Patterns, predictors, and patient-reported reasons for antidepressant discontinuation in the WHO World Mental Health Surveys

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Abstract

Background. Despite their documented efficacy, substantial proportions of patients discontinue antidepressant medication (ADM) without a doctor’s recommendation. The current report integrates data on patient-reported reasons into an investigation of patterns and predictors of ADM discontinuation.

Methods. Face-to-face interviews with community samples from 13 countries (n = 30 697) in the World Mental Health (WMH) Surveys included n = 1890 respondents who used ADMs within the past 12 months.

Results. 10.9% of 12-month ADM users reported discontinuation-based on recommendation of the prescriber while 15.7% discontinued in the absence of prescriber recommendation. The main patient-reported reason for discontinuation was feeling better (46.6%), which was reported by a higher proportion of patients who discontinued within the first 2 weeks of treatment than later. Perceived ineffectiveness (18.5%), predisposing factors (e.g. fear of dependence) (20.0%), and enabling factors (e.g. inability to afford treatment cost) (5.0%) were much less commonly reported reasons. Discontinuation in the absence of prescriber recommendation was associated with low country income level, being employed, and having above average personal income. Age, prior history of psychotropic medication use, and being prescribed treatment from a psychiatrist rather than from a general medical practitioner, in comparison, were associated with a lower probability of this type of discontinuation. However, these predictors varied substantially depending on patient-reported reasons for discontinuation.

Conclusion. Dropping out early is not necessarily negative with almost half of individuals noting they felt better. The study underscores the diverse reasons given for dropping out and the need to evaluate how and whether dropping out influences short- or long-term functioning.

Introduction

Major depressive disorder (MDD) is among the most common mental disorders, affecting an estimated 4.4 percent of the world’s population each year (Cipriani et al., 2018; World Health Organization, 2017). Depression increases morbidity and mortality (Goldstein et al., 2020; Lépine & Briley, 2011; Wang et al., 2020) and is one of the larger contributors to disability worldwide (GBD, 2017 DALYs & HALE Collaborators, 2018). The economic costs of major depression are enormous (Chisholm et al., 2016; Chiu, Lebebaum, Cheng, de Oliveira, & Kurdyak, 2017; Kessler, 2012; Tanner et al., 2020; Yamabe, Liebert, Flores, & Pashos, 2019).

Several effective treatments for MDD exist, including a wide range of antidepressant medications (ADMs), psychological therapies, brain stimulation therapies (e.g. transcranial magnetic stimulation, electroconvulsive therapy, deep brain stimulations) and others (Barth et al., 2016; Cipriani et al., 2018; Moshe et al., 2021). ADMs are by far the most frequently used of these treatments given their low cost and ease of administration (Brody & Gu,
ADM use for treatment of MDD has increased in recent years (Mojtabai & Olfson, 2014; Scholten, Batelaan, & Van Balkom, 2020). In addition, ADMs are often prescribed for anxiety as well as for other mental and physical conditions (e.g., headache, pain, insomnia, gastrointestinal disorders) (Gardarsdottir, Heerdink, van Dijk, & Egberts, 2007; Wu et al., 2012). Among the reasons for the widespread use of ADMs are the empirical support for their positive effects, their low-cost relative to other treatments, and their accessibility in countries where access to other treatments is limited.

Despite their demonstrated efficacy, an estimated 33–60 percent of patients who begin ADMs discontinue even when this is not recommended by their treatment provider (Fornaro et al., 2023; Wells, Clerkin, Ellis, & Beevers, 2014). Discontinuation usually occurs within the first 3 months of beginning treatment even though recommendations are for continued use over much longer durations (6–9 months) (American Psychiatric Association, 2010; National Institute for Health and Care Excellence [NICE], 2009; Olfson, Marcus, Tedeschi, & Wan, 2006). As might be expected, discontinuation is associated with an increased likelihood of relapse and risk of suicide (Liu et al., 2021; Sirey et al., 2017; Van Leeuwen et al., 2021). In some patients there can be a wide range of symptoms often referred to as part of the ‘antidepressant withdrawal syndrome’ (e.g., flu-like symptoms, dizziness, shaking, fatigue, electric shock sensations, anxiety, emotional lability, lowering of mood, irritability, and bouts of crying) (Clarke et al., 2022; Fornaro et al., 2023; Gastaldon et al., 2022; Sørensen, Jørgensen, & Munkholm, 2022). Many of these symptoms can be enduring (Davies, Pauli-Jones, & Montagu, 2018).

