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Perceived helpfulness of bipolar disorder treatment: Findings from the World Health Organization World Mental Health Surveys

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Abstract

Objectives: To examine patterns and predictors of perceived treatment helpfulness for mania/hypomania and associated depression in the WHO World Mental Health Surveys.

Methods: Face-to-face interviews with community samples across 15 countries found n = 2,178 who received lifetime mania/hypomania treatment and n = 624 with lifetime mania/hypomania who received lifetime major depression treatment. These respondents were asked whether treatment was ever helpful and, if so, the number of professionals seen before receiving helpful treatment. Patterns and predictors of treatment helpfulness were examined separately for mania/hypomania and depression.

Results: 63.1% (mania/hypomania) and 65.1% (depression) of patients reported ever receiving helpful treatment. However, only 24.5–22.5% were helped by the first professional seen, which means that the others needed to persist in help seeking after initial unhelpful treatments in order to find helpful treatment. Projections find only 22.9% (mania/hypomania) and 43.3% (depression) would persist through a series of unhelpful treatments but that the proportion helped would increase substantially if persistence increased. Few patient-level significant predictors of helpful treatment emerged and none consistently either across the two components (i.e., provider-level helpfulness and persistence after earlier unhelpful treatment) or for both mania/hypomania and depression. Although prevalence of treatment was higher in high-income than low/middle-income countries, proportional helpfulness among treated cases was nearly identical in the two groups of countries.

Conclusions: Probability of patients with mania/hypomania and associated depression obtaining helpful treatment might increase substantially if persistence in help-seeking increased after initially unhelpful treatments, although this could require seeing numerous additional treatment providers. In addition to investigating reasons

for initial treatments not being helpful, messages reinforcing the importance of persistence should be emphasized to patients.

KEYWORDS
bipolar disorder, patient-reported outcomes, treatment effectiveness

1 | INTRODUCTION

Bipolar disorder is rated as one of the most burdensome diseases from a societal perspective[1] despite its comparatively low lifetime prevalence[2] because of the combination of high recurrence[3] and very high impairment.[4] Recurrence and impairment are complex, most likely associated with the burden of comorbid psychiatric disorders and medical diseases and the effectiveness of treatment. Whereas studies of the efficacy and effectiveness of bipolar disorder treatment almost always focus on symptomatic response,[5,6] patient-centered definitions can also be important both in their own right[7] and in helping uncover issues important to patients that are not assessed in treatment trials[8] that can influence treatment adherence.[9] Knowing about these issues can help identify needs not being met by treatment and inform policy and service responses to address these needs.[10] One neglected aspect of research on patient-centered evaluations of treatment effectiveness involves lifetime pathways to care. These pathways typically involve the patient contacting multiple professionals before being helped.[11] This help-seeking process is more complex in the case of bipolar disorder than many other conditions because patterns and predictors of help-seeking might differ for manic/hypomanic and depressive episodes – especially for patients who do not have a long-term stable relationship with a treater. An evaluation of these pathways requires information about the sequence of contacts with health professionals following the onset of the syndrome, the probability of receiving treatment considered helpful from each professional seen, and the probability of persisting in help seeking after receiving treatment considered unhelpful.[12,13] Decomposing treatment pathways into these components can provide important insights into modifiable predictors of successful transitions. In the current report, we present data on the prevalence and predictors of perceived treatment helpfulness for manic/hypomanic episodes and associated depressive episodes from respondents in the World Health Organization (WHO) World Mental Health (WMH) surveys, a large cross-national series of community epidemiological surveys of the prevalence and correlates of common mental disorders.

2 | MATERIALS AND METHODS

2.1 | Sample

The WMH surveys are coordinated surveys administered to probability samples of adults (ages 18+) in the non-institutionalized household populations of countries throughout the world.[14] The data in the current report come from 16 national and regional WMH surveys carried out in 15 countries: 9 surveys in countries classified by the World Bank as high-income (national surveys in Argentina, Australia, New Zealand, Northern Ireland, Poland, Portugal, Saudi Arabia, and the United States, and a regional survey in Murcia Spain) and 7 surveys in countries classified as low-/middle-income (national surveys in Colombia, Lebanon, Mexico, and Peru, and regional surveys in Sao Paulo Brazil, Medellin Colombia, and Shenzhen in the People's Republic of China [PRC]) (Appendix Table S1). The two surveys in Colombia were administered to separate samples in 2003 (national sample of urban areas) and 2011–2012 (the city of Medellin). Eight national surveys were based on representative household samples, whereas the three others were based on all urbanized areas in the country (Argentina, Columbia, and Mexico). The field dates ranged from 2001–03 (the United States) to 2013–16 (Saudi Arabia). Response rates ranged from 50.4% (Poland) to 97.2% (Medellin, Colombia). The weighted average response rate was 69.2% across all surveys.

Access to the cross-national World Mental Health 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 via the Inter-University Consortium for Political and Social Research (ICPSR).[15]

2.2 | Measures

Interviews were carried out by lay interviewers who completed a 40-hour structured interviewer training program and passed a practice test before carrying out interviews. Interviewer work was closely monitored by supervisors who completed a 6-day training program with staff of the WMH Data Collection Coordination Centre (DCCC) and implemented a centralized quality control protocol developed by the DCCC.[16] Interviews were carried out face-to-face in the homes of respondents after obtaining informed consent using procedures approved by local Institutional Review Boards. All study procedures adhered to recognized human subjects research standards as outlined by the Declaration of Helsinki. Translation of the interview schedule from the original English version to other languages was completed using a standardized WHO translation, back-translation, and harmonization protocol.[17] This required culturally competent bilingual clinicians in the participating countries to review, modify, and approve the key phrases used to describe symptoms of all disorders assessed in the survey.

2.2.1 | Mania/hypomania

History of mania/hypomania was assessed using DSM-IV criteria with the fully structured World Health Organization Composite International Diagnostic Interview (CIDI) Version 3.0.[18] Respondents were classified as meeting criteria for lifetime mania if they ever had a manic episode, defined as a time lasting 7 days or longer (or hospitalization) with elevated mood plus at least three other symptoms, or irritable mood plus at least four other symptoms, with the mood disturbance resulting in marked impairment, psychotic features, or need for hospitalization. Respondents who did not meet criteria for lifetime mania were classified as having lifetime hypomania if they had a period lasting 4 days or longer when they experienced symptoms similar to those of mania (i.e., elevated mood with three other symptoms or irritable mood with four other symptoms) with an unequivocal change in functioning but not necessarily the marked impairment seen in mania. Diagnoses excluded cases with plausible organic causes. A CIDI validity study carried out in conjunction with several WMH surveys[19,20] found very good concordance (κ=0.79–0.94) between diagnoses of lifetime mania/hypomania based on the CIDI and blinded follow-up diagoses based on the Structured Clinical Interview for DSM-IV (SCID).[21]

2.2.2 | Major depressive episode

The CIDI was also used to assess major depressive episode (MDE). Respondents were classified as meeting criteria for lifetime MDE if they ever had a time lasting 2 weeks or longer when most of the day nearly every day they had dysphoria or markedly diminished pleasure or interest in all or almost all activities and five or more of nine symptoms that were present most of the day nearly every day and caused significant distress or impairment. Blinded clinical reappraisal interviews using the Structured Clinical Interview for DSM-IV (SCID) as the gold standard in a probability subsample of WMH respondents across several WMH surveys found good concordance (κ=0.53) between diagnoses based on the CIDI and those based on the SCID.[19]

2.2.3 | Helpfulness of treatment

Diagnostic sections of the CIDI in most participating countries ended with a question series that asked respondents, "Did you ever in your life talk to a medical doctor or other professional about your [episodes of the focal disorder]?" "Other professionals" were defined broadly to include "psychologists, counselors, spiritual advisors, herbalists, acupuncturists, and other healing professionals." Respondents who said they talked to a professional were then asked how old they were the first time they talked to a professional about this problem and whether they ever got treatment for this problem that "you considered *helpful* or *effective*." Respondents who reported ever receiving helpful treatment were then asked, "How many professionals did you *ever* talk to about [the focal disorder] up to and including the first time you ever got helpful treatment?" Respondents who reported that they never received helpful treatment, in comparison, were asked, "How many professionals did you *ever* talk to about [the focal disorder]?" This question series was included in all participating countries in the mania/hypomania section of the survey and in all but five countries (the exceptions being Colombia, Mexico, New Zealand, Peru, and the United States) in the depression section of the survey.

