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ORIGINAL ARTICLE

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The prevalence and burden of bipolar disorder: findings from the Global Burden of Disease Study 2013

Alize J Ferrari[1,2,3] | Emily Stockings[4] | Jon-Paul Khoo[2] | Holly E Erskine[1,2,3] | Louisa Degenhardt[3,4,5] | Theo Vos[3] | Harvey A Whiteford[1,2,3]

[1]The University of Queensland, School of Public Health, Herston, QLD, Australia

[2]Queensland Centre for Mental Health Research, Wacol, QLD, Australia

[3]University of Washington, Institute for Health Metrics and Evaluation, Seattle, WA, USA

[4]University of New South Wales, National Drug and Alcohol Research Centre, Sydney, NSW, Australia

[5]University of Melbourne, Melbourne School of Population and Global Health, Melbourne, VIC, Australia

Correspondence
Alize Ferrari, Queensland Centre for Mental Health Research, The Park Centre for Mental Health, Wacol, QLD, Australia.
Email: alize_ferrari@qcmhr.uq.edu.au

Objectives: We present the global burden of bipolar disorder based on findings from the Global Burden of Disease Study 2013 (GBD 2013).

Methods: Data on the epidemiology of bipolar disorder were obtained from a systematic literature review and assembled using Bayesian meta-regression modelling to produce prevalence by country, age, sex and year. Years lived with disability (YLDs) were estimated by multiplying prevalence by disability weights quantifying the severity of the health loss associated with bipolar disorder. As there were no years of life lost (YLLs) attributed to bipolar disorder, YLDs equated to disability-adjusted life years (DALYs) as a measure of total burden.

Results: There were 32.7 million cases of bipolar disorder globally in 1990 and 48.8 million in 2013; equivalent to a 49.1% increase in prevalent cases, all accounted for by population increase and ageing. Bipolar disorder accounted for 9.9 million DALYs in 2013, explaining 0.4% of total DALYs and 1.3% of total YLDs. There were 5.5 million DALYs recorded for female individuals and 4.4 million for male individuals. DALYs were evident from age 10 years, peaked in the 20s, and decreased thereafter. DALYs were relatively constant geographically.

Conclusions: Despite being relatively rare, bipolar disorder is a disabling illness due to its early onset, severity and chronicity. Population growth and aging are leading to an increase in the burden of bipolar disorder over time. It is important that resources be directed towards improving the coverage of evidence-based intervention strategies for bipolar disorder and establishing strategies to prevent new cases of the disorder.

KEYWORDS

bipolar disorder, disability, epidemiology, global burden of disease, prevalence

Bipolar disorder is a chronic and severe mental disorder, characterized by irregular acute episodes of depressed, elevated, and mixed mood states.[1,2] Efficacious psychopharmacological and psychosocial treatments exist, but misdiagnosis and delayed diagnosis are common.[3,4] Treatment rates for bipolar disorder remain low, especially in low- and middle-income settings.[5]

High-quality data on the epidemiology of bipolar disorder are essential for formulating effective mental health policy and service planning. For instance, data on the prevalence, incidence, and excess mortality of bipolar disorder assist in the identification of those needing treatment and aid in facilitating access. Epidemiological data can also inform equitable distribution of health system resources, such as the distribution of funds between health promotion, treatment, and research. In addition to epidemiological data, policy makers need to be provided with complete and current information about the health impacts of bipolar disorder in comparison to other diseases and injuries[5,6]; for this, burden of disease estimates are an important metric.