The focus on ADM discontinuation has long been recognized as important for treatment planning. Findings from multiple studies have suggested that disorder severity, low income, lack of insurance, public v. private insurance, ethnic minority status, younger age, and comorbid anxiety and substance use are associated with discontinuation (Akincigil et al., 2007; Bambauer, Soumerai, Adams, Zhang, & Ross-Degnan, 2007; Ji & Hong, 2020; Samples & Mojtabai, 2015; Warden, Rush, Trivedi, Fava, & Wisniewski, 2007). However, the great majority of prior studies were characterized by either small samples, investigation of single clinical settings or geographical locales, evaluation of only one or two ADMs, or drawing on prescriber, electronic, or pharmacy records to infer actual use v. discontinuation. Little attention has been accorded reports by individuals themselves who are taking ADMs in community contexts (Kato et al., 2021; Samples & Mojtabai, 2015). Direct reports are critical to understanding who has continued or discontinued medication, the reasons for discontinuation, the timing of discontinuation over the course of treatment, and whether the decision to discontinue was based on the patient or the prescriber. Moreover, not everyone who discontinues fails to respond to treatment. Consequently, it is important to evaluate when and for whom discontinuation was ill advised. Thus, it is important to work with broadly defined samples and to look more directly than in prior studies at use reported by individuals themselves, the reasons for discontinuation, and evaluation of clinical status.

The purpose of the current report was to present the results of a study of ADM discontinuation in samples of the general population across many countries in the World Mental Health (WMH) surveys. We evaluated the diagnoses of the people who use ADMs with special attention to depression and anxiety and, importantly, we examined patient-reported reasons for discontinuing ADMs.

Methods

Sample

The World Health Organization’s (WHO) World Mental Health (WMH) surveys are a coordinated set of community epidemiological surveys administered to probability samples of adults in the non-institutionalized household population in countries throughout the world (Scott, de Jonge, Stein, & Kessler, 2018). Data for the current report are from 15 WMH surveys in 13 countries. Four of the countries were low- or middle-income countries (LMICs) as per the World Bank’s classification (Fantom & Serajuddin, 2016): Colombia (2 surveys), Mexico, Peru and Romania. The other nine were high-income countries (HICs): Argentina, Belgium, France, Germany, Italy, Netherlands, Portugal, Spain (two surveys), and the United States. It should be noted that a larger number of WMH surveys asked about 12-month medication use, but only the 15 considered here included the question series about reasons for use. All samples were based on multi-stage clustered area probability household designs; they were nationally representative in nine surveys, representative of all urbanized areas in two others, and representative of selected regions or Metropolitan areas in the others (online Supplementary Table S1). Average response rate weighted by sample size was 69.6%.

Measures

The interview

Interviews were administered face-to-face in respondents’ homes after obtaining informed consent. Local ethics or institutional review committees at each site 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 assessed core mental disorders and was administered to all respondents. Part II assessed additional disorders and correlates and was administered to 100% of Part I respondents with any disorder, plus 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 weighted Part II prevalence estimates being equivalent to Part I estimates (Heeringa et al., 2008). Of the 30,697 Part II respondents, we focused on the 1890 who were users of ADMs in the past 12 months but who had no evidence of bipolar disorder (i.e., neither met criteria for lifetime bipolar disorder in the diagnostic assessment nor reported bipolar disorder as a reason for their ADM use). Each of these individuals was asked about up to three medications (and up to five in some surveys). In the few cases where a patient reported using more than this number of medications, we sampled this maximum number randomly from those used and weighted the respondent’s data to adjust for the under-sampling. A total of 2,139 ADM uses were included among the sampled medications for these 1,890 respondents. These are the cases considered in the current report.

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.

Diagnoses

The survey instrument was the WHO Composite International Diagnostic Interview (CIDI) Version 3.0 (Kessler & Ustün, 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. Diagnoses based on the CIDI had good concordance with diagnoses based on blinded clinical reappraisal interviews using the Structured Clinical Interview for DSM-IV (SCID; [First, Spitzer, Gibbon, and Williams, 2002]) as the gold standard (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 use**

ADM use was defined as taking an ADM at any time in the past 12 months. Information on use was captured by presenting respondents with a list of psychotropic medications using both generic and trade names and asking about use 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 ‘medications 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, 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 with expertise in global public health (DV, CW) 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. In addition, 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. One of these questions was: ‘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, marital problems, not getting along with others, poor work performance, alcohol or drug problems, poor concentration, and poor memory. Multiple reasons could be reported, which is important because some of the ‘other’ reasons are also symptoms of MDD and anxiety disorders. Respondents were then asked if they were still taking each medication; if not, whether they discontinued on their own or based on the recommendation of their prescribing health professional. A series of follow-up questions asked about reasons for ADM discontinuation (see online Supplementary Table S2 for the interview questions).

