade[15] | Corina Benjet[16] | Ronny Bruffaerts[17] | José-Miguel Caldas-de-Almeida[18] | Stephanie Chardoul[19] | Giovanni de Girolamo[20] | Oye Gureje[21] | Josep M. Haro[22] | Elie G. Karam[23,24] | Aimee Karam[23,24] | Viviane Kovess-Masfety[25] | Fernando Navarro-Mateu[26,27,28] | Daisuke Nishi[29] | José Posada-Villa[30] | Annelieke Roest[31] | Juan Carlos Stagnaro[32] | Cristian Vladescu[33] | Daniel V. Vigo[34] | Ronald C. Kessler[6] | the WHO World Mental Health Survey collaborators

[1]Department of Psychiatry & Neuroscience Institute, SAMRC Unit on Risk & Resilience in Mental Disorders, University of Cape Town, Cape Town, South Africa | [2]Department of Psychology, Yale University, New Haven, Connecticut, USA | [3]Faculty of Medicine, University of Southampton, Southampton, UK | [4]School of Public Health, The University of Queensland, Herston, Australia | [5]Queensland Centre for Mental Health Research, The Park Centre for Mental Health, Wacol, Queensland, Australia | [6]Department of Health Care Policy, Harvard Medical School, Boston, Massachusetts, USA | [7]Department of Psychiatry, University of Oxford, Oxford, UK | [8]School of Medicine and Population Health, University of Sheffield, Sheffield, UK | [9]Department of Social Medicine, Postgraduate Program in Public Health, Federal University of Espírito Santo, Vitória, Brazil | [10]Department of Internal Medicine, Center for Reducing Health Disparities, UC Davis Health System, Sacramento, California, USA | [11]College of Medicine, Al-Qadisiya University, Diwaniya Governorate, Diwaniya, Iraq | [12]Health Services Research Unit, IMIM-Hospital del Mar Medical Research Institute, Barcelona, Spain | [13]Pompeu Fabra University (UPF), Barcelona, Spain | [14]CIBER en Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain | [15]Núcleo de Epidemiologia Psiquiátrica - LIM 23, Instituto de Psiquiatria Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil | [16]Department of Epidemiologic and Psychosocial Research, National Institute of Psychiatry Ramón de la Fuente Muñiz, Mexico City, Mexico | [17]Universitair Psychiatrisch Centrum - Katholieke Universiteit Leuven (UPC-KUL), Leuven, Belgium | [18]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 | [19]Survey Research Center, Institute for Social Research, University of Michigan, Ann Arbor, Michigan, USA | [20]IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy | [21]Department of Psychiatry, University College Hospital, Ibadan, Nigeria | [22]Parc Sanitari Sant Joan de Déu, CIBERSAM, Universitat de Barcelona, Barcelona, Spain | [23]Department of Psychiatry and Clinical Psychology, Faculty of Medicine, St George University of Beirut, Beirut, Lebanon | [24]Institute for Development, Research, Advocacy and Applied Care (IDRAAC), Beirut, Lebanon | [25]Ecole des Hautes Etudes en Santé Publique (EHESP), Paris Descartes University, Paris, France | [26]Unidad de Docencia, Investigación y Formación en Salud Mental, Gerencia Salud Mental, Servicio Murciano de Salud, Murcia, Spain | [27]Biomedical Research Institute of Murcia Pascual Parrilla–IMIB, Murcia, Spain | [28]CIBER Epidemiology and Public Health-Murcia, Murcia, Spain | [29]Department of Mental Health, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan | [30]Colegio Mayor de Cundinamarca University, Faculty of Social Sciences, Bogota, Colombia | [31]Department of Developmental Psychology, Faculty of Behavioral and Social Sciences, University of Groningen, Groningen, the Netherlands | [32]Departamento de Psiquiatría y Salud Mental, Facultad de Medicina, Universidad de Buenos Aires, Buenos Aires, Argentina | [33]National Institute for Health Services Management, Bucharest, Romania | [34]Department of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada

**Correspondence:** Daniel V. Vigo (daniel.vigo@ubc.ca)

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## ABSTRACT

**Background:** Anxiolytic medications, particularly benzodiazepines, are widely prescribed, giving impetus to long-standing debates about how often these agents should be employed in clinical practice. There are, however, few cross-country studies

Professor Dan Stein was a beloved colleague, with a rare combination of wisdom, humility, and bonhomie that made working with him a reward unto itself. He made countless contributions to the fields of clinical psychiatry, psychiatric epidemiology, and psychopharmacology. In a testament of his love for our field and unparallelled work ethic, he submitted the final revisions to this posthumous article days before his passing.

of the pharmacoepidemiology of these agents. We report on the frequency of anxiolytic medication 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 World Mental Health (WMH) Surveys asked about anxiolytic medication use anytime in the prior 12 months in conjunction with validated fully structured diagnostic interviews. Treatment questions were administered independently of diagnoses to all respondents.

**Results:** A weighted 5.6% ($n = 4079$) of respondents reported anxiolytic medication use within the past 12 months; the vast majority comprised benzodiazepine use, and use was highest amongst respondents with a subthreshold major depressive episode (MDE) (25.2%) and a 12-month MDE (19.8%). Rates were significantly higher in high-income countries (HICs) than low- and middle-income countries (LMICs) (8.5% vs. 2.2%, $\chi^2_1 = 559.6$, $p < 0.001$). Short-acting benzodiazepines and z-drugs were most commonly used for sleep (66.5% and 85.5%), while intermediate-acting benzodiazepines and long-acting benzodiazepines were most commonly used either for sleep (37.9% and 30.1%) or anxiety (33.3% and 32.0%). Across all conditions, anxiolytic medications were reported as *very* effective by 55.7% of users and *somewhat* effective by an additional 32.2% of users, with similar proportions in HICs and LMICs. Negative predictors of high perceived effectiveness were a 12-month MDE and taking anxiolytic medication for comorbid anxiety and depression.