In this paper, we summarize the epidemiology and burden of bipolar disorder based on findings from the Global Burden of Disease Study 2013 (GBD 2013).[7–9] GBD 2013 is the latest analysis of disease burden associated with 306 diseases and injuries, across 188 countries. Based on an approach introduced by the World Bank's World Development Report of 1993,[10] GBD 2013 makes use of disability-adjusted life years (DALYs) to quantify disease burden. Although other methods for quantifying burden exist, the DALY was the first metric to incorporate both the mortality and morbidity associated with a given disease or injury. Within the DALY, mortality is quantified as the years of life lost (YLLs) to premature mortality and morbidity as years lived with disability (YLDs). YLLs and YLDs are summed to estimate DALYs so that one DALY is equivalent to the loss of a healthy year of life due to a particular disease or injury.[7–9]

GBD 2010, which preceded GBD 2013, estimated burden for 20 mental and substance use disorders, which as a group were the leading cause of YLDs and the 5th leading cause of DALYs globally. Bipolar disorder explained 7% of DALYs due to mental and substance use disorders and was ranked as the 45th leading cause of DALYs and the 17th leading cause of YLDs worldwide in 2010.[11,12] In GBD 2010, DALYs for bipolar disorder were entirely made up of non-fatal burden (i.e. YLDs). YLLs were estimated using cause of death records which follow the International Classification of Diseases, Tenth Revision (ICD-10) rules for attributing deaths to a single "direct" cause.[2] All deaths due to bipolar disorder as the "underlying" cause were attributed to its direct physical cause (e.g. suicides due to bipolar disorder were allocated to the GBD 2013 injuries cause group). For this reason, there were no documented deaths and no YLLs "directly" due to bipolar disorder and YLDs equated to DALYs.[12]

As GBD 2013 presents a complete re-analysis of burden using updated data and methodology, it supersedes all earlier burden of disease estimates.[7–9] Such regular updating of health statistics allows us to evaluate changes in disease burden and the impact of health programmes over time, which is critical for informing policy decisions, health services and research priorities. This paper updates the prevalence and burden of bipolar disorder to 2013. We investigate trends in prevalence and burden by country, region, age, sex and year and summarize GBD 2013 methods for quantifying the burden of bipolar disorder.

1 | METHODS

1.1 | Overview

The method used to estimate the prevalence and burden of bipolar disorder in GBD 2013 was similar to that used in GBD 2010.[12] Epidemiological data were obtained from systematic reviews of the literature and assembled using Bayesian meta-regression modelling to produce prevalence by country, region, age, sex, and year. YLDs were estimated by combining prevalence with health state-specific disability weights which quantified the severity of the health loss associated with bipolar disorder. As was the case in GBD 2010, no YLLs were estimated for bipolar disorder and YLDs equated to DALYs.

1.2 | Case definition

According to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) and ICD-10, bipolar disorder is a chronic mood disorder with little or no complete remission. It involves the experience of one or more manic or hypomanic episodes, which can be accompanied by a major depressive episode. A manic episode is characterized by elevated, expansive, or irritable mood for at least 1 week while a hypomanic episode is characterized by symptoms of a manic episode which are less severe for at least 4 days. A major depressive episode is characterized by depressed mood for at least 2 weeks.[1,2]

In GBD 2013, we estimated burden for the entire spectrum of bipolar disorder simultaneously, rather than individually for each subtype of the disorder. This included cases meeting DSM-IV-TR or ICD-10 diagnostic criteria for bipolar I disorder (manic episodes usually alternating with a depressive episode), bipolar II disorder (alternating hypomanic and depressive episodes) and/or cyclothymia (subsyndromal hypomanic and depressive symptom phases) and/or bipolar disorder not otherwise specified (clinically significant symptoms of bipolar disorder which do not meet criteria for the other diagnoses).[1,2] Cases due to a general medical condition or substance-induced cases were not included.

1.3 | Prevalence estimation

1.3.1 | Literature review

A systematic review of the literature was conducted to assemble existing data on the prevalence, incidence, remission and excess mortality of bipolar disorder. An existing systematic review conducted between January 1980 and December 2008[13] was updated to December 2013. Methods for both searches adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[14] and comprised three stages. Stage one entailed searches of electronic databases (Medline, Embase and PubMed). The search string used has been provided as Supporting Information (Data S1). Stage two involved searches of grey literature sources. This included reports issued by government institutions, ongoing international collaborative research projects, and other mental health interest groups. The final stage was an ongoing process that involved expert consultation to critically review shortlisted studies and suggest additional data sources.