2.2.4 | Predictors

We examined five classes of predictors of the reported helpfulness of treatment: socio-demographics at the time of first treatment, lifetime comorbid conditions as of that time, treatment type, treatment timing, and childhood adversities. The predictors in each class were as follows: *Sociodemographics* included age (continuous), sex, marital status (married, never married, previously married), and education (in quartiles defined by within-country distributions). *Lifetime comorbid conditions* were limited to any anxiety disorder and any substance use disorder because these were the only two major classes of disorders assessed in common across all WMH surveys. We examined only these broad classes of comorbid conditions rather than more specific comorbidities because the sample size in the analysis of patients treated for bipolar disorder was too small to support more nuanced analyses of specific comorbidities. Anxiety disorders included generalized anxiety disorder, panic disorder, agoraphobia with or without panic disorder, post-traumatic stress disorder, specific phobia, and social phobia. Substance use disorders included alcohol and illicit drug abuse and dependence. All these disorders were assessed with the CIDI. We also included among the predictors a dichotomy defining whether the respondent had a history of mania versus hypomania. In the models predicting helpfulness of MDE treatment, we additionally included a series of dichotomous predictors for whether the respondent previously received helpful mania/hypomania treatment, unhelpful treatment, or no mania/hypomania treatment. In the models predicting helpfulness of mania/hypomania treatment, in comparison, we included dichotomous predictors for whether the respondent previously received helpful MDE treatment, unhelpful MDE treatment, MDE treatment of unknown helpfulness (in the case of the five countries that did not include questions about the helpfulness of MDE treatment), no MDE treatment, or they did not have MDE. *Treatment type* was defined as the cross-classification of variables for: (i) whether the respondent reported receiving medication, talk therapy, or both, as of the age of first mania/hypomania treatment; and; (ii) types of treatment professionals seen as of that age, including mental health specialists (psychiatrist, psychiatric nurse, psychologist, psychiatric social worker, and mental health counselor), primary care providers, human services providers (social worker or counselor in a social services agency, and spiritual advisor), and complementary/alternative medicine providers (other type of healer

TABLE 1 Lifetime prevalence of DSM-IV mania/hypomania and MDE with lifetime mania/hypomania, proportion of cases with lifetime mania/hypomania and MDE with lifetime mania/hypomania who obtained treatment, and proportion of treated cases who perceived treatment as helpful

	All countries pooled			High-income countries pooled			Low-/middle-income countries pooled		
	%	(SE)	(n)	%	(SE)	(n)	%	(SE)	(n)
I. Lifetime mania/hypomania									
Prevalence of lifetime mania/hypomania	2.3	(0.1)	(91,416)	2.7	(0.1)	(58,991)	1.6	(0.1)	(32,425)
χ^2_1	74.7*								
Proportion who obtained mania/hypomania treatment (among mania/hypomania cases)†	26.6	(1.3)	(2,178)	28.9	(1.5)	(1,705)	19.3	(2.2)	(473)
χ^2_1	10.7*								
Proportion who perceived mania/hypomania treatment as helpful (among mania/hypomania cases who received treatment)†,‡	63.1	(2.4)	(598)	63.0	(2.5)	(503)	63.5	(6.1)	(95)
χ^2_1	0.0								
II. Lifetime MDE with lifetime mania/hypomania									
Prevalence of lifetime MDE with mania/hypomania	1.2	(0.1)	(55,206)	1.3	(0.1)	(36,919)	0.9	(0.1)	(18,287)
χ^2_1	10.8*								
Proportion who obtained depression treatment (among MDE with mania/hypomania cases)§	43.9	(2.6)	(624)	47.9	(3.0)	(481)	31.9	(4.8)	(143)
χ^2_1	7.1*								
Proportion who perceived depression treatment as helpful (among MDE with mania/hypomania cases who received treatment)§,¶	65.1	(3.9)	(280)	64.6	(4.2)	(235)	67.3	(9.3)	(45)
χ^2_1	0.1								

Abbreviations: MDE, major depressive episode; SE, standard error.

*Significant at the.05-level, two-sided design-based test.

†Cases are based on three conditions: (i) Respondents obtained mania/hypomania treatment; (ii) Year of first mania/hypomania treatment was 1990 or later; and (iii) Age of onset of mania/hypomania was the year of first mania/hypomania treatment or earlier.

‡Cases are based on four conditions: (i) Respondents obtained mania/hypomania treatment; (ii) Year of first mania/hypomania treatment was 1990 or later; (iii) Age of onset of mania/hypomania was the year of first mania/hypomania treatment or earlier; and (iv) Respondents obtained helpful mania/hypomania treatment.

§Cases are based on three conditions: (i) Respondents obtained depression treatment; (ii) Year of first depression treatment was 1990 or later; and (iii) Age at onset of MDE with mania/hypomania was the year of first depression treatment or earlier.

¶Cases are based on four conditions: (i) Respondents obtained depression treatment; (ii) Year of first depression treatment was 1990 or later; (iii) Age at onset of MDE with mania/hypomania was the year of first depression treatment or earlier; and (iv) Respondents obtained helpful depression treatment.

or self-help group). We recognize that human services professionals and complementary/alternative medicine providers cannot deliver evidence-based care for bipolar disorder, but these types of providers were nonetheless included in the analysis because they were reported by substantial proportions of patients as having been sought out for help with mania/hypomania or depression. *Treatment timing* included a dichotomous measure for whether the respondent's first attempt to seek treatment for the focal syndrome (i.e., either mania/hypomania or MDE) occurred before 2000 or subsequently (2000 being the average mid-point between the start of observation and survey field dates) and a continuous variable for length of delay in years between age-of-onset of mania/hypomania and age of initially seeking treatment. *Childhood adversities* (CAs) included a count of 7 CAs that we have referred to previously[22] as indicators of maladaptive family functioning (physical abuse, sexual abuse, neglect, parental mental disorder, parental substance use disorder, parental

criminal behavior, and family violence) and a count of 5 other CAs (parental death, parental divorce, other loss of a parent, physical illness, and economic adversity).

2.3 | Analysis methods

The interviews were in two parts. Part I was administered to all respondents and assessed core DSM-IV mental disorders (n = 91,416 respondents across all surveys). Part II assessed additional disorders and correlates and was administered to 100% of respondents who screened positive for any lifetime Part I disorder and a probability subsample of other Part I respondents (n = 49,546). Individual weights were applied to adjust for discrepancies between the sample and population distributions on census demographic and geographic variables. Part II respondents were additionally weighted to adjust for differential probabilities of selection into Part II. The Part II sample was used in the analyses reported here given that information about some comorbidities, sectors of treatment, and CAs were all in Part II.