**Data analysis**

Weights were applied within surveys to adjust for differences in within-household probabilities of selection and to calibrate the data to match Census population distributions on socio-demographic and geographic variables. Part II data were then weighted to adjust for differential probabilities of selection into Part II. Cross-tabulations were used to examine gross associations between ADM discontinuation and clinical variables as well as patient-reported reasons for discontinuation. The time-to-discontinuation distribution by week and the projected cumulative probability of discontinuation by 1 year (52 weeks) were estimated using the two-part actuarial survival curve method implemented in SAS 9.4 (SAS Institute Inc, 2013). Given the sparseness of the data on discontinuation after the first 6 weeks, the survival curves in subsequent weeks were smoothed using a 4-week moving average. Discrete-time survival analysis with person-week as the unit of analysis was then used to examine predictors of discontinuation (Hosmer, Lemeshow, & May, 2008). These models had a probit link function with robust standard errors (Tabatabai et al., 2014). This was done both for discontinuation overall and for discontinuation due to specific types of reasons. Coefficients and coefficients ± 2 of their design-based SEs were then exponentiated to create risk ratios (RRs) and 95% confidence intervals (CIs). Significance of RR sets defining a single categorical variable (e.g. the dummy variables defining ADM classes) was evaluated with Wald χ² tests based on design-corrected coefficient variance–covariance matrices. Statistical significance was evaluated consistently using two-sided design based 0.05-level tests. 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 Institute Inc, 2013) that adjusts estimates of SEs and CIs for the weighting and clustering of observations in the WMH surveys.

**Results**

**Sample characteristics**

The great majority of observations in the sample came from HICs (87.1%) (Table 1). Median (inter-quartile range) age was 49 (37–59). 72.8% were female, 62.6% were married and 22.1% previously married. The distribution of education using pooled within-country categories was 22.6% high, 25.6% high-average, 23.9% low-average, and 20.8% low. The distribution of family income using pooled within-country categories was 22.2% high, 25.6% high-average, 23.9% low-average, and 20.8% low. The distribution of family income using pooled within-country categories was 23.2% high, 27.2% high-average, 23.4% low-average, and 26.2% low.

**Clinical characteristics by treatment status**

73.3% (n = 1573) of ADMs were still being used at the time of interview compared to 10.9% (n = 238) discontinued based on prescriber’s advice and 15.7% (n = 328) discontinued by the patient in the absence of prescriber advice (henceforth referred to as discontinuation ‘by the patient’). Table 2 provides
information on clinical characteristics of the sample by ADM treatment status (currently using, discontinued on prescriber’s advice, discontinued by patient). Significantly higher proportions of the first two subgroups than the third were from HICs (89.0–85.4% v. 79.4%, \( \chi^2 = 14.4, p < 0.001 \)). The three subgroups also differed significantly in duration of use, with much higher proportions of those who discontinued than those still using having durations of 1–2 weeks (27.7–27.4% v. 4.7%) or 3–6 weeks (23.1–21.9% v. 7.1%). Durations of 7+ weeks were much more common among patients who were still using than those who discontinued on their own or discontinued on prescriber’s advice (88.2% v. 49.2–50.7%; \( \chi^2 = 225.6, p < 0.001 \)).

The three subgroups did not differ significantly in the other clinical characteristics considered in Table 2. Most patients in all three subgroups used SSRIs (56.5–59.9%) rather than in either older (28.7–31.3%) or newer (8.8–14.8%) ADMs. The plurality across subgroups had diagnoses of 12-month threshold MDE and/or anxiety disorder (41.4–47.6%) followed by either subthreshold 12-month MDE and/or anxiety disorder either in the absence (23.4–28.3%) or presence (19.4–22.2%) of lifetime MDE and/or anxiety disorder. Patient-reported reasons for ADM use were also comparable across subgroups, with depression-only (33.1–38.4%) and anxiety-only (20.7–26.1%) the most common reasons.