**Conclusion:** These data do not definitely answer the question of how often benzodiazepines should be prescribed in clinical practice, but they usefully inform discussions of how to optimize their use. It is noteworthy that anxiolytic medications, particularly benzodiazepines, are largely prescribed for anxiety and sleep, and that they are widely perceived to be either very or somewhat effective by users. However, more targeted prescription of these agents may be necessary; in particular antidepressant intervention should be prioritized in the pharmacotherapy of major depressive disorder.

## 1 | Introduction

Since their discovery in the 1960s, benzodiazepines have been commonly used for anxiolysis and sedation, and in some countries several (with intermediate or long half-life) are approved for anxiety disorders such as generalized anxiety disorder and panic disorder, while others (with a short or intermediate half-life) are approved for insomnia (Junkes et al. 2024; López-Muñoz et al. 2011). Given their improved safety profile, benzodiazepines replaced earlier anxiolytic and sedative agents such as the barbiturates and meprobamate. Concerns about benzodiazepine adverse events, most notably tolerance and dependence, gave impetus to development of newer agents such as buspirone and pregabalin for generalized anxiety disorder, and 'z-drugs' (such as zopiclone) for insomnia. The introduction of selective serotonin reuptake inhibitors provided clinicians with additional efficacious and well-tolerated options for the treatment of anxiety disorders (Baldwin et al. 2014; Bandelow et al. 2023).

There are nevertheless several reasons for the widespread use of benzodiazepines (Balon et al. 2020; Dubovsky and Marshall 2022; Silberman et al. 2023). Anxiety disorders are the most prevalent of mental disorders, and they are associated with significant distress and impairment (Stein et al. 2017). Furthermore, anxiety and anxiety adjacent symptoms such as agitation and insomnia are key symptoms in a range of mental health conditions, including major depressive disorder (MDD), where anxiety is now recognized as a specifier that deserves targeted intervention (Maj et al. 2020). Notably, a large evidence-base of randomized controlled trials (RCTs) demonstrates the efficacy of benzodiazepines for anxiety disorders and anxiety adjacent symptoms. These agents generally have low costs relative to other treatments, and they are accessible in countries where access to psychological services is limited (Dubovsky and Marshall 2022).

There are also important reasons for judicious use of benzodiazepines (Dell'osso and Lader 2013; Lader 2014; Peppin et al. 2021). There is robust evidence for the short-term efficacy of benzodiazepines in some anxiety disorders such as generalized anxiety disorder, but little evidence of efficacy in other conditions such as posttraumatic stress disorder and obsessive-compulsive disorder. Benzodiazepines are associated with a range of important adverse events. With longer-term use, there are fewer data on efficacy, and more concerns about the risk of tolerance and the potential for dependence and abuse. Still, meta-analysis of anxiety disorder trials suggests that for some disorders, benzodiazepines may be associated with greater efficacy and fewer adverse events than antidepressants (Bighelli et al. 2016; Gomez et al. 2018; Offidani et al. 2013). Clinical judgment is therefore needed to weigh the benefits that may follow from the use of benzodiazepines, the risk of the underlying conditions for which treatment is being provided, the risks of long-term benzodiazepine use, and potential risks associated with other treatments (Baldwin et al. 2013).

Epidemiological data may be useful in informing this debate (Cosci et al. 2015; Fisher et al. 2012; Kurko et al. 2015; Soumerai et al. 2024). In a national registry study in Luxembourg, around 80% of benzodiazepine users were short-term or intermittent users, while the rest were continuous users. The authors predicted and confirmed that specific benzodiazepines with short and intermediate half-lives (alprazolam and triazolam) were associated with continuous and high-dose use (Cloos et al. 2015). Comparison of prescription data before and after triplicate benzodiazepine regulations in New York State found that although benzodiazepine prescription decreased, there was an increase in prescription of older more dangerous agents, indicating the need

for alternative approaches to optimize benzodiazepine use (Weintraub et al. 1991).

Despite this evidence, there are few published cross-country comparisons of the pharmacoepidemiology of benzodiazepines (Huerta et al. 2016). Comparative data from low- and middle-income countries is particularly scant (Campanha et al. 2020). Further, extant studies have largely drawn on administrative data on prescriptions received rather than on respondent reports of benzodiazepine use. Fundamental questions therefore remain about the use of benzodiazepines, including the conditions for which they are used and how effective they are perceived to be.

The World Health Organization (WHO) World Mental Health (WM) surveys provide an important resource to address these questions. This is 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/) (Scott et al. 2017). We earlier used this dataset to report on the use of antidepressants, including the conditions for which they are used and how effective they are perceived to be, in countries of varying income levels across the world (Kazdin et al. 2023). An additional publication on the use of mood-stabilizers and antipsychotic medications is under way.