The analysis sample was limited to people with first lifetime mania/hypomania treatment during or after 1990 to reduce the potential effects of recall bias. We investigated two component probabilities that together make up the probability of a patient eventually receiving helpful treatment: (i) the probability that a given treatment professional was perceived as being helpful; and (ii) the probability that the patient persisted in help seeking from another treatment professional after a prior unhelpful treatment. We calculated the cumulative probability distributions of each component separately using discrete-count survival analysis.[23] We stopped after six treatment professionals because this was the last number in pooled analyses across all countries where at least n = 30 patients received treatment. We then carried out parallel survival analyses of the predictors of these two component outcomes pooled across all professionals seen using standard discrete-count methods and a logistic link function[24] followed by a patient-level model to predict overall probability of ever receiving helpful treatment regardless of number of professionals seen. We also investigated interactions of significant predictors with country income group and historical time (a dummy variable for treatment beginning after 2000). These analyses were carried out separately for the helpfulness of treatment for mania/hypomania and for MDE.

Because the WMH samples were based on clustered designs and used weighting to adjust for differential probabilities of selection, design-based methods were used to estimate the standard errors (SEs) of coefficient estimates based on the Taylor series linearization method[25] implemented in SAS 9.4 (RRID:SCR_008567).[26] Logistic regression coefficients and these coefficients +/- 2 standard errors were exponentiated to create odds ratios (ORs) and 95% confidence intervals (CIs). The significance of sets of coefficients 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 .05 level tests.

3 | RESULTS

3.1 | Prevalence and perceived helpfulness of treatment

Lifetime prevalence (SE) of mania/hypomania was 1.6% (0.1) in low-/middle-income countries, 2.7% (0.1) in high-income countries, and 2.3% (0.1) in the total sample (Table 1, Part I). Approximately one-quarter (26.6% [1.3]) of respondents with lifetime mania/hypomania across all countries reported ever being treated and 63.1% (2.4) of those treated reported ever obtaining treatment they considered helpful. The probability of ever receiving treatment was significantly higher in high-income countries than in low-/middle-income countries (28.9% vs. 19.3%; $p = 0.001$), but the probability of treated patients describing the treatment as helpful was nearly identical in high-income and low-/middle-income countries (63.0% vs. 63.5%; $p = 0.932$).

Lifetime prevalence of MDE with lifetime mania/hypomania was 0.9% (0.1) in low-/middle-income countries, 1.3% (0.1) in high-income countries, and 1.2% (0.1) across all countries (Table 1, Part II). Fewer than half (43.9% [2.6]) of these respondents reported ever obtaining MDE treatment and 65.1% (3.9) of the latter reported that the treatment was helpful. Although respondents in high-income countries had a significantly higher probability of obtaining MDE treatment than did those in low-/middle-income countries (47.9% vs. 31.9%; $p = 0.007$), probability of the treatment being perceived as helpful was similar in the two subsamples (64.6% vs. 67.3%; $p = 0.80$).

3.2 | Conditional and cumulative probabilities of treatment helpfulness

Mania/hypomania treatment from the first professional seen was considered helpful by 24.5% (1.5) of respondents in the total sample, with a higher proportion in low-/middle-income than high-income countries (30.8% [1.8] vs. 23.2% [1.7]; $p = 0.002$) (Table 2, Part I). Among patients who persisted in help seeking after receiving initially unhelpful treatment, the cumulative probability of eventually receiving helpful treatment rose from 48.5% (2.6) when seeing two professionals to 85.4% (3.1) when seeing up to six professionals. The 85.4% projected rate is roughly 3.5 times the proportion of patients who were helped by the first professional seen (i.e., 85.4/24.5), which means that fewer than one third of the patients who could receive helpful treatment with persistent help seeking received such help from the first professional seen (i.e., 1/3.5). These patterns were relatively comparable across country income levels, although probabilities of receiving helpful treatment were consistently somewhat higher in low-/middle-income countries.

MDE treatment from the first professional seen was considered helpful by 22.5% (2.4) of respondents in the total sample and did not differ significantly by country income level (Table 2, Part II). Among patients who persisted in seeking help from more than one professional after receiving initially unhelpful treatment, the cumulative probability of eventually receiving helpful treatment rose from

TABLE 2 Conditional and cumulative probabilities of mania/hypomania treatment and depression treatment being perceived as helpful after each professional seen, among respondents with: I) lifetime DSM-IV mania/hypomania disorder who obtained mania/hypomania treatment and II) lifetime DSM-IV MDE with lifetime mania/hypomania who obtained depression treatment

	Conditional probability									Cumulative probability								
	All			High-income countries			Low-/middle-income countries			All			High-income countries			Low-/middle-income countries		
Number of professionals seen after which treatment was perceived as helpful	%	(SE)	(n)	%	(SE)	(n)	%	(SE)	(n)	%	(SE)	(n)	%	(SE)	(n)	%	(SE)	(n)
I. Mania/hypomania treatment perceived as helpful																		
1	24.5	(1.5)	(598)	23.2	(1.7)	(503)	30.8	(1.8)	(95)	24.5	(1.5)	(598)	23.2	(1.7)	(503)	30.8	(1.8)	(95)
2	31.8	(2.0)	(328)	29.1	(2.3)	(285)	47.7	(3.2)	(43)	48.5	(2.6)	(598)	45.6	(2.7)	(503)	63.8	(7.1)	(95)
3	34.1	(3.6)	(192)	34.6	(3.9)	(168)	29.9	(8.4)	(24)	66.1	(2.9)	(598)	64.4	(3.2)	(503)	74.6	(6.3)	(95)
4	19.2	(4.5)	(99)	21.6	(5.1)	(86)	1.4	(1.4)	(13)	72.6	(2.9)	(598)	72.1	(3.3)	(503)	75.0	(6.3)	(95)
5	14.4	(4.2)	(53)	11.2	(4.1)	(46)	34.0	(15.3)	(7)	76.5	(2.9)	(598)	75.2	(3.2)	(503)	83.5	(7.4)	(95)
6	37.9	(8.8)	(32)	36.4	(8.9)	(30)	95.2	(0.0)	(2)	85.4	(3.1)	(598)	84.2	(3.4)	(503)	99.2	(1.1)	(95)
II. Depression treatment perceived as helpful																		
1	22.5	(2.4)	(280)	21.7	(2.3)	(235)	26.6	(7.8)	(45)	22.5	(2.4)	(280)	21.7	(2.3)	(235)	26.6	(7.8)	(45)
2	29.2	(3.4)	(172)	24.4	(3.4)	(145)	53.0	(8.2)	(27)	45.2	(4.1)	(280)	40.7	(4.0)	(235)	65.5	(10.6)	(45)
3	24.2	(4.0)	(97)	23.7	(4.3)	(86)	28.9	(8.9)	(11)	58.5	(4.5)	(280)	54.8	(4.7)	(235)	75.5	(9.5)	(45)
4	24.2	(9.1)	(55)	26.7	(9.9)	(49)	0.0	(0.0)	(6)	68.5	(5.1)	(280)	66.8	(5.7)	(235)	75.5	(9.5)	(45)
5	11.6	(6.1)	(38)	9.8	(6.1)	(33)	29.2	(22.2)	(5)	72.2	(5.2)	(280)	70.1	(5.9)	(235)	82.6	(7.9)	(45)
6	21.6	(7.6)	(31)	19.8	(7.6)	(28)	57.8	(0.0)	(3)	78.2	(5.5)	(280)	76.0	(6.2)	(235)	92.7	(6.5)	(45)

Abbreviations: MDE, major depressive episode; SE, standard error.

45.2% (4.1) when seeing two to 78.2% (5.5) when seeing up to six professionals, which, as with treatment of mania/hypomania, is roughly 3.5 times the proportion of patients who were helped by the first professional seen (i.e., 78.2/22.5). As with mania/hypomania, the incremental pattern was relatively comparable across country income levels, although probabilities of receiving helpful treatment were consistently somewhat higher in low-/middle-income countries.