Studies were included if sufficient information was provided on the methodology and sample characteristics to determine the external validity of findings. Cross-sectional or longitudinal studies (with a minimum follow-up period of 2 years) reporting prevalence, incidence, remission or excess mortality associated with bipolar disorder were required. The minimum follow-up period was imposed on longitudinal studies to allow sufficient time for observation of outcomes. For prevalence, we included point (current/past month) or past year estimates. Lifetime estimates were excluded as they are more susceptible to recall bias.[15–18] For incidence, we included rates with person-years of follow-up as the denominator. For remission, we included remission

estimates from prospective general population cohort studies with a naturalistic follow-up of cases until they no longer fulfilled diagnostic criteria for bipolar disorder. For excess mortality, we included estimates of relative risk or a standardized mortality ratio. Included data were collected from samples representative of the general population. Studies were excluded if samples could be considered at greater or lesser risk compared to the general population (e.g. inpatients, pharmacological treatment samples, veterans, or refugees). *Caseness* was established from clinical thresholds proposed by DSM or ICD.[1,2] As stated previously, burden was estimated for the entire spectrum of bipolar disorder simultaneously. Studies reporting separate estimates for bipolar I disorder, bipolar II disorder, cyclothymia, and/or bipolar disorder not otherwise specified were included if sufficient data were provided to sum the disorder-specific estimates. At a minimum, studies needed to report on bipolar I and bipolar II disorder. No limitation was set on the language of publication.

1.3.2 | DisMod-MR 2.0 modelling

The extracted epidemiological data were entered into DisMod-MR 2.0, a Bayesian meta-regression tool used to meta-analyze data on prevalence.[7,19] DisMod-MR 2.0 was based on the same incidence-prevalence-mortality (IPM) mathematical model[19] used in earlier GBD studies. However, unlike DisMod-MR 1.0 (the earlier version of the tool used in GBD 2010) which used a negative-binomial rate model,[19] DisMod-MR 2.0 used a log rate model to estimate prevalence.[7] Due to constraints on computing time, DisMod-MR 1.0 prevalence estimates were limited to a regional consistency check between parameters. The much faster Dismod-MR 2.0 allowed a full "cascade," i.e., a sequence of analyses from: (i) global, (ii) super-regional, (iii) regional, and (iv) country-level estimations. This ensured that prevalence estimates were consistent at all levels of the cascade. At the global level, the country-specific input data from our systematic literature review were used to estimate super-region priors using a mixed effects nonlinear regression model. The super-region models were informed by these priors passed down from the global fit and in turn its results were fed back into regional estimates and then country-level disaggregation. The final DisMod-MR 2.0 output included prevalence by sex, for 20 age groups, six reference years (1990, 1995, 2000, 2005, 2010, and 2013), 21 regions, 188 countries and the subnational locations (11 subregions of the United Kingdom, 31 provinces of China, and 32 states of Mexico) included in the study. The national estimates for the latter three countries were aggregates of the subnational estimates. Rather than exclude countries with absent raw epidemiological data, we made use of data from surrounding countries and regions to predict prevalence for all countries with missing data. Regions were defined according to GBD 2013's grouping of broad geographical regions or continents. Each region consisted of at least two countries, grouped based on country-specific rates of child/adult mortality and major causes of death. More information about the tool has been presented elsewhere.[7,19]