### Time to discontinuation

Survival analysis was used to estimate conditional hazards of discontinuation by the patient as a function of number of weeks of use as well as the cumulative probability of such discontinuation by weeks of use. Curves were smoothed because of the relatively small sample size (Fig. 1). A projected 19.0% (S.E. = 0.1%) of patients would be expected to discontinue after 1 year, with a significantly lower proportion in HICs (17.7%, S.E. = 0.1%) than...
LMICs (28.5%, S.E. = 0.4%; \( \chi^2_1 = 13.3, p < 0.001 \)). The highest hazard of discontinuation was after 1 week of use (1.5%) and was again significantly lower in HICs (1.3%, S.E. = 0.1%) than LMICs (3.8%, S.E. = 0.9%; \( \chi^2_1 = 396.3, p < 0.001 \)).

### Reasons for discontinuation

Reported reasons for discontinuation by the patient were categorized rationally into four broad categories based on previous conceptual frameworks: (Henshaw & Freedman-Doan, 2009; Magaard, Seeralan, Schulz, & Brütt, 2017) lack of continued need, perceived treatment ineffectiveness, enabling factors (pressure to quit from friends or family; inability to afford treatment), and predisposing factors (fear of dependence; wanting to solve the problem on one’s own). The most commonly reported reason for discontinuation was lack of continued need, largely due to feeling better (46.6%) (Table 3). Strikingly, a significantly higher proportion of patients who discontinued after 1–2 weeks (51.4%) than either 3–6 weeks (32.8%) or 7 + weeks (50.0%; \( \chi^2_1 = 7.6, p = 0.022 \)) reported feeling better as a reason for discontinuation despite it typically taking longer than 2 weeks for ADM effects to be felt. More detailed analyses found that lack of continued need was reported by equal proportions of users of SSRIs and TCAs (48.4% vs. 49.6%), but a lower proportion of patients using newer ADMs (32.2%) and a considerably higher proportion of patients using other (than TCAs) older ADMs (70.8%; \( \chi^2_1 = 9.0, p = 0.029 \)) (online Supplementary Table S3). Disorder status was also associated negatively with lack of continued need as a reason.
for discontinuation ($\chi^2 = 13.6, p = 0.003$) due to a much higher proportion among patients with subthreshold disorder (65.8%) and lower among other patients (38.8%) than among patients with threshold (12-month or lifetime) disorders (40.8–45.2%) (online Supplementary Table S3). Lack of continued need as a reason for discontinuation was also significantly associated with reason for ADM use ($\chi^2 = 18.5, p = 0.002$) due to lower proportions of discontinued among patients who used for other (than sleep) physical reasons or other single reasons (than depression, anxiety, or sleep) (31.8–25.0%) than those who used for depression, anxiety, or sleep (47.4–57.0%) (online Supplementary Table S3).

Predisposing factors were the next most common reasons for discontinuation (20.0%) (Table 3). Probability of reporting these reasons was not related to time to discontinuation ($\chi^2 = 3.8, p = 0.15$). However, more detailed analyses found that predisposing factors were more common among users of SSRIs and newer ADMS (22.8–30.4%) than TCAs and other older ADMS (10.7–5.7%; $\chi^2 = 16.1, p = 0.001$) and much lower among patients without a mental disorder or 12-month subthreshold problems (0.0) and those using for poor sleep (4.9%) than others (14.3–33.8%; $\chi^2 = 156.1, p < 0.001$) (online Supplementary Table S3).

Perceived ineffectiveness was the next most common reason for discontinuation (18.5%) (Table 3) due to a combination of reports that the medication was not working (14.3%) and that the patient experienced side-effects (5.1%). Perceived ineffectiveness was less likely to be reported as a reason among patients who discontinued after 1–2 weeks (14.3%) than after 3 or more weeks, but this difference was not significant (21.0–19.8%, $\chi^2 = 5.2, p = 0.08$). More detailed analyses not reported in Table 3 found that ineffectiveness was less likely to be reported as a reason for discontinuation among patients with 12-month subthreshold diagnoses (7.8%) than others (18.7–24.3%; $\chi^2 = 12.2, p = 0.007$), and by patients who used ADMS for sleep, other physical problems, or multiple problems (11.9–13.1%) than other single reasons (20.6–28.6%; $\chi^2 = 22.4, p < 0.001$) (online Supplementary Table S3). Enabling (5.0%) and other (14.2%) reasons for discontinuation were less common (Table 3).