3.3 | Persistence of treatment seeking

Among respondents with lifetime mania/hypomania who were not helped by the first professional they saw, 76.0% (1.8) in the total sample and relatively comparable proportions in high- and low-/middle-income countries (77.1% [2.1] vs. 70.4% [2.8]) persisted in seeing a second professional (Table 3, Part I). This conditional probability remained relatively stable for up to four subsequent professionals seen in the total sample (67.6–80.4%) as well as in high-income countries (68.0–80.4%), but the number of patients who saw a second professional in low-/middle-income countries was too small (n = 27) to produce stable estimates of subsequent conditional probabilities of persistence in help seeking. Unlike cumulative probability of receiving helpful treatment, which, by definition, *increases* as number of professionals seen increases, cumulative probability of help-seeking persistence *decreases* as number of professionals seen increases. This cumulative probability of persistence through six professionals was 22.9% (4.2) in the total sample, with a similar pattern in high-income countries (25.5% [4.6]) but a much lower cumulative probability in low-/middle-income countries (4.9% [4.8]).

Among respondents with lifetime MDE, 80.6% (2.8) persisted in seeing a second professional after receiving initially unhelpful treatment, with very similar proportions in high- and low-/middle-income countries (80.7 [2.7] - 80.0% [8.7]) (Table 3, Part II). As with treatment of mania/hypomania, conditional probabilities of help-seeking persistence were fairly stable up through six professionals seen in the total sample (78.0–92.9%) and high-income countries (79.1–96.2%) but the number persisting after the second professional seen was too small in low-/middle-income countries (n = 16) to generate stable estimates of subsequent conditional probabilities. Cumulative probability estimates showed that 43.3% (6.3) of patients persisted in help seeking from up to six professionals in the total sample, with a somewhat higher proportion in high-income countries (46.8% [6.6]) and a much lower proportion in low-/middle-income counties (18.6% [10.5]).

3.4 | Predictors of receiving helpful treatment for mania/hypomania

Among patients who sought treatment for mania/hypomania, patient-level odds of receiving helpful treatment (i.e., Model 3) were reduced significantly among patients who had long delays between age-of-onset (AOO) and age of first seeking treatment (OR [95%CI] =0.97 [0.94–0.99]), received treatment from a general medical professional (0.51 [0.33–0.79]), received prior unhelpful treatment for MDE (0.11 [0.04–0.30]), and had mania as opposed to hypomania (0.56 [0.36–0.89]) (Table 4). The reduced ORs for treatment delays and lifetime mania were due to significantly reduced help-seeking persistence (i.e., Model 2; 0.96 [0.94–0.99] for treatment delays and 0.57 [0.36–0.90] for mania vs. hypomania). Receiving treatment from a general medical professional, in comparison, was associated with a significantly reduced provider-level OR of treatment helpfulness (0.54 [0.39–0.76]). The OR associated with receiving unhelpful lifetime MDE treatment was due to reduced odds of both provider-level treatment helpfulness (0.19 [0.08–0.46]) and help-seeking persistence (0.41 [0.22–0.77]). Having lifetime MDE but never receiving MDE treatment, finally, was associated with significantly increased odds of receiving helpful treatment for mania/hypomania compared to patients with no history of MDE (1.63 [1.01–2.64]) due to increased help-seeking persistence (1.86 [1.11–3.12]). Treatment by mental health specialists with psychotherapy and complementary/alternative medicine providers was both associated with significantly reduced odds of provider-level helpfulness and significantly increased odds of help-seeking persistence. These opposite-sign associations cancelled out to create non-significant associations of these variables with receiving helpful treatment at the patient level.

Significant interactions were found between country income level and two predictors: treatment type and MDE treatment (Appendix Table S2). These interactions were complex. Mental health specialty treatment with medication and complementary/alternative treatment were associated with significantly increased odds of both provider-level helpfulness and help-seeking persistence in low-/middle-income countries but not in high-income countries, but the significant associations were based on a small number of cases (Appendix Tables S3-S4). Never having MDE treatment was associated with significantly elevated odds of help-seeking persistence for mania/hypomania in high-income countries but significantly reduced odds of both provider-level helpfulness and persistence in low-/middle-income countries. We also looked for but failed to find any significant interactions between the other variables in Table 4 and historical time in predicting helpfulness of treatment (Appendix Table S5).

3.5 | Predictors of receiving helpful treatment for MDE

Among patients who sought treatment for MDE, patient-level odds of the treatment being helpful (i.e., Model 3) were increased significantly among those who received two or more types of treatment (4.68 [1.22–18.00]), had one or more prior lifetime anxiety disorders (2.33 [1.10–4.96]), and previously received helpful treatment for mania/hypomania (14.47 [4.20–49.85]) (Table 5). Decomposition showed that the increased OR for receiving two or more types of treatment was due to non-significantly increased odds of both provider-level helpfulness (i.e., Model 1) and help-seeking

TABLE 3 Conditional and cumulative probabilities of persistence with treatment after previous unhelpful attempts, among respondents with: I) lifetime DSM-IV mania/hypomania disorder who obtained mania/hypomania treatment, and II) lifetime DSM-IV MDE with mania/hypomania who obtained depression treatment

	I. Conditional probability									II. Cumulative probability								
	All			High-income countries			Low-/middle-income countries			All			High-income countries			Low-/middle-income countries		
Number of professionals seen if not helped by the previous one	%	(SE)	(n)	%	(SE)	(n)	%	(SE)	(n)	%	(SE)	(n)	%	(SE)	(n)	%	(SE)	(n)
I. Persistence of mania/hypomania treatment																		
2	76.0	(1.8)	(443)	77.1	(2.1)	(379)	70.4	(2.8)	(64)	76.0	(1.8)	(443)	77.1	(2.1)	(379)	70.4	(2.8)	(64)
3	80.4	(1.9)	(234)	80.4	(2.1)	(207)	80.8	(1.8)	(27)	61.2	(3.0)	(443)	62.0	(3.1)	(379)	56.9	(9.7)	(64)
4	76.9	(3.4)	(127)	77.0	(3.8)	(109)	76.3	(3.7)	(18)	47.0	(3.7)	(443)	47.7	(4.0)	(379)	43.4	(8.6)	(64)
5	67.6	(7.7)	(76)	68.0	(8.6)	(64)	65.6	(16.0)	(12)	31.8	(4.2)	(443)	32.4	(4.6)	(379)	28.5	(9.8)	(64)
6	72.0	(7.4)	(44)	78.7	(7.0)	(39)	17.1	(7.5)	(5)	22.9	(4.2)	(443)	25.5	(4.6)	(379)	4.9	(4.8)	(64)
II. Persistence of depression treatment																		
2	80.6	(2.8)	(208)	80.7	(2.9)	(175)	80.0	(8.7)	(33)	80.6	(2.8)	(208)	80.7	(2.9)	(175)	80.0	(8.7)	(33)
3	78.0	(4.4)	(126)	79.1	(4.9)	(110)	69.5	(6.4)	(16)	62.9	(5.1)	(208)	63.8	(5.6)	(175)	55.6	(12.6)	(33)
4	81.3	(4.1)	(70)	81.5	(4.5)	(63)	79.7	(5.9)	(7)	51.1	(5.7)	(208)	52.0	(6.2)	(175)	44.3	(14.2)	(33)
5	92.9	(4.1)	(42)	96.2	(2.1)	(36)	69.1	(22.2)	(6)	47.5	(5.9)	(208)	50.0	(6.2)	(175)	30.6	(13.0)	(33)
6	91.3	(5.0)	(34)	93.7	(4.4)	(30)	60.7	(23.9)	(4)	43.3	(6.3)	(208)	46.8	(6.6)	(175)	18.6	(10.5)	(33)

Abbreviations: MDE, major depressive episode; SE, standard error.

persistence (i.e., Model 2), that the increased OR of prior anxiety was due to significantly increased persistence (2.82 [1.54–5.18]), and that the significantly increased OR of prior helpful mania/hypomania treatment was due to significantly increased odds of both provider-level helpfulness (1.93 [1.07–3.48]) and help-seeking persistence (10.41 [3.67–29.55]). No significant interactions were found between any of these predictors and either country income level (Appendix Table S6) or historical time (Appendix Table S7).