A number of expert prior settings were used to guide the DisMod-MR 2.0 analysis. We assumed zero incidence before age 10 years and after age 80 years as this led to the most plausible fit to the data obtained from our systematic review. Remission was set to a maximum of 0.05 (i.e., 5% per annum) in agreement with expert advice suggesting no, or very little, sustained remission from bipolar disorder.[20,21] Study-level covariates were used to accommodate some of the between-study variability in the raw prevalence data. A prevalence type covariate was used (effect size: 0.51, 95% uncertainty: 0.34–0.75) to adjust all data points derived from point/past-month prevalence upwards, towards the level they would have been if the study had captured 12-month prevalence. We set 12-month prevalence as the desirable level due to the episodic nature of bipolar disorder.[1,2] Estimates of point prevalence surveying symptoms experienced in the past 30 days or less may fail to diagnose cases of bipolar disorder in a residual state, thereby underestimating prevalence. Other potential sources of between-study variability such as sample coverage (community vs national), completeness of bipolar disorder diagnosis (inclusion of bipolar I and II only vs the entire spectrum of bipolar disorder), study response rate (≥80% vs <80% response rate), and version of diagnostic criteria use to define bipolar disorder (DSM or ICD criteria), were investigated using study-level covariates, although none of these had a statistically significant effect on prevalence.[13]

1.4 | Burden quantification

GBD 2013 estimated burden (as YLDs) by multiplying prevalence estimates from DisMod-MR 2.0 by three disability weights representative of the disability experienced during depressive, manic and residual states of bipolar disorder.[7]

1.4.1 | Disability weights

To estimate disability weights in GBD 2013, data from the GBD 2010 Disability Weights Measurement Study[22] were used in addition to data collected from another four European countries.[23,24] In all of these studies, a range of lay descriptions which together reflected all non-fatal outcomes from the diseases and injuries in GBD 2013 were used. Community-based surveys were conducted in Bangladesh, Indonesia, Peru, the United Republic of Tanzania, the USA, Hungary, Italy, Sweden, and the Netherlands. An open-access internet survey in English, Spanish, and Mandarin was also available. These surveys made use of a pair-wise comparison method, asking respondents to nominate which of two randomly selected health states they considered the healthier.[7] Responses were anchored on a scale of 0 (healthy) to 1 (death) using a series of additional questions which compared the benefits of lifesaving and disease prevention programmes for a subset of the 220 GBD 2010 health states. For bipolar disorder, there was only a marginal change between disability weights from GBD 2010 and GBD 2013, within overlapping bounds of uncertainty.[22–24]

In order to capture the range of severity in the presentation of bipolar disorder, disability weights were determined for three health states, generated according to the DSM-IV-TR description of the disorder.[1] These were manic, depressive, and residual health states. A manic state involved elevated, expansive, or irritable mood. A depressive state involved depressed mood, or loss of interest in daily

activities. A residual state involved depressive or manic symptoms which are below the threshold for a manic or depressive episode. A separate review of the literature was also conducted to capture epidemiological survey data on the proportion of bipolar cases in each health state. Health state-specific proportions from six studies were meta-analysed to generate a total proportion of bipolar disorder cases experiencing manic, depressive, and residual states.[25] These were used to allocate total bipolar disorder prevalent cases (estimated by DisMod-MR 2.0) to each health state-specific disability weight. The GBD 2013 lay descriptions, severity proportions and disability weights are summarized in Table 1. The meta-analysis of health state-specific proportions is provided as Supporting Information (Data S2).

1.4.2 | Comorbidity adjustments

In GBD studies, burden is estimated for each cause one by one. As individuals may experience more than one disease or injury at a given point in time, burden estimates were also corrected for comorbidity. To do so, microsimulation methods were used to create hypothetical populations of 40 000 individuals in each age, sex, year, and country combination. Individuals were exposed to the independent probability of experiencing any sequela or combination of sequelae included in GBD 2013. The probability of being exposed to each sequela was equivalent to its prevalence in the population. The combined disability weight for each simulated individual experiencing two or more sequelae was estimated using a multiplicative function, i.e. taken as 1 minus the cross-product of 1 minus the disability weight for each sequela. The difference between the average disability weight in individuals experiencing only one sequela and the multiplicatively combined disability weight in those experiencing two or more sequelae was taken as the "comorbidity correction." The average comorbidity correction for each sequela was applied to the corresponding location-, age-, sex-, and year-specific YLD.