**Predictors of discontinuation**

Survival analysis found that country income group was the only predictor of discontinuation by the patient that varied in importance by time of discontinuation ($\chi^2 = 10.8, p = 0.005$). The other predictors had RRs that were consistent across person-weeks in univariable analyses (online Supplementary Table S4). The subset of the latter predictors that had significant univariable associations pooled across person-weeks was included in a multivariable model (Table 4). RR of discontinuation in that model was highest in weeks 1–2 (RR = 7.4) and intermediate in weeks 3–6 (RR = 3.9) relative to weeks 7 + (RR = 1.0). RR was four-fold as high in LMICs as HICs in weeks 1–2, two-fold as high in LMICs as HICs in weeks 3–6, and equal in LMICs compared to HICs between 7–52 weeks. In addition, being employed and having high/high-average family income were associated with elevated RR of discontinuation (RR = 1.4), whereas age, history of prior psychotropic medication use, and receiving the ADM prescription from a mental health professional rather than from a general medical practitioner were all associated with significant reduced RRs of discontinuation (RR = 0.6–0.8). Finally, patient education...
and disorder severity, both of which had significantly elevated univariable RRs with discontinuation, were nonsignificant in the multivariable model (RR = 1.3).

These multivariable predictors of discontinuation were then decomposed through reported reasons by estimating the model separately for the four broad types of reasons considered here (Table 4). Time to discontinuation, although related to all four types of reasons, was most strongly related to predisposing reasons and least strongly related to enabling reasons. The higher discontinuation rates of LMICs than HICs as a function of time to discontinuation were exclusive to need and enabling factors for discontinuation in weeks 1–2 and enabling factors for discontinuation in weeks 3–6. Socio-economic predictors were consistently related to continued need, with education also related to enabling factors. Age, in comparison, was related only to treatment ineffectiveness and predisposing factors. Prior psychotropic medication use and disorder severity, in comparison, were related exclusively to discontinuation due to enabling factors.

**Table 3. Reasons for discontinuation by patient**

<table>
<thead>
<tr>
<th>Reasons for Discontinuation</th>
<th>Weeks Used Before Discontinuation by Patient</th>
<th>Total</th>
<th>1–2</th>
<th>3–6</th>
<th>7+</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%a (s.e.)</td>
<td>%a (s.e.)</td>
<td>%a (s.e.)</td>
<td>%a (s.e.)</td>
<td>χ²b df</td>
</tr>
<tr>
<td><strong>Lack of continued need</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Felt better</td>
<td>46.6 (2.8)</td>
<td>51.4 (4.6)</td>
<td>32.8 (5.0)</td>
<td>50.0 (4.1)</td>
<td>7.6* 2</td>
</tr>
<tr>
<td>No longer neededc</td>
<td>1.8 (0.6)</td>
<td>0.0 (0.0)</td>
<td>2.0 (1.5)</td>
<td>2.7 (1.1)</td>
<td>0.0 1d</td>
</tr>
<tr>
<td>Total</td>
<td>48.4 (2.8)</td>
<td>51.4 (4.6)</td>
<td>34.9 (5.0)</td>
<td>52.7 (3.9)</td>
<td>7.3* 2</td>
</tr>
<tr>
<td><strong>Treatment ineffectiveness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication not working</td>
<td>14.3 (1.2)</td>
<td>13.0 (2.1)</td>
<td>17.3 (3.1)</td>
<td>13.7 (1.8)</td>
<td>1.8 2</td>
</tr>
<tr>
<td>Side effects</td>
<td>5.1 (1.0)</td>
<td>2.1 (0.7)</td>
<td>6.5 (2.2)</td>
<td>6.1 (1.3)</td>
<td>7.2* 2</td>
</tr>
<tr>
<td>Total</td>
<td>18.5 (1.3)</td>
<td>14.3 (2.2)</td>
<td>21.0 (3.4)</td>
<td>19.8 (1.9)</td>
<td>5.2 2</td>
</tr>
<tr>
<td><strong>Predisposing factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fear of dependence</td>
<td>15.3 (1.5)</td>
<td>23.2 (3.7)</td>
<td>12.1 (3.7)</td>
<td>12.5 (1.6)</td>
<td>9.4* 2</td>
</tr>
<tr>
<td>Wanted to solve problem on own</td>
<td>7.1 (1.4)</td>
<td>6.8 (1.3)</td>
<td>8.8 (3.9)</td>
<td>6.5 (1.4)</td>
<td>0.6 2</td>
</tr>
<tr>
<td>Total</td>
<td>20.0 (2.0)</td>
<td>25.0 (3.5)</td>
<td>20.9 (4.3)</td>
<td>16.9 (2.3)</td>
<td>3.8 2</td>
</tr>
<tr>
<td><strong>Enabling factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pressured to quitf</td>
<td>4.2 (0.8)</td>
<td>4.3 (0.5)</td>
<td>2.6 (1.6)</td>
<td>4.8 (1.6)</td>
<td>0.8 2</td>
</tr>
<tr>
<td>Couldn’t afford treatment</td>
<td>1.0 (0.4)</td>
<td>2.5 (1.3)</td>
<td>0.0 (0.0)</td>
<td>0.5 (0.0)</td>
<td>12.7* 1d</td>
</tr>
<tr>
<td>Total</td>
<td>5.0 (0.9)</td>
<td>6.2 (1.4)</td>
<td>2.6 (1.6)</td>
<td>5.4 (1.6)</td>
<td>1.7 2</td>
</tr>
<tr>
<td><strong>Other reasons</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any other reason</td>
<td>14.2 (1.9)</td>
<td>8.9 (4.6)</td>
<td>26.4 (4.6)</td>
<td>11.9 (1.5)</td>
<td>12.6 2</td>
</tr>
<tr>
<td>(n)</td>
<td>(328)</td>
<td>(87)</td>
<td>(67)</td>
<td>(174)</td>
<td></td>
</tr>
</tbody>
</table>