4 | DISCUSSION

Across 15 countries combined, 63.1% of adults with a lifetime history of treated DSM-IV mania/hypomania reported ever obtaining treatment they considered helpful. The comparable proportion among patients with lifetime mania/hypomania who obtained treatment for a major depressive episode was 65.1%. The latter proportion is very similar to the one found in a parallel WMH study of helpful treatment for non-bipolar major depressive disorder.[12] Proportions were very similar in high-income (63.0%–64.6%) and low-/middle-income (63.5%–67.3%) countries despite probability of ever seeking treatment being considerably higher in high-income than low-/middle-income countries.

In both groups of countries, only about one fourth of patients received helpful treatment from the first professional seen and persistence was required to achieve the considerably higher rates of eventual helpfulness reported by respondents. Our projections suggest that more than 85% of the patients seeking treatment for mania/hypomania and 78% for major depression would have received helpful treatment if they had persisted with up to six professionals. However, based on observed patterns, we estimated that only 22.9% of patients seeking treatment for mania/hypomania and 43.3% for depression would have persisted in help-seeking efforts up through that many professionals if they were not helped by any of the first five professionals seen.

Although we do not know the reasons fewer than one fourth of patients experienced their first treatment for mania/hypomania or depression as helpful, this finding is indirectly consistent with previous research in clinical samples that time from bipolar illness onset to first maintenance treatment is nearly a decade.[27,28] Two large-scale surveys of patients with bipolar disorder carried out 8 years apart by the Depression and Bipolar Support Alliance found similar results, with patients reporting that it took them up to a decade of seeking help before obtaining an accurate bipolar diagnosis.[29,30] Consistent with our failure to find a time trend in the WMH data in reducing this delay, the two DBSA surveys found no evidence for the length of delay in obtaining an accurate diagnosis decreasing over time in the 8 years between these two surveys.

Findings such as these emphasize the importance of improving early detection of bipolar disorder in the general medical sector, where treatment is initially sought by most bipolar patients, and increasing the speed of referral of such patients from primary care to specialty care settings where appropriate medication can be prescribed. These findings also make it clear that ongoing efforts to increase the speed with which appropriate treatments are found for individual patients are of great importance in sustaining patient engagement. It is also important to make patients aware that optimal treatments for bipolar disorder vary across patients for reasons that are not yet well understood, requiring a certain amount of trial and error in arriving at an optimal treatment plan. Inoculating patients against unrealistic expectations about the speed of finding an effective treatment, coupled with the use of measurement-based care (MBC) to increase opportunities to detect patients' negative evaluations, might help provide encouragement for patients whose initial treatments are unhelpful while these patients are still engaged.[31] Such an approach was used, for example, in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BP), where MBC was used to help establish clear patient expectations for treatment[32] that led to improvements in guideline-concordant treatment decisions that improved clinical outcomes.[33] In addition, for patients who disengage from treatment, rapid proactive follow-up to determine the reasons and to ensure appropriate referral may be helpful.

We are unaware of previous research with which to compare the findings that 63.1%–65.1% of patients in the WMH sample eventually obtained helpful treatment. Typical treatment studies evaluate episode treatment response rather than lifetime treatment response, focus on symptom-based criteria rather than patient-centered criteria of treatment helpfulness, and are based on samples with exclusions that make them unrepresentative of the general population represented in the WMH sample.

Within the context of those substantial differences, it is worth noting that the proportions of WMH respondents who reported being helped were higher than the proportion of bipolar patients found to have good long-term treatment response in observational studies of treatment samples,[34] possibly suggesting that patients in the community have a broader definition of helpfulness than the definitions used in clinical studies. We also found less consistent evidence for significant predictors of patient-reported helpfulness than in the clinical literature on predictors of treatment response,[35-37] suggesting that the determinants of patient perceptions of treatment helpfulness might be different from the determinants of clinical definitions of treatment success. It is noteworthy in this regard that most of the significant patient-level predictors of perceived helpfulness predicted persistence in help seeking after earlier unhelpful treatments rather than perceived helpfulness of specific treatment encounters.

The extent to which perceived helpfulness relates to definitions of successful treatment outcomes in clinical trials is difficult to determine. It is clear, though, that the two are overlapping rather than distinct given that perceptions such as those of treatment helpfulness, quality of life, optimism about the future, and purpose in life all relate directly to morbidity[9,38] and mortality.[39,40] Thus, the perceptions that patients have at the end of treatment are not trivial. Direct tests of perceived helpfulness and treatment outcome have not been reported in a way that would permit drawing firm conclusions.

TABLE 4 All countries: Factors associated with helpful mania/hypomania treatment and persistence (pooled across professionals seen), and perceived helpfulness of treatment (person level), among people with lifetime DSM-IV mania/hypomania disorder who obtained treatment

	Model 1: Predicting helpful treatment pooled across professionals seen					Model 2: Predicting persistence pooled across treatment failure					Model 3: Predicting perceived helpfulness of treatment across mania/hypomania patients				
	Prevalence			Multivariate		Prevalence			Multivariate		Prevalence			Multivariate	
	Mean/%	(SE)	(n)	OR	(95% CI)	Mean/%	(SE)	(n)	OR	(95% CI)	Mean/%	(SE)	(n)	OR	(95% CI)
Age of first mania/hypomania treatment	29.7	(0.6)	(1,383)	1.01	(0.99–1.02)	29.3	(0.6)	(1,008)	0.99	(0.97–1.02)	29.9	(0.5)	(598)	1.00	(0.98–1.02)
χ^2_1	0.87					0.31					0.01				
Gender															
Female	57.2	(3.2)	(1,383)	1.05	(0.75–1.47)	57.1	(3.9)	(1,008)	1.13	(0.74–1.73)	56.7	(2.1)	(598)	1.17	(0.77–1.79)
Male	42.8	(3.2)	(1,383)	1.00	-	42.9	(3.9)	(1,008)	1.00	-	43.3	(2.1)	(598)	1.00	-
χ^2_1	0.09					0.35					0.54				
Marital Status															
Never married	53.0	(2.9)	(1,383)	0.76	(0.57–1.01)	53.6	(3.5)	(1,008)	1.40	(0.89–2.20)	52.2	(1.9)	(598)	0.96	(0.61–1.51)
Previously married	19.1	(2.2)	(1,383)	0.90	(0.62–1.29)	19.0	(2.5)	(1,008)	1.55	(0.96–2.52)	17.8	(1.4)	(598)	1.07	(0.65–1.75)
Currently married	28.0	(2.5)	(1,383)	1.00	-	27.5	(3.0)	(1,008)	1.00	-	30.0	(1.6)	(598)	1.00	-
χ^2_2	3.68					3.69					0.16				
Education															
Low	11.9	(2.3)	(1,383)	0.73	(0.49–1.08)	12.5	(2.8)	(1,008)	0.85	(0.46–1.60)	10.6	(1.0)	(598)	0.80	(0.43–1.50)
Low-average	26.2	(3.1)	(1,383)	1.06	(0.73–1.53)	25.9	(3.5)	(1,008)	0.88	(0.54–1.45)	24.8	(2.1)	(598)	1.28	(0.78–2.11)
High-average	35.4	(3.0)	(1,383)	1.10	(0.80–1.51)	34.6	(3.5)	(1,008)	0.84	(0.49–1.42)	36.4	(2.1)	(598)	1.16	(0.64–2.11)
Student	12.4	(1.7)	(1,383)	0.74	(0.32–1.72)	13.3	(2.0)	(1,008)	0.47*	(0.24–0.94)	13.6	(1.7)	(598)	0.47	(0.20–1.14)
High	14.0	(1.7)	(1,383)	1.00	-	13.6	(1.9)	(1,008)	1.00	-	14.6	(1.4)	(598)	1.00	-
χ^2_4	5.94					5.75					7.53				
Treatment delay (years)†	5.3	(0.4)	(1,383)	1.00	(0.98–1.01)	5.3	(0.5)	(1,008)	0.96*	(0.94–0.99)	5.3	(0.3)	(598)	0.97*	(0.94–0.99)
χ^2_1	0.50					8.95*					6.04*				
Started mania/hypomania treatment >= 2000 (vs. 1990–1999)	53.4	(3.0)	(1,383)	1.14	(0.80–1.62)	50.8	(3.6)	(1,008)	0.81	(0.50–1.31)	59.3	(1.7)	(598)	1.06	(0.71–1.58)
χ^2_1	0.54					0.72					0.07				
Treatment type‡															
Mental health specialist + psychotherapy	64.5	(2.5)	(1,383)	0.63*	(0.46–0.86)	65.5	(3.0)	(1,008)	1.95*	(1.01–3.77)	60.0	(1.8)	(598)	0.95	(0.47–1.91)
Mental health specialist + medication	67.9	(2.4)	(1,383)	0.70	(0.46–1.08)	70.7	(2.5)	(1,008)	1.61*	(1.01–2.57)	55.7	(1.9)	(598)	1.26	(0.71–2.25)