Here we build on this prior work to report on the cross-country use of benzodiazepines, including the conditions for which they are used and how effective they are perceived to be. Given important clinical differences between benzodiazepines with different half-lives, as well as previous epidemiological work differentiating these medications by half-life, we classified benzodiazepines into short-acting, intermediate-acting, and long-acting agents, and this represents the large majority of the medication use covered in this paper. Given partial overlaps in debates about benzodiazepines and z-drugs (Huerta et al. 2016; Nutt 2005), as well as in their underlying mechanisms of action, we also report here on the use of z-drugs.

As noted earlier, the benzodiazepines replaced earlier anxiolytic and sedative agents such as the barbiturates and meprobamate, and newer drugs such as hydroxyzine, buspirone and pregabalin were in turn developed for generalized anxiety disorder. These agents are not covered in other WMH papers on psychiatric medications, and if included here would represent only a small minority of the medication use covered. From a neuroscientific point of view, these agents have entirely different mechanisms of action, and are used for a range of indications other than anxiolysis and sedation. However, from an epidemiological perspective, they potentially provide a useful contrast with the main focus here on benzodiazepines and z-drugs, and so we have chosen to include them in the analysis, as a miscellaneous group of "anxiolytic medications".

The paper covers several questions. First, we examine use of anxiolytic medications (i.e., short-acting, intermediate-acting and long-acting benzodiazepines, z-drugs, and miscellaneous) in 20 countries of varying income levels across the world. Second, we evaluate the diagnoses of the people who use anxiolytic medication, paying special attention to anxiety disorders and major depressive episodes. Third, we examine the reasons given by respondents for anxiolytic medication use. Finally, we examine how effective respondents perceive their anxiolytic medications to be overall and as a function of reasons for use.

## 2 | Methods

### 2.1 | Sample

Data are included from 22 WMH surveys with adult respondents (18 years or older) in 20 countries. Ten surveys were carried out in low- or middle-income countries (LMICs; Brazil, Bulgaria, 2 surveys in Colombia, Iraq, Lebanon, Mexico, Nigeria, Peru, and Romania) and 12 in high-income countries (HICs; Argentina, Belgium, France, Germany, Israel, Italy, Japan, the Netherlands, Portugal, 2 surveys in Spain, and the United States). Thirteen of these surveys were based on nationally representative multi-stage 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 (Supporting Information 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 carried out 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). *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*.

### 2.2 | Measures

#### 2.2.1 | Diagnoses

The survey instrument was the WHO Composite International Diagnostic Interview (CIDI) Version 3.0 (Kessler and Üstün 2004), a fully structured interview generating diagnoses of lifetime and 12-month DSM-IV disorders. The conditions considered here are anxiety disorders including agoraphobia, generalized anxiety disorder, panic disorder, post-traumatic stress disorder, social phobia and specific phobia, as well as major depressive episode (MDE). Blinded clinical reappraisal diagnostic interviews using the Structured Clinical Interview for DSM-IV (SCID) (First et al. 1997) as gold standard found good concordance with CIDI diagnoses (Haro et al. 2006). We

categorized respondents into four hierarchically-ordered categories of anxiety disorders, reflecting recency and severity (i.e., 12-month anxiety disorder includes respondents who met full criteria for at least one anxiety disorder; lifetime anxiety disorder includes other respondents who met lifetime criteria for at least one anxiety disorder; partial anxiety disorder includes other respondents who met 12-month subthreshold criteria for at least one anxiety disorder, and respondents who had none of these conditions). The same four categories were used to define MDE hierarchically (i.e., 12-month MDE; lifetime MDE for other respondents who met lifetime criteria for MDE; partial MDE for other respondents who met 12-month subthreshold criteria for MDE; and respondents who had none of these conditions). We also created a four-category hierarchical variable that combined scores on the separate four-category MDE and anxiety disorder variables.

#### 2.2.2 | Anxiolytic Medication Use

Anxiolytic medication users were defined as those who took an anxiolytic medication at any time in the past 12 months. Information on use was captured by presenting respondents with a list of available 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 antidepressants, anxiolytics (including sedatives and hypnotics), antipsychotics, mood stabilizers, and other psychotropic agents—the current paper focuses only on anxiolytic medications. Respondents were instructed to *include medicines even if you took them only once*. Because anxiolytic medication administration policies vary across countries, the medication list was modified for each country. Information was gathered on a total of 56 anxiolytic medications (Supporting Information S1), which were categorized for analysis into short-acting benzodiazepines, intermediate-acting benzodiazepines, long-acting benzodiazepines, z-drugs, and miscellaneous agents. Two clinical psychiatrists with expertise in public health (DJS, DV) independently reviewed responses (which involved selecting from country-specific lists including generic and brand names) and classified anxiolytic medications into the five 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 the latter surveys for the subset of analyses that considered two of these additional questions.

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 (Supplementary Table 3). Respondents could report multiple reasons, which is important because some of the "other" reasons are also symptoms of anxiety disorders.
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 5 psychotropic medications in 6 European countries (Belgium, France, Germany, Italy, Netherlands, Spain) and up to three in other countries. These numbers captured well over 90% of anxiolytic medication uses in each survey.

### 2.3 | 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 for design effects. Logistic regression analysis was used to examine predictors of respondent reports about the effectiveness of specific anxiolytic medication classes. In cases where the predictors were categorical (e.g., anxiolytic medication 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 $\pm$ 2 of their design-based standard errors (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, indicating 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 anxiolytic medication classes) was evaluated with Wald $\chi^2$ tests based on design-corrected coefficient variance-covariance matrices. Statistical significance was evaluated consistently using 2-sided design based 0.05-level tests.