Although probabilities of the co-occurrence of bipolar disorder with other diseases and injuries may be dependent, all probabilities of comorbidity were modelled as independent in GBD 2013 as we could not identify sufficient data to confidently generate these dependent probabilities by age and sex. We explored the contribution of dependent and independent comorbidity in the Medical Expenditure Panel Surveys in the USA and found that independent comorbidity captured most of the comorbidity, once age was accounted for. This supplementary analysis and GBD 2013's methodology for comorbidity correction have been presented in more detail elsewhere.[7,26]

2 | RESULTS

2.1 | Systematic review

Figure 1 summarizes the results of our systematic literature review. The GBD 2010 search strategy identified 36 prevalence and excess all-cause mortality studies.[12,13] The GBD 2013 literature update identified eight additional studies. This culminated in a final data set of 38 prevalence studies from 26 countries and six excess all-cause mortality studies from five countries. Although our review identified two studies reporting the incidence of bipolar disorder, these were excluded from analysis as reported estimates (0% and 0.1%)[27,28] were implausibly low compared to reported prevalence estimates and would have underestimated the incidence of the full spectrum of bipolar disorder across the entire lifespan. There were no studies reporting on complete remission which for GBD purposes was equivalent to cure rather than a reduction in symptom levels. Table 2 shows the countries for which epidemiological data were available for bipolar disorder. A full list of the included data sources is provided as Supporting Information (Data S3).

2.2 | Modelled prevalence data

Using DisMod-MR 2.0, we estimated 32.7 million (95% uncertainty: 28.8–36.5 million) cases of bipolar disorder globally in 1990 and 48.8 million (43.5–54.4 million) in 2013; equivalent to a 49.1% (46.7% to 52.2%) increase in prevalent cases between 1990 and 2013. The increase in prevalent cases was entirely attributed to demographic shifts in population size and age composition between 1990 and 2013. The age-standardized prevalence rate of bipolar disorder remained unchanged between 1990 (0.7%, 0.6%–0.7%) and 2013 (0.7%, 0.6%–0.8%).

Table 3 shows estimated age-standardized prevalence rates for bipolar disorder by sex, year, region and the 25 most populous countries. Rates for all 188 countries are provided as Supporting Information (Table S1). Although there was some variation in prevalence between

TABLE 1 Global Burden of Disease Study 2013 severity proportions and disability weights for bipolar disorder

Health state	Lay description	Severity proportion[a]	Disability weight
Depressive	Has constant sadness and has lost interest in usual activities. The person has some difficulty in daily life, sleeps badly, has trouble concentrating, and sometimes thinks about harming himself (or herself)	0.23 (0.10–0.39)	0.40 (0.27–0.53)
Manic	Is hyperactive, hears and believes things that are not real, and engages in impulsive and aggressive behaviour that endangers the person and others	0.21 (0.12–0.33)	0.49 (0.34–0.65)
Residual	Has mild mood swings, irritability and some difficulty with daily activities	0.52 (0.28–0.77)	0.03 (0.02–0.05)

The table is formulated based on data presented elsewhere.[23–25]

[a]Refers to the proportion of bipolar disorder cases within each health state; severity proportions and disability weight are presented with 95% ranges of uncertainty.