(Continues)

TABLE 4 Continued

	Model 1: Predicting helpful treatment pooled across professionals seen					Model 2: Predicting persistence pooled across treatment failure					Model 3: Predicting perceived helpfulness of treatment across mania/hypomania patients				
	Prevalence			Multivariate		Prevalence			Multivariate		Prevalence			Multivariate	
	Mean/%	(SE)	(n)	OR	(95% CI)	Mean/%	(SE)	(n)	OR	(95% CI)	Mean/%	(SE)	(n)	OR	(95% CI)
General medical	68.1	(2.7)	(1,383)	0.54*	(0.39–0.76)	71.0	(3.1)	(1,008)	0.98	(0.62–1.56)	61.9	(1.9)	(598)	0.51*	(0.33–0.79)
Complementary/alternative medicine	31.2	(3.2)	(1,383)	0.63*	(0.45–0.88)	34.3	(3.9)	(1,008)	1.87*	(1.15–3.04)	22.2	(1.5)	(598)	1.10	(0.61–1.98)
Human services	26.1	(3.2)	(1,383)	1.00	-	29.1	(3.8)	(1,008)	1.00	-	20.0	(1.8)	(598)	1.00	-
χ^2_4	19.12*					11.52*					11.26*				
Exactly 2 or more of the above	74.5	(2.0)	(1,383)	1.09	(0.68–1.75)	77.7	(2.0)	(1,008)	1.79	(0.91–3.50)	62.9	(2.0)	(598)	1.33	(0.65–2.73)
χ^2_1	0.13					2.89					0.59				
χ^2_5	40.66*					67.11*					12.36*				
Anxiety disorders§															
Any anxiety disorders	70.0	(2.4)	(1,383)	1.24	(0.92–1.68)	70.8	(2.8)	(1,008)	0.85	(0.60–1.19)	65.2	(1.9)	(598)	1.01	(0.70–1.47)
No anxiety disorder	30.0	(2.4)	(1,383)	1.00	-		29.2	(2.8)	(1,008)	1.00	-	34.8	(1.9)	(598)	1.00
χ^2_1	2.07					0.91					0.00				
Substance use disorders¶															
Any substance use disorders	46.6	(2.9)	(1,383)	0.97	(0.69–1.35)	48.5	(3.5)	(1,008)	1.55*	(1.01–2.37)	39.3	(2.0)	(598)	1.30	(0.80–2.12)
No substance use disorder	53.4	(2.9)	(1,383)	1.00	-	51.5	(3.5)	(1,008)	1.00	-	60.7	(2.0)	(598)	1.00	-
χ^2_1	0.04					4.06*					1.14				
Got helpful lifetime MDE Treatment	19.5	(2.3)	(1,383)	1.29	(0.88–1.88)	17.4	(2.8)	(1,008)	1.40	(0.70–2.80)	20.1	(1.7)	(598)	1.81	(0.85–3.85)
Got unhelpful lifetime MDE treatment	6.7	(1.2)	(1,383)	0.19*	(0.08–0.46)	8.5	(1.5)	(1,008)	0.41*	(0.22–0.77)	6.4	(1.0)	(598)	0.11*	(0.04–0.30)
Got lifetime MDE treatment but unknown helpfulness††	23.7	(2.7)	(1,383)	0.88	(0.62–1.24)	24.4	(3.3)	(1,008)	1.83*	(1.24–2.69)	20.5	(1.3)	(598)	1.29	(0.81–2.05)
Had lifetime MDE but never got MDE treatment	17.0	(2.7)	(1,383)	1.01	(0.69–1.48)	17.9	(3.4)	(1,008)	1.86*	(1.11–3.12)	13.4	(1.2)	(598)	1.63*	(1.01–2.64)
Did not have lifetime MDE	33.0	(2.5)	(1,383)	1.00	-	31.7	(2.9)	(1,008)	1.00	-	39.7	(2.1)	(598)	1.00	-
χ^2_4	18.84*					39.27*					28.04*				
χ^2_6	20.34*					46.18*					33.47*				
Have lifetime mania	31.9	(2.9)	(1,383)	0.79	(0.53–1.18)	33.2	(3.5)	(1,008)	0.57*	(0.36–0.90)	29.8	(2.0)	(598)	0.56*	(0.36–0.89)
Have lifetime hypomania	68.1	(2.9)	(1,383)	1.00	-	66.8	(3.5)	(1,008)	1.00	-	70.2	(2.0)	(598)	1.00	-
χ^2_1	1.34					5.71*					6.11*				
Childhood adversities															

(Continues)

TABLE 4 Continued

	Model 1: Predicting helpful treatment pooled across professionals seen					Model 2: Predicting persistence pooled across treatment failure					Model 3: Predicting perceived helpfulness of treatment across mania/hypomania patients				
	Prevalence			Multivariate		Prevalence			Multivariate		Prevalence			Multivariate	
	Mean/%	(SE)	(n)	OR	(95% CI)	Mean/%	(SE)	(n)	OR	(95% CI)	Mean/%	(SE)	(n)	OR	(95% CI)
Family dysfunction‡‡	47.6	(2.7)	(1,383)	0.76	(0.56–1.03)	48.9	(3.3)	(1,008)	1.60*	(1.06–2.40)	44.2	(1.8)	(598)	1.14	(0.78–1.66)
Other§§	19.9	(2.7)	(1,383)	1.37*	(1.03–1.80)	19.8	(3.3)	(1,008)	0.73	(0.46–1.16)	20.8	(1.3)	(598)	1.07	(0.69–1.66)
χ^2_2	5.99*					7.46*					0.63				
Global χ^2_{24}	140.54*					192.16*					126.78*				

Abbreviations: CI, confidence interval; MDE, major depressive episode; OR, odds ratio; SE, standard error.

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

†Treatment delay (years) = Age at first mania/hypomania treatment − Age at onset of mania/hypomania.

‡Treatment providers: mental health specialists (psychiatrist, psychiatric nurse, psychologist, psychiatric social worker, and mental health counselor), primary care providers, human services providers (social worker or counselor in a social services agency, spiritual advisor), and complementary/alternative medicine (other type of healer or self-help group).

§Lifetime anxiety disorders include generalized anxiety disorder, panic disorder, agoraphobia with or without panic disorder, post-traumatic stress disorder, specific phobia, and social phobia.