*Significant at the 0.05 level, two-sides design-based test.

Estimate treats row variable as numerator and column variable as denominator. For example, the % or ‘Felt Better’ (46.6%) is the % of those that stopped medication because they felt better among the Total.

χ² tests evaluate the significance of differences in distributions across subgroups defined by the columns.

Believed problem would get better without medication.

df test leaving out 0 cell.

We also asked about embarrassment, but no patient reported this as a reason for discontinuation.

Someone in personal life pressured the patient to quit.

**Discussion**

The study provided information on ADM discontinuation among 1890 individuals spanning 13 countries. SSRIs were the most frequently used ADM, encompassing more than half the sample. Depression and anxiety were the primary reasons for taking ADMs. Reasons for using ADMs did not vary by type of medication. Treatment was discontinued in 10.9% of cases based on the recommendation of the prescriber and an additional 15.7% of patients discontinued on their own. Discontinuing by either criterion was higher in LMICs than HICs within the first several weeks of treatment. Discontinuation did not vary systematically as a function of the initial reason for taking ADMs. Patients were less likely to discontinue on their own if the ADM had been prescribed by a psychiatrist in contrast to a general medical practitioner.

Among the noteworthy findings is that roughly half of discontinuation, whether based on the prescriber or the patient’s own decision, occurred because the patient felt better. It is noteworthy, though, that this reason for discontinuation was more common among patients who discontinued within 1–2 weeks of initiating...
minimal improvement was seen as feeling better. The latter is that the expectations of these patients were low and that even a better could mean that patients improved in ways that affected continuation more generally and specialty for general practitioners. Of course, patients are not randomly assigned to type of prescriber due to a lower rate of discontinuation among individuals whose prescriber was a psychiatrist than a general practitioner. Although feeling better was by far the most frequent reason for discontinuation, 20.0% of the patients who discontinued given for discontinuation, 20.0% of the patients who discontinued treatment, which is before the time ADMs effects are typically found to exist, indicating that the term ‘feeling better’ might mean something other than episode remission. There is no way to evaluate this issue objectively with the WMH data, though, as information was not collected about symptom profiles at the time of discontinuation.

Interestingly, ADM discontinuation as a function of type of prescriber due to a lower rate of discontinuation among individuals whose prescriber was a psychiatrist than a general practitioner. Of course, patients are not randomly assigned to type of prescriber, so conclusions about the basis of this difference cannot be determined here. Even so, this difference warrants further research in case there are differences in prescribing practices that can be identified and that would help reduce rates of discontinuation more generally and specialty for general practitioners.

That early discontinuation often occurred because patients felt better could mean that patients improved in ways that affected their daily lives even if not their symptoms. It could also mean that the expectations of these patients were low and that even a minimal improvement was seen as feeling better. The latter is the interpretation typically made in clinical research (Anderson, Bautista, & Hoppe, 2019; Bai, Yang, Chen, & Gao, 2020; Cuijpers, Noma, Karyotaki, Cipriani, & Furukawa, 2019; Kullgard, Holmqvist, & Andersson, 2022). However, our result suggests than this assumption deserves more careful consideration. The patient perspective is critically important and warrants more serious investigation in future research to clarify the relationships among acceptability of treatment, termination that is genuinely premature, and satisfactory improvement from the perspective of the patient (Montoya et al., 2016).