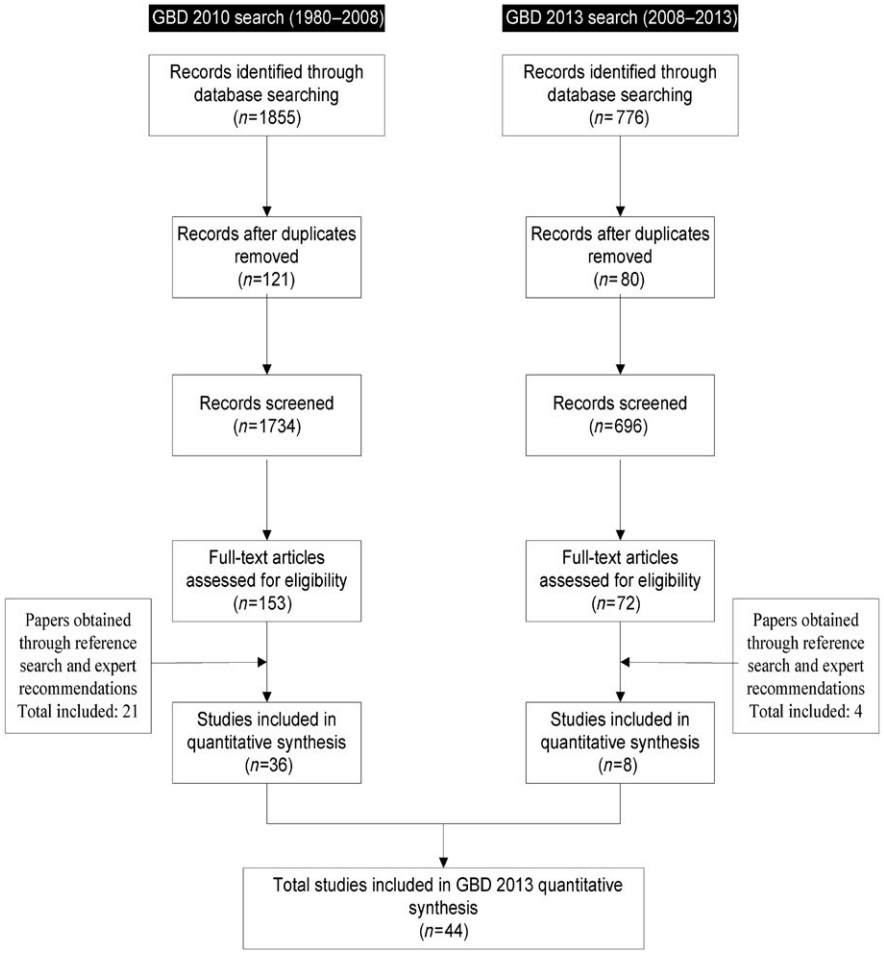

FIGURE 1 Flow chart summarizing findings from the systematic literature review of epidemiological data for bipolar disorder.The literature search conducted for GBD 2010 has also been presented elsewhere[14]

countries, many estimates fell within overlapping bounds of uncertainty when compared to other countries or the global average.

Globally, the male to female prevalence ratio was 0.8 (0.5–1.1) in 2013. Figure 2 illustrates changes in the prevalence of bipolar disorder across the lifespan. Prevalence was evident from 10 years of age, peaked in the early 20s, and then decreased steadily with age thereafter. Figure 3 compares the global prevalence of bipolar disorder across the lifespan for 2013 to the prevalence distribution of other GBD 2013 mental disorders occurring in adulthood (i.e., major depressive disorder, dysthymia, anxiety disorder, and schizophrenia). The distribution of bipolar disorder prevalence across the lifespan resembled that of schizophrenia more so than the other mental disorders. Both these disorders had lower prevalence and similar age distributions compared to major depressive disorder, dysthymia, and anxiety disorder, which had considerably higher prevalence, and were evident at very young ages.

2.3 | Burden of bipolar disorder

Bipolar disorder was responsible for 6.6 million (4.2–9.9 million) DALYs in 1990 and 9.9 million (6.3–14.8 million) DALYs in 2013, all accounted for by YLDs. In 1990, it ranked as the 76th leading cause of global DALYs (explaining 0.3% of total DALYs) and the 19th leading cause of YLDs (explaining 1.2% of total YLDs). In 2013, it ranked as the 54th leading cause of global DALYs (explaining 0.4% of total DALYs) and the 16th leading cause of YLDs (explaining 1.3% of total YLDs).

Among the mental and substance use disorders assessed in GBD 2013, bipolar disorder was the fifth leading cause of DALYs (after major depressive disorder, anxiety disorder, schizophrenia, and alcohol use disorders, respectively). It accounted for 5.7% of the burden due to mental and substance use disorders. In spite of the significantly lower global prevalence of bipolar disorder compared to dysthymia (see Fig. 3), the two disorders explained similar proportions of global DALYs and YLDs given the higher disability weights associated