## 3 | Results

### 3.1 | Prevalence and Associations of Anxiolytic Medication Use With MDE and Anxiety Disorders

Of the $n$ = 49,919 Part-II WMH survey respondents that were analyzed, a weighted 5.6% ($n$ = 4079) reported using anxiolytic medications in the 12 months before the interview (Table 1). Use was considerably more prevalent in HICs than LMICs (8.5% vs. 2.2%, $\chi^2_1 = 559.6$, $p < 0.001$). Use was highest amongst respondents with partial MDE (25.2%) and 12-month MDE (19.8%), lower among respondents with partial anxiety disorder (15.0%) and 12-month anxiety disorders (14.3%), lower still among respondents with lifetime MDE (12.3%) and lifetime anxiety disorder (10.7), and lowest among respondents with no 12-month, lifetime, or partial MDE (3.5%) and no 12-month, lifetime, or partial anxiety disorders (2.5%). For each of these categories, use was considerably more prevalent in HICs than

**TABLE 1** | Prevalence of anxiolytic medication use by anxiety disorder and MDE histories within and across country income groups ($n$ = 49,919).

| | Total | | High-income | | Low- and middle-income | | HIC vs. LMIC $\chi^2_1$ |
|---|---|---|---|---|---|---|---|
| | % | (SE) | % | (SE) | % | (SE) | |
| Anxiety disorder | | | | | | | |
| 12-month | 14.3 | (0.5) | 20.5 | (0.8) | 6.3 | (0.5) | 200.6[a] |
| Lifetime[b] | 10.7 | (0.6) | 14.7 | (0.9) | 3.6 | (0.6) | 67.7[a] |
| Partial[c] | 15.0 | (0.6) | 21.9 | (0.9) | 5.7 | (0.5) | 199.3[a] |
| None[d] | 2.5 | (0.1) | 3.9 | (0.2) | 1.1 | (0.1) | 158.3[a] |
| MDE | | | | | | | |
| 12-month | 19.8 | (0.7) | 26.9 | (1.1) | 9.3 | (0.8) | 135.4[a] |
| Lifetime[b] | 12.3 | (0.5) | 16.9 | (0.6) | 4.5 | (0.6) | 95.2[a] |
| Partial[c] | 25.2 | (1.2) | 32.0 | (1.6) | 14.4 | (1.6) | 49.5[a] |
| None[d] | 3.5 | (0.1) | 5.6 | (0.2) | 1.4 | (0.1) | 282.4[a] |
| Total | 5.6 | (0.1) | 8.5 | (0.2) | 2.2 | (0.1) | 559.6[a] |

Abbreviations: MDE: major depressive episode; LMIC: low- and middle-income countries.
[a]Significant at the 0.05 level, two-sided test.
[b]Lifetime: Meet full criteria for lifetime MDE/anxiety disorder, excluding 12-month MDE or anxiety disorder.
[c]Partial: Did not meet full criteria but has 12-month symptoms or selected depression or anxiety as reason for medication use.
[d]None: Did not meet criteria for 12-month, lifetime, or partial MDE or anxiety disorder.

**TABLE 2** | The distributions of anxiety disorder and MDE among anxiolytic medication users ($n$ = 4079).

| | Total | | High-income | | Low- and middle- income | | $\chi^2_1$ HIC vs. LMIC |
|---|---|---|---|---|---|---|---|
| | % | (SE) | % | (SE) | % | (SE) | |
| Anxiety disorder | | | | | | | |
| 12-month | 25.5 | (1.0) | 25.1 | (1.0) | 27.4 | (1.7) | 1.4 |
| Lifetime[a] | 9.3 | (0.6) | 10.1 | (0.6) | 6.1 | (0.8) | 13.0[b] |
| Partial | 31.8 | (1.1) | 32.6 | (1.1) | 28.4 | (1.8) | 3.9[b] |
| None | 33.3 | (1.2) | 32.2 | (1.2) | 38.1 | (2.0) | 6.9[b] |
| MDE | | | | | | | |
| 12-month | 18.7 | (0.7) | 18.5 | (0.8) | 19.6 | (1.5) | 0.5 |
| Lifetime[a] | 14.5 | (0.5) | 15.6 | (0.6) | 9.7 | (1.1) | 16.8[b] |
| Partial | 12.7 | (0.6) | 12.2 | (0.7) | 15.4 | (1.3) | 4.8[b] |
| None | 54.1 | (1.0) | 53.8 | (1.1) | 55.4 | (2.0) | 0.5 |
| Anxiety disorder or MDE | | | | | | | |
| 12-month | 33.7 | (1.0) | 33.1 | (1.1) | 36.5 | (1.9) | 2.5 |
| Lifetime | 14.4 | (0.6) | 15.5 | (0.6) | 9.2 | (0.9) | 25.2[b] |
| Partial | 26.8 | (1.0) | 26.7 | (1.1) | 27.0 | (1.9) | 0.0 |
| None | 25.2 | (1.0) | 24.7 | (1.1) | 27.3 | (1.9) | 1.4 |

Abbreviations: MDE: major depressive episode; LMIC: low- and middle-income countries.
[b]Significant at the 0.05 level, two-sided test.
[a]See Table 1 for definitions of lifetime, partial, and none.

LMICs, but the pattern of distribution was remarkably similar in HICs and LMICs, with use highest in partial and 12-month MDE, followed by partial and 12-month anxiety disorder, and then by lifetime anxiety disorder and none of these conditions.