Although feeling better was by far the most frequent reason given for discontinuation, 20.0% of the patients who discontinued treatment on their own reported predisposing factors (e.g. fear of dependence, wanting to resolve problems on one’s own) as reasons and 18.5% reported ineffectiveness of treatment. We evaluated whether discontinuation by the patient could be predicted and found several reliable predictors, including low country income level, being employed, and having above average personal income. Age, prior history of psychotropic medication use, and being prescribed treatment from a mental health professional

### Table 4. Multivariable predictors of discontinuation by patient

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Need</th>
<th>Ineffective</th>
<th>Predisposing</th>
<th>Enabling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person-weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–2</td>
<td>7.4* (5.0–10.9)</td>
<td>5.7* (3.1–10.7)</td>
<td>7.2* (3.5–15.0)</td>
<td>15.6* (7.6–31.7)</td>
<td>6.3* (1.8–22.4)</td>
</tr>
<tr>
<td>3–7</td>
<td>3.9* (2.6–6.0)</td>
<td>2.5* (1.1–5.6)</td>
<td>4.6* (1.9–11.1)</td>
<td>5.4* (2.5–11.5)</td>
<td>1.0 (0.1–8.1)</td>
</tr>
<tr>
<td>7–52 (REF)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \chi^2 )</td>
<td>116.1*</td>
<td>31.2*</td>
<td>33.0*</td>
<td>58.9*</td>
<td>8.4*</td>
</tr>
<tr>
<td>County income level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LMIC 1–2 weeks</td>
<td>4.0* (2.2–7.5)</td>
<td>7.2* (3.1–16.8)</td>
<td>0.7 (0.1–4.0)</td>
<td>0.4 (0.1–2.1)</td>
<td>8.5* (1.8–40.3)</td>
</tr>
<tr>
<td>LMIC 3–6 weeks</td>
<td>2.0 (0.8–4.7)</td>
<td>2.3 (0.5–11.3)</td>
<td>0.6 (0.1–3.3)</td>
<td>0.7 (0.2–2.4)</td>
<td>12.6* (1.1–142.7)</td>
</tr>
<tr>
<td>LMIC 7–52 weeks</td>
<td>0.9 (0.4–1.7)</td>
<td>0.9 (0.4–2.3)</td>
<td>0.3 (0.0–1.8)</td>
<td>0.5 (0.1–2.2)</td>
<td>1.0 (0.1–8.1)</td>
</tr>
<tr>
<td>( \chi^2 )</td>
<td>20.9*</td>
<td>21.3*</td>
<td>2.3</td>
<td>2.1</td>
<td>10.7*</td>
</tr>
<tr>
<td>Socio-economic status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>1.4* (1.0–1.9)</td>
<td>2.0* (1.2–3.3)</td>
<td>0.7 (0.1–1.4)</td>
<td>1.0 (0.6–1.9)</td>
<td>1.6 (0.5–4.8)</td>
</tr>
<tr>
<td>High/low-average education*</td>
<td>1.3 (0.8–2.2)</td>
<td>3.7* (1.8–7.4)</td>
<td>1.6 (0.7–3.7)</td>
<td>1.3 (0.6–2.8)</td>
<td>8.5* (1.8–40.2)</td>
</tr>
<tr>
<td>High/high-average income</td>
<td>1.4* (1.0–1.9)</td>
<td>1.7* (1.0–2.9)</td>
<td>1.1 (0.6–1.9)</td>
<td>1.4 (0.8–2.6)</td>
<td>0.7 (0.3–1.9)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (in decades)</td>
<td>0.8* (0.7–0.9)</td>
<td>0.9 (0.8–1.0)</td>
<td>0.8* (0.6–0.9)</td>
<td>0.7* (0.5–0.8)</td>
<td>0.9 (0.7–1.2)</td>
</tr>
<tr>
<td>Prior psychotropic use*</td>
<td>0.6* (0.5–0.9)</td>
<td>0.7 (0.4–1.2)</td>
<td>0.8 (0.4–1.6)</td>
<td>0.6 (0.3–1.1)</td>
<td>0.2* (0.1–0.5)</td>
</tr>
<tr>
<td>Disorder severity*</td>
<td>1.3 (0.9–1.7)</td>
<td>1.0 (0.7–1.6)</td>
<td>1.6 (0.9–2.8)</td>
<td>1.2 (0.6–2.1)</td>
<td>3.6* (1.2–10.9)</td>
</tr>
<tr>
<td>Rx by MH professional</td>
<td>0.6* (0.4–0.9)</td>
<td>0.6 (0.3–1.0)</td>
<td>0.9 (0.5–1.6)</td>
<td>0.4* (0.2–0.8)</td>
<td>0.5 (0.1–1.9)</td>
</tr>
</tbody>
</table>