¶Substance use disorders include alcohol and/or drug abuse and alcohol or drug dependence but not abuse.

††Helpfulness of MDE treatment questions was not assessed for five surveys (Colombia, Peru, Mexico, New Zealand, and the United States).

‡‡Family dysfunction includes physical abuse, sexual abuse, neglect, parent mental disorder, parent substance disorder, parent criminal behavior, and family violence.

§§Other includes parent died, parent divorced, other parent loss, physical illness, and economic adversity.

TABLE 5 All countries: Factors associated with helpful depression treatment and persistence (pooled across professionals seen), and perceived helpfulness of depression treatment (person level), among people with lifetime DSM-IV MDE with mania/hypomania who obtained depression treatment

	Model 1: Predicting helpful depression treatment pooled across professionals seen					Model 2: Predicting persistence pooled across depression treatment failure					Model 3: Predicting perceived helpfulness of depression treatment across patients				
	Prevalence			Multivariate		Prevalence			Multivariate		Prevalence			Multivariate	
	Mean/%	(SE)	(n)	OR	(95% CI)	Mean/%	(SE)	(n)	OR	(95% CI)	Mean/%	(SE)	(n)	OR	(95% CI)
Age of first depression treatment	26.4	(0.9)	(783)	1.00	(0.98–1.03)	25.7	(1.0)	(599)	1.01	(0.98–1.05)	27.3	(0.6)	(280)	0.98	(0.93–1.04)
χ^2_1	0.07					0.84					0.36				
Gender															
Female	58.3	(6.1)	(783)	1.03	(0.60–1.74)	58.2	(7.1)	(599)	0.50*	(0.29–0.87)	58.6	(3.6)	(280)	0.81	(0.38–1.73)
Male	41.7	(6.1)	(783)	1.00	-	41.8	(7.1)	(599)	1.00	-	41.4	(3.6)	(280)	1.00	-
χ^2_1	0.01					6.01*					0.30				
Marital Status															
Never married	51.6	(6.1)	(783)	0.85	(0.55–1.32)	52.5	(6.9)	(599)	1.27	(0.64–2.53)	50.9	(3.5)	(280)	1.23	(0.60–2.50)
Previously married	13.9	(4.0)	(783)	0.69	(0.31–1.51)	13.7	(4.4)	(599)	1.02	(0.29–3.51)	12.8	(2.4)	(280)	1.23	(0.25–5.99)
Currently married	34.5	(6.3)	(783)	1.00	-	33.9	(7.2)	(599)	1.00	-	36.3	(3.4)	(280)	1.00	-
χ^2_2	1.05					0.56					0.40				
Education															
Low	5.8	(2.8)	(783)	1.58	(0.53–4.69)	5.3	(3.2)	(599)	3.11	(0.44–22.18)	5.6	(1.3)	(280)	3.12	(0.53–18.39)
Low-average	18.8	(3.0)	(783)	1.42	(0.59–3.45)	16.6	(3.1)	(599)	0.72	(0.33–1.60)	23.5	(2.8)	(280)	0.91	(0.28–2.97)
High-average	41.4	(6.7)	(783)	1.26	(0.59–2.69)	42.8	(7.6)	(599)	0.50	(0.21–1.18)	36.5	(3.6)	(280)	0.69	(0.18–2.55)
Student	22.6	(4.3)	(783)	0.64	(0.27–1.51)	24.9	(4.9)	(599)	0.66	(0.29–1.47)	21.4	(2.9)	(280)	0.27	(0.07–1.09)
High	11.4	(2.1)	(783)	1.00	-	10.5	(2.1)	(599)	1.00	-	13.0	(1.7)	(280)	1.00	-
χ^2_4	7.51					5.19					6.92				
Depression treatment delay (years)†	6.0	(1.0)	(783)	1.01	(0.97–1.05)	5.7	(1.2)	(599)	1.00	(0.96–1.03)	6.2	(0.6)	(280)	1.03	(0.97–1.08)
χ^2_1	0.11					0.01					0.94				
Started depression treatment >= 2000 (vs. 1990–1999)	49.0	(6.3)	(783)	1.45	(0.87–2.43)	45.0	(7.2)	(599)	0.37*	(0.18–0.75)	65.2	(3.2)	(280)	1.14	(0.53–2.49)
χ^2_1	2.05					7.65*					0.12				

(Continues)

TABLE 5 (Continued)

	Model 1: Predicting helpful depression treatment pooled across professionals seen					Model 2: Predicting persistence pooled across depression treatment failure					Model 3: Predicting perceived helpfulness of depression treatment across patients				
	Prevalence			Multivariate		Prevalence			Multivariate		Prevalence			Multivariate	
	Mean/%	(SE)	(n)	OR	(95% CI)	Mean/%	(SE)	(n)	OR	(95% CI)	Mean/%	(SE)	(n)	OR	(95% CI)
Treatment type[‡]															
Mental health specialist + psychotherapy	44.4	(6.0)	(783)	0.52*	(0.32–0.85)	44.1	(6.9)	(599)	1.47	(0.71–3.04)	45.0	(3.2)	(280)	0.47	(0.22–1.02)
Mental health specialist + medication	75.1	(4.1)	(783)	0.53	(0.26–1.09)	76.4	(4.6)	(599)	3.28*	(1.03–10.39)	60.5	(3.2)	(280)	1.17	(0.40–3.40)
General medical	71.7	(6.3)	(783)	0.60	(0.32–1.09)	73.7	(7.2)	(599)	2.98*	(1.26–7.06)	63.5	(3.1)	(280)	1.07	(0.42–2.76)
Complementary/ alternative medicine	35.5	(7.3)	(783)	0.66	(0.36–1.18)	38.3	(8.3)	(599)	3.99*	(1.63–9.72)	21.0	(3.3)	(280)	1.23	(0.38–3.96)
Human services	30.9	(7.2)	(783)	1.00	-	34.3	(8.2)	(599)	1.00	-	19.4	(3.3)	(280)	1.00	-
χ^2_4	7.63					17.40*					5.43				
Exactly 2 or more of the above	80.1	(3.2)	(783)	1.88	(0.78–4.53)	81.8	(3.3)	(599)	2.17	(0.64–7.33)	64.0	(3.2)	(280)	4.68*	(1.22–18.00)
χ^2_1	1.95					1.55					5.05*				
χ^2_5	7.79					59.53*					18.02*				
Anxiety disorders[§]															
Any anxiety disorders	79.3	(3.1)	(783)	0.84	(0.51–1.39)	80.6	(3.5)	(599)	2.82*	(1.54–5.18)	68.2	(3.1)	(280)	2.33*	(1.10–4.96)
No anxiety disorder	20.7	(3.1)	(783)	1.00	-	19.4	(3.5)	(599)	1.00	-	31.8	(3.1)	(280)	1.00	-
χ^2_1	0.47					11.27*					4.83*				
Substance use disorders[¶]															
Any substance use disorders	35.9	(5.7)	(783)	0.97	(0.59–1.61)	36.0	(6.5)	(599)	0.49*	(0.26–0.92)	34.5	(3.4)	(280)	0.50	(0.23–1.07)
No substance use disorder	64.1	(5.7)	(783)	1.00	-	64.0	(6.5)	(599)	1.00	-	65.5	(3.4)	(280)	1.00	-
χ^2_1	0.01					4.91*					3.23				
Got helpful lifetime mania/ hypomania treatment	31.9	(4.4)	(783)	1.93*	(1.07–3.48)	27.1	(4.8)	(599)	10.41*	(3.67–29.55)	33.8	(2.6)	(280)	14.47*	(4.20–49.85)
Got unhelpful lifetime mania/hypomania treatment	23.7	(5.3)	(783)	0.70	(0.30–1.63)	26.8	(6.4)	(599)	0.76	(0.41–1.40)	18.7	(2.5)	(280)	0.58	(0.24–1.41)