We also looked at the distribution of anxiety disorders and MDE at the person-medication level of analysis (Table 2). One-fourth (25.2%) of all use occurred among respondents who did not meet criteria for either an anxiety disorder or MDE (33.3% without an anxiety disorder, 54.1% without a MDE), with the remainder consisting of 33.7% with a 12-month disorder (25.5% anxiety disorder, 18.7% MDE), 14.4% with a lifetime but not 12-month disorder (9.3% anxiety disorder, 14.5% MDE), and 26.8% with a subthreshold 12-month disorder (31.8% anxiety disorder,

12.7% MDE). These patterns were strikingly similar in HICs and LMICs, with some statistically significant but substantively minor differences.

## 3.2 | Use of Anxiolytic Medications by Class

Intermediate-acting benzodiazepines were the anxiolytic medication class most commonly used in the past year across surveys (53.3%), followed by long-acting benzodiazepines (34.0%), other anxiolytic medications (13.0%) and z-drugs (10.0%) (Table 3). These percentages sum to more than 100% because 16.0% of respondents used two or more anxiolytic medication classes in the past year. Intermediate-acting benzodiazepines were more commonly used than long-acting benzodiazepines in HICs compared to LMICs (57.2% vs. 35.4%, $\chi^2_1 = 74.8$, $p < 0.001$), whereas long-acting benzodiazepines were more commonly used than intermediate-acting benzodiazepines in LMICs compared to HICs (55.9% vs. 29.1%, $\chi^2_1 = 112.3$, $p < 0.001$). Z-drugs were also more commonly used in HICs compared to LMICs (11.6% vs. 2.8%, $\chi^2_1 = 49.9$, $p < 0.001$), while rates of use of short-acting benzodiazepines, and of two or more anxiolytic medications, were similar in HICs and LMICs.

## 3.3 | Reasons for Anxiolytic Medication Use

Most respondents reported a single reason for anxiolytic medication use. Intermediate-acting and long-acting benzodiazepines were largely used for the single reasons of anxiety (33.3% and 32.0%) and poor sleep (37.9% and 30.1%) (Table 4). Short-acting benzodiazepines and especially z-drugs, in comparison, were largely used for poor sleep (66.5% and 85.5%). While other anxiolytic medications were also used largely for anxiety (23.8%) and sleep (34.2%), they had the highest rate of use across types for other physical symptoms (7.2%) and other symptoms (21.5%). Relatively few respondents gave multiple reasons for their use. Intermediate-acting benzodiazepines, long-acting benzodiazepines, and other anxiolytic medications were used for both anxiety and depression (5.7%, 4.2%, 2.6% respectively) as well as for anxiety without depression (5.5%, 5.5%, 2.8% respectively). Short-acting benzodiazepines and z-drugs were more likely to be used for anxiety without depression (5.3% and 2.1%). Taken together, differences in reasons for use across anxiolytic medication classes were statistically significant as a set ($\chi^2_{32=}398.3$, $p < 0.001$).

### 3.3.1 | Patterns and Predictors of Perceived Treatment Effectiveness

Anxiolytic medications were perceived to be *very* effective by 55.7% of users and *somewhat* effective by an additional 32.2%, with similar rates in HICs (55.0%, 32.2%) versus. LMICs (60.7%, 24.7%; $\chi^2_1 = 8.2$, $p = 0.004$). For very effective treatment, anxiolytic medications were differentially effective as a function of MDE recency and severity ($\chi^2_3 = 9.9$, $p = 0.019$) as well as reasons for use ($\chi^2_8 = 27.2$, $p = 0.001$), with anxiolytic medications reported less effective in those with 12-month MDE (OR = 0.8, 95% CI 0.7–0.9) and in those using anxiolytic medication for both anxiety and depression (OR = 0.5, 95% CI 0.3–0.7) (Table 5). For very or somewhat effective treatment, anxiolytic medications were differentially effective as a function of reasons for use ($\chi^2_8 = 19.3$, $p = 0.013$), with anxiolytic medications reported as less effective in those using anxiolytic medication for other reasons (OR = 0.6, 95% CI 0.4–1.0) and more effective in those using these agents for anxiety and another reason other than depression (OR = 3.5, 95% CI 1.7–7.0).

We repeated these analyses separately in HICs and in LMICs. In HICs, predictors were largely the same as those in the overall sample (Supplement Table 4a-4b). In HICs, for very effective treatment anxiolytic medications were again differentially effective as a function of MDE recency and severity ($\chi^2_3 = 8.1$, $p = 0.044$) and reasons for use ($\chi^2_8 = 20.3$, $p = 0.009$), and for very or somewhat effective treatment, anxiolytic medications were again differentially effective as a function of reasons for use ($\chi^2_8 = 24.5$, $p = 0.002$). In LMICs, for both very effective treatment and very or somewhat effective treatment anxiolytic medications were differentially effective as a function of anxiety disorder recency and severity ($\chi^2_3 = 19.9$, $p = 0.001$ and $\chi^2_3 = 8.9$, $p = 0.031$ respectively). In both very effective treatment and very or somewhat effective treatment anxiolytic medications were reported as less effective in those with 12-month anxiety disorder (OR = 0.5, 95% CI 0.3–0.9 and OR = 0.5 95% CI 0.3–0.9 respectively) and more effective in those with lifetime anxiety disorder (OR = 3.5, 95% CI 1.8–6.9 and OR = 3.7 95% CI 1.5–9.2 respectively). Furthermore, for very effective treatment anxiolytic medications