Abbreviations: RR, relative risk; 95% CI, 95% confidence interval of RR.
*High, high-average, and low-average education were Coded 1; low education was Coded 0.
*In past 2 years.
*Severe/moderate (Coded 1) v. mild/none (Coded 0).
*Number of person-weeks in the analysis, noting that all person-weeks of patients who did not report lack of continued need as a reason for discontinuation were coded to NO on dropout in the ‘Need’ model, all person-weeks of patients who did not report treatment ineffectiveness as a reason for discontinuation were coded to NO on dropout from the ‘ineffective’ model, etc.
*Significant at the 0.05 level, two-sided design-based test.
rather than from a general medical practitioner, in comparison, were associated with low probability of discontinuation. Importantly, we found that most of these predictors differed in importance as a function of the reasons for discontinuation. This is critical to note for future research as well as for efforts to develop pre-treatment risk models to target preventive interventions. There are important clinical implications of this variation both for predicting discontinuation and different for predicting outcomes with which discontinuation can be associated. For example, it is possible that discontinuing because treatment was ineffective might influence the likelihood of seeking further treatment. Improved understanding of the outcomes of those who discontinue would also be an important line of research.

**Limitations**

The study has several noteworthy limitations. First, data were based on retrospective respondent self-reports about medication use and treatment discontinuation over the past 12 months. Self-reports are subject to recall bias. However, prior research has found good agreement between self-reports of medication use and objective data such as pharmacy and prescription records (e.g. Boudreau et al. 2004; Cotterchio, Kreiger, Darlington, & Steingart, 1999; Kwon et al. 2003).

Second, information of key characteristics of the ADMs used was not collected, such as ADM dose. Nor did we evaluate the timeline of taking ADMs in relation to the occurrence of symptoms or reports of ADM effectiveness. The latter is important because evaluations of ADM effectiveness at the time of interview might be different than evaluations at the time of terminating ADM use. Nor did we obtain information about symptom profiles either at the beginning of treatment or at the time of treatment discontinuation, which could have been used to confirm patient reports about feeling better as a reason for discontinuation. Third, although we made comparisons across different conditions (e.g. anxiety, depression), between patients whose prescriptions came from mental health specialists vs. primary care treatment providers, and by ADM class, we could not draw any causal inferences about these factors, as none of them was randomized. Instead, results involving these correlates should be interpreted as providing only descriptive information about patterns of discontinuation. Similarly, our comparisons across income level were limited by the relatively small sample size of the same in LMICs.

**Conclusions**

We conducted a large-scale study of ADM discontinuation based on general population samples in 13 countries. We examined reasons for discontinuation, timing of discontinuation, and descriptive correlates. The findings convey the importance of evaluating discontinuation in a finer-grained fashion than is usually the case given that approximately half of the patients who discontinued on their own did so because, based on their own self-reports, they felt better. These data have important implications for understanding patterns and predictors of ADM discontinuation that recognize variation in reasons for discontinuing aimed at guiding preventive interventions. Attention to those at risk for discontinuing and not improving could lead to better strategies to improve clinical care.

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Competing interest. In the past 3 years, Dr Kessler was a consultant for Cambridge Health Alliance, Canandaigua VA Medical Center, Holmusk, Partners Healthcare, Inc., RallyPoint Networks, Inc., and Sage Therapeutics. He has stock options in Cerebral Inc., Mirah, PYM, Roga Sciences and Verisense Health. Dr Navarro-Mateu reports non-financial support from Otsuka outside the submitted work. In the past 3 years, Dr Harris has received personal fees from RAND Corporation outside the submitted work. In the past 3 years, Dr Stein has received honoraria from Discovery Vitality, Johnson & Johnson, Kanna, L’Oreal, Lundbeck, Orion, Sanofi, Servier, Takeda, and Vistagen. All other authors declare no conflict of interest.

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Ethical standards. 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.

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