(Continues)

TABLE 5 (Continued)

	Model 1: Predicting helpful depression treatment pooled across professionals seen					Model 2: Predicting persistence pooled across depression treatment failure					Model 3: Predicting perceived helpfulness of depression treatment across patients				
	Prevalence			Multivariate		Prevalence			Multivariate		Prevalence			Multivariate	
	Mean/%	(SE)	(n)	OR	(95% CI)	Mean/%	(SE)	(n)	OR	(95% CI)	Mean/%	(SE)	(n)	OR	(95% CI)
Had lifetime mania/hypomania but never got mania/hypomania treatment	44.4	(6.1)	(783)	1.00	-	46.1	(6.9)	(599)	1.00	-	47.4	(3.3)	(280)	1.00	-
χ^2_2	7.61*					20.80*					22.58*				
χ^2_4	13.33*					27.78*					25.34*				
Have lifetime mania	37.0	(5.2)	(783)	1.05	(0.70–1.58)	37.0	(5.9)	(599)	1.16	(0.57–2.35)	32.4	(3.1)	(280)	2.06	(0.95–4.45)
Have lifetime hypomania	63.0	(5.2)	(783)	1.00	-	63.0	(5.9)	(599)	1.00	-	67.6	(3.1)	(280)	1.00	-
χ^2_1	0.06					0.16					3.34				
Childhood adversities															
Family dysfunction††	36.5	(6.8)	(783)	0.85	(0.44–1.62)	36.9	(7.8)	(599)	1.98	(0.93–4.23)	35.0	(2.8)	(280)	1.37	(0.61–3.10)
Other‡‡	11.9	(2.0)	(783)	1.16	(0.62–2.15)	10.4	(1.8)	(599)	0.82	(0.34–2.00)	17.9	(2.0)	(280)	0.76	(0.34–1.73)
χ^2_2	0.29					3.26					0.82				
Global χ^2_{22}	42.85*					279.61*					118.22*				

MDE, major depressive episode; SE, standard error; OR, odds ratio; CI, confidence interval.

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

†Treatment delay (years) = Age at first depression treatment – Age at onset.

‡Treatment providers: mental health specialists (psychiatrist, psychiatric nurse, psychologist, psychiatric social worker, and mental health counselor), primary care providers, human services providers (social worker or counselor in a social services agency, spiritual advisor), and complementary/alternative medicine (other type of healer or self-help group).

§Anxiety disorders include generalized anxiety disorder, panic disorder, agoraphobia with or without panic disorder, post-traumatic stress disorder, specific phobia and social phobia.

¶Substance use disorders include alcohol and/or drug abuse and alcohol or drug dependence but not abuse.

††Family dysfunction includes physical abuse, sexual abuse, neglect, parent mental disorder, parent substance disorder, parent criminal behavior, and family violence.

‡‡Other includes parent died, parent divorced, other parent loss, physical illness, and economic adversity.

Among the reasons is that many competing factors (e.g., severity of patient symptoms and premorbid social competence) that might well relate to perceived helpfulness have long been known to influence therapeutic change.[41] Yet, adjacent literatures focus on perceptions of diverse facets of treatment and therapeutic change. For example, patient expectations for improvement, perceptions of the helpfulness of the relationship with the therapist (therapeutic alliance), perceptions of few obstacles or barriers to treatment, and views of the acceptability of the treatment procedures are all positively related to therapeutic change in the small-to-moderate range.[42-47] These findings might lead to the argument that helpfulness as a perception is valuable in its own right given its associations with improved functioning and symptom change.

We know of no previous research that attempted to decompose patterns or predictors of perceived helpfulness of treatment in the way we did here. Even so, important limitations exist in our approach that could be improved in future studies.[48] First, we were unable to corroborate respondent recall of lifetime disorders and treatment timing. Both types of recall might have been flawed in ways that biased estimates of the extent to which treatment is helpful and the correlates of treatment being helpful. Second, the assessment of perceived helpfulness of treatment was based on a single question asking respondents about whether and when they "talk(ed) to" a professional about their disorder and follow-up questions about whether they ever received "helpful or effective" treatment and the number of professionals talked to up to the time helpful-effective treatment was obtained. We have no way of knowing whether these were formal or therapeutic consultations, the type(s) or appropriateness of clinical activities undertaken, or how encounters with a team of professionals were counted. Nor do we know how patients determined whether treatment was helpful. Third, we included human services and complementary/alternative medicine providers in the count of treatment providers despite the fact that they cannot deliver evidence-based care for bipolar disorder, as these providers were reported by substantial proportions of patients as having been sought out for help for with their manic/hypomanic or depressive symptoms. This made it impossible for us to estimate the number of healthcare providers seen before helpful treatment was obtained. Fourth, we had no way to know if unmeasured variables influenced either perceived treatment helpfulness or persistence after prior unhelpful treatments.

Despite these limitations, the findings are provocative and might be used to guide future studies that attempt to disaggregate patient treatment pathways using in-depth interviewing in an effort to improve treatment delivery and decrease steps in the pathway that must be traversed before treatment is considered helpful. Such insights could be valuable both in terms of reducing symptom duration prior to receiving helpful treatment and in reducing the economic waste of providing unhelpful treatment. Precision treatment assignment holds great promise in this regard but remains an underdeveloped area of investigation.[49,50] The current results suggest that a more practical approach in the short term might be to emphasize to patients that treatment is a trial and error enterprise that requires persistence even if it is implemented in accordance with current Bipolar Disorder Treatment Guidelines.[51] Whether improving perceived helpfulness of treatment would reduce the likelihood of future negative outcomes (e.g., suicidality, course of illness, onset of comorbidities) is an important question that will require controlled studies evaluating long-term outcomes.

Perceived helpfulness of treatment is an important healthcare outcome from a patient-centered perspective. Findings from this large, community sample are encouraging in that about two thirds of lifetime help seekers eventually received treatment they perceived as helpful. But findings also suggested that this percentage might increase substantially if patients persisted in help seeking after earlier treatment failures. Evidence remains to be obtained about the extent to which individualized, targeted treatment can reduce the number of steps in the pathway to helpful treatment.

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CONFLICT OF INTERESTS

Dr. Nierenberg serves on scientific advisory boards for Alkermes, Jazz Pharmaceuticals, Sage Pharmaceuticals, Otsuka, and Neuronetics. He was a consultant for Acadia Pharmaceuticals, Esai, Myriad, Merck, Ginger, Protogenics, Neurogenics, and Clexio. He also reports receiving honoraria from Sunovion and Neurostar. Dr. Navarro-Mateu reports non-financial support from Otsuka outside the submitted work. In the past 3 years, Dr. Kessler was a consultant for Datastat, Inc., RallyPoint Networks, Inc., Sage Pharmaceuticals, and Takeda. The remaining coauthors report no competing interests.

AUTHORS' CONTRIBUTIONS

AAN, MGH, AEK, NS, DVV, JA, SL, JJM, FNM, KMS, and RCK have made substantial contributions to conception and design. NS, WTC, JA, YA, GB, BB, JMC, JMH, CH, AK, SL, FNM, JPV, KMS, JCS, MCV, and RCK contributed substantially to the acquisition of data. AAN, MGH, AEK, VPP, DVV, HNZ, JMH, AK, SL, JJM, and RCK contributed to the analysis and interpretation of data. AAN, MGH, AEK, VPP, HNZ, and RCK were involved in drafting the manuscript and NS, DVV, WTC, JA, YA,GB, BB, JMC, JMH, CH, AK, SL, JJM, FNM, JPV, KMS, JCS, and MCV revised it critically for important intellectual content. All authors have given final approval of the version to be published. All authors have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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SUPPORTING INFORMATION

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

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