**TABLE 3** | Among anxiolytic medication users, distribution of anxiolytic medication classes by country income group ($n = 4079$)[a].

| | Total | | High-income | | Low- and middle-income | | $\chi^2_1$ HIC vs. LMIC |
|---|---|---|---|---|---|---|---|
| | % | (SE) | % | (SE) | % | (SE) | |
| Short-acting Bz | 2.8 | (0.3) | 2.8 | (0.3) | 2.4 | (0.7) | 0.4 |
| Intermediate-acting Bz | 53.3 | (1.0) | 57.2 | (1.1) | 35.4 | (2.1) | 74.8[b] |
| Long-acting Bz | 34.0 | (1.0) | 29.1 | (1.1) | 55.9 | (2.3) | 112.3[b] |
| Z-drugs | 10.0 | (0.7) | 11.6 | (0.8) | 2.8 | (0.5) | 49.9[b] |
| Other Anx med | 13.0 | (0.7) | 12.9 | (0.8) | 13.5 | (1.5) | 0.1 |
| 2+ Anx med in the past year | 16.0 | (0.7) | 16.3 | (0.8) | 14.6 | (1.3) | 1.2 |

Abbreviations: Anx Med: Anxiolytic Medications; Bz: benzodiazepine, LMIC: low- and middle-income countries.
[b]Significant at the 0.05 level, two-sided test.
[a]See Appendix Table 2 for classifications for types of anxiolytic medications.

**TABLE 4** | Distribution of reasons for taking anxiolytic medications, among all anxiolytic medications taken ($n = 4147$)[b].

| | | S-Bz | | I-Bz | | L-Bz | | Z-Drugs | | Other Anx Med | | Total/ Any Anx Med | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | %[b] | (SE) | % | (SE) | % | (SE) | % | (SE) | % | (SE) | % | (SE) |
| Single Reason[a] | Anxiety | 10.4 | (1.8) | 33.3 | (1.5) | 32.0 | (1.9) | 2.0 | (0.8) | 23.8 | (3.4) | 28.6 | (1.1) |
| | Depression | 6.0 | (2.5) | 8.3 | (0.7) | 9.2 | (1.0) | 3.0 | (1.4) | 6.8 | (1.5) | 7.8 | (0.5) |
| | Poor sleep | 66.5 | (5.3) | 37.9 | (1.7) | 30.1 | (1.8) | 85.5 | (2.6) | 34.2 | (3.6) | 40.5 | (1.3) |
| | Other physical | 3.7 | (2.4) | 1.9 | (0.6) | 4.7 | (0.9) | 0.5 | (0.2) | 7.2 | (1.5) | 3.1 | (0.4) |
| | Reasons Other reason | 5.8 | (3.6) | 6.3 | (0.7) | 12.5 | (1.5) | 3.9 | (1.4) | 21.5 | (2.4) | 9.2 | (0.7) |
| Multiple reasons | Anxiety and depression | 0.7 | (0.5) | 5.7 | (0.6) | 4.2 | (0.6) | 1.5 | (0.6) | 2.6 | (0.8) | 4.5 | (0.4) |
| | Anxiety and not depression, +1 | 5.3 | (2.7) | 5.5 | (0.7) | 5.5 | (0.8) | 2.1 | (0.8) | 2.8 | (1.3) | 4.9 | (0.5) |
| | Depression and not anxiety, +1 | 0.4 | (0.4) | 0.9 | (0.2) | 1.1 | (0.4) | 0.0 | (0.0) | 0.5 | (0.3) | 0.8 | (0.2) |
| | No anxiety, no depression, +2 | 1.2 | (1.0) | 0.4 | (0.1) | 0.7 | (0.3) | 1.6 | (1.0) | 0.6 | (0.4) | 0.6 | (0.1) |

Abbreviations: Anx Med, Anxiety Medication; S-Bz, short-acting benzodiazepine; I-Bz, intermediate-acting benzodiazepine; L-Bz, long acting benzodiazepine.
[a]$\chi^2_{32=}398.3$, $p < 0.001$.
[b]Sample is based on a person-medication file (each Anx Med taken is a separate record). Dropped data from surveys: Iraq, Nigeria, Brazil, Bulgaria, Lebanon, Israel, Japan, due to the surveys not asking about reasons for medication. For the remaining 15 surveys, another 45 records were dropped due to missing responses from the reasons questions. See Supplementary Table 3 for classifications for reasons for medication.

were reported as less effective among those without anxiety disorder (OR = 0.5, 95% CI 0.3–0.8).

## 4 | Discussion

Several limitations of this work deserve emphasis. First, respondents may underreport or deny benzodiazepine use due to stigma, recall bias, or concerns about confidentiality. Second, data came from self-reports of treatment effectiveness rather than from clinician-rated standardized symptom measures or objective measures of sleep. Third, information about several key characteristics of anxiolytic medication use, such as dose and duration were not obtained, and we did not assess the temporal relationship between anxiolytic medication use and symptom occurrence. Fourth, although we made comparisons across different classes of anxiolytic medications, respondents were not randomly assigned to anxiolytic medication class, limiting conclusions about the differential effectiveness of anxiolytic medication classes. Fifth, we did not consider the combined use of antidepressant and anxiolytic medications, which may be useful in certain clinical contexts. Relatedly, it is possible that some who reported taking anxiolytic medication for depression, were prescribed these agents primarily for treatment of anxiety symptoms in depression.

Consistent with our interest in long-standing debates about benzodiazepines and related drugs, the vast majority of data reported on here pertains to the use of short-acting, intermediate-acting and long-acting benzodiazepines and z-drugs. Nevertheless, we also reported on the much less frequent use of a range of miscellaneous anxiolytic medications. The inclusion of this miscellaneous group cannot be justified on the basis of mechanism of action or of indication for prescription. While some of the agents in this miscellaneous group have long been primarily used for anxiolysis and sedation, or are registered for the treatment of GAD, others are much less commonly used as anxiolytic medications and/or have other indications. From an epidemiological perspective, the less frequent use of these medications prevented further subclassification based on mechanism of action or indication for prescription, and instead their inclusion as a group allowed for comparison with benzodiazepines and z-drugs. Still, any interpretation of such comparisons needs to bear in mind the heterogeneity of this group.

Despite these limitations and considerations, the study provides informative data on the use of several anxiolytic medication classes in a large sample of individuals across 20 countries. 5.6% of respondents across these countries reported anxiolytic medication use in the past 12 months. In comparison, an earlier parallel analysis of antidepressant use in the World Mental Health Surveys found that 3.1% of respondents reported use of these agents in the previous 12 months (Kazdin et al. 2023). Benzodiazepines comprise the vast majority of anxiolytic medication use, a finding that is consistent with a broad range of prior epidemiological work highlighting the widespread use of these agents (Dell'osso and Lader 2013; Junkes et al. 2024; López-Muñoz et al. 2011). While other anxiolytic medications are less commonly used, the ongoing use of outdated and dangerous agents such as the barbiturates is concerning.

There are considerably higher rates of anxiolytic medication use in HICs than LMICs. This finding is consistent with our earlier work on antidepressant use (Kazdin et al. 2023), and treatment gaps in anxiety disorders (Alonso et al. 2018). Several reasons may be driving this difference. First, lower relative personal income and higher health related out-of-pocket costs can be assumed for respondents in LMICS versus HICs, which would inevitably result in lower use of medication. Second, there may be significant differences in availability of prescribers and of medication among LMICs and HICs, and this may contribute to differences in medication use. Third, there may be more

**TABLE 5** | Predictors of perceived treatment effectiveness ($n = 4126$)[a].

| | Very effective | | Very/somewhat effective | |
|---|---|---|---|---|
| | OR | (95% CI) | OR | (95% CI) |
| I. MDE | | | | |
| 12-Month | 0.8[b] | (0.7–0.9) | 0.8[b] | (0.7–1.0) |
| Lifetime[c] | 1.1 | (1.0–1.3) | 1.2 | (0.9–1.5) |
| Partial | 1.1 | (0.9–1.3) | 1.0 | (0.8–1.3) |
| None | 1.0 | (0.9–1.2) | 1.0 | (0.8–1.3) |
| $\chi^2_3$ | 9.9[b] | | 5.8 | |
| II. Anxiety disorder | | | | |
| 12-Month | 1.0 | (0.8–1.2) | 1.0 | (0.8–1.2) |
| Lifetime[c] | 1.1 | (0.8–1.3) | 1.0 | (0.7–1.4) |
| Partial | 1.1 | (0.9–1.3) | 1.1 | (0.8–1.4) |
| None | 0.9 | (0.8–1.1) | 1.0 | (0.8–1.4) |
| $\chi^2_3$ | 1.6 | | 0.5 | |
| III. Anxiolytic medication classes | | | | |
| Short-acting benzodiazepines | 0.8 | (0.5–1.2) | 1.0 | (0.6–1.7) |
| Intermediate-acting benzodiazepines | 1.1 | (0.9–1.3) | 1.3[b] | (1.0–1.6) |
| Long-acting benzodiazepines | 1.0 | (0.8–1.2) | 0.8 | (0.7–1.1) |
| Z-drugs | 1.2 | (0.9–1.7) | 0.9 | (0.6–1.4) |
| Other anxiolytic medications | 1.0 | (0.8–1.3) | 1.1 | (0.8–1.5) |
| $\chi^2_4$ | 2.5 | | 8.6 | |
| IV. Single reasons | | | | |
| Anxiety | 1.1 | (0.9–1.4) | 0.9 | (0.6–1.3) |
| Depression | 0.7 | (0.5–1.0) | 0.7 | (0.5–1.2) |
| Poor sleep | 1.1 | (0.9–1.3) | 0.9 | (0.6–1.3) |
| Other physical reasons | 1.0 | (0.6–1.7) | 0.8 | (0.5–1.4) |
| Other reasons | 1.2 | (0.8–1.6) | 0.6[b] | (0.4–1.0) |
| Multiple reasons | | | | |
| Anxiety and depression | 0.5[b] | (0.3–0.7) | 0.7 | (0.4–1.1) |
| Anxiety and not depression, +1 | 1.4 | (1.0–2.1) | 3.5[b] | (1.7–7.0) |
| Depression and not anxiety, +1 | 1.4 | (0.7–2.6) | 1.1 | (0.4–3.0) |
| No anxiety, no depression, +2 | 1.0 | (0.5–2.2) | 1.4 | (0.4–5.6) |
| $\chi^2_8$ | 27.2[b] | | 19.3[b] | |

Abbreviation: MDE: major depressive episode.
[b]Significant at the 0.05 level, two-sided test.
[a]Controlling for survey. 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 $n = 4192$. Another 66 records were dropped due to missing values for the questions asking about reasons for treatment and effectiveness, further reducing the sample to 4126.
[c]See Table 1 for definitions of lifetime, partial, and none.

attitudinal barriers to use of anxiolytic medications in LMICs than HICs. There is a clear public health and investment case for scaling up interventions for anxiety disorders and MDD in LMICs (Chisholm et al. 2016); this should include judicious use of antidepressants and benzodiazepines (Baldwin et al. 2013).

Intermediate-acting benzodiazepines were the anxiolytic medication class most commonly used across surveys, followed by long-acting benzodiazepines. The finding that intermediate-acting benzodiazepines were more commonly prescribed than long-acting benzodiazepines in HICs, while long-acting benzodiazepines were more commonly prescribed than intermediate-acting benzodiazepines in LMICs may reflect the readier availability of less expensive longer-acting agents, or a preference for agents that require less frequent administration in some contexts. The more common use of z-drugs in HICs than LMICs likely reflects the more recent availability of these agents and their higher costs.

The use of intermediate-acting and long-acting benzodiazepines for both anxiety and poor sleep, and of short-acting benzodiazepines and especially z-drugs for poor sleep is consistent with clinical guidelines, which rest in turn on the evidence base of RCTs (Balon et al. 2020; Dubovsky and Marshall 2022). Thus, for example, both alprazolam (intermediate-acting) and clonazepam (long-acting) are FDA-approved for the treatment of panic disorder. The increased use of other anxiolytic medications for other physical symptoms and other symptoms, may reflect the evidence base that some of these agents, such as pregabalin, are useful for pain symptoms in some clinical contexts, or may indicate that such agents are turned to when more commonly prescribed agents fail.

Most of the survey respondents who used anxiolytic medications reported that they were very effective and a large majority reported that they were at least somewhat effective, with similar patterns in HICs and LMICs. These findings are consistent with the large evidence-base of RCTs employing clinician-rated measures to demonstrate the efficacy of these agents (Balon et al. 2020; Dubovsky and Marshall 2022). Although the RCT evidence-base derives predominantly from work in HICs, clinicians from around the world have emphasized the usefulness of these agents (Silberman et al. 2023). Self-evaluation of effectiveness in community populations is a useful complement to such work because it allows for the evaluation to take into account individuals' own views about the benefits they experience from treatment in everyday life on the dimensions that matter most to them (Stein et al. 2021).

Anxiolytic medications were more commonly used by respondents with subthreshold and 12-month MDE than by those with subthreshold and 12-month anxiety disorder. Indeed, 45.9% of all use was by respondents with 12-month, lifetime, or subthreshold MDE. These patterns were strikingly similar in HICs and LMICs. Furthermore, anxiolytic medications were reported more effective among respondents who used these medications for anxiety and another reason other than depression, and less effective among respondents with 12-month MDE as well as among respondents who used these agents for both anxiety and depression. These findings are consistent with clinical guidelines which emphasize the importance of antidepressant treatment for individuals with MDD.

The data presented here do not definitely answer the question of how often benzodiazepines should be prescribed in clinical practice, but they usefully inform discussions of how best to optimize their use. The results provide an important complement to the evidence from controlled treatment trials by reporting on perceived effectiveness outside of the context and restrictions of such work. It is reassuring to find that anxiolytic medications, particularly benzodiazepines, are largely prescribed in the general population for anxiety and sleep, and that they are widely perceived to be either very or somewhat effective by users. However, more targeted prescription of these agents may be necessary given that a meaningful proportion of use was reported to be for depression and antidepressant intervention should be prioritized in the pharmacotherapy of MDD.

## Author Contributions

D.J.S., A.E.K, C.V., D.V.V. and R.C.K. conceptualized and designed the study. A.A-H., J.A., L.H.A., C.B., J-M C-de-A., G.de.G., A.R.O.G., J.M.H., E.G.K., A.K., V.K-M., F.N-M., D.S., J.P-V., and C.V. acquired and analyzed the data. D.J.S., A.E.K., C.V., D.V., and R.C.K. interpreted the data. N.A.S. created new software used in the work, and I.H. conduced analyses using this. D.J.S., A.E.K., D.S.B.,M.G.H., I.H., J.R.P., N.A.S., P.W., M.C.V, A.A-H., J.A., L.H.A., C.B., J-M.C-de-A, G.deG., A.R.O.G., J.M.H., E.G.K., A.K., V.K-M., F.N-M., D.S., J.P-V., C.V., D.V.V. and R.C.K. drafted the work or substantively revised it. All authors read and approved the final manuscript.


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### Ethics Statement

At all survey sites, the local ethics or institutional review committee reviewed and approved the protocol to ensure protection of human subjects, in line with appropriate international and local guidelines. Details of the ethics committees for the WMH surveys can be viewed at this link: http://www.hcp.med.harvard.edu/wmh/ftpdir/WMH_Ethics_approval.pdf.

### Consent

The authors have nothing to report.

### Conflicts of Interest

The authors declare no conflicts of interest.

### Data Availability Statement

Access to the cross-national World Mental Health (WMH) data is governed by the organizations funding and responsible for survey data collection in each country. These organizations made data available to the WMH consortium through restricted data sharing agreements that do not allow us to release the data to third parties. The exception is that the U.S. data are available for secondary analysis.

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## Supporting Information

Additional supporting information can be found online in the Supporting Information section.

**Supporting Information S1:** hup70031-sup-0001-suppl-data.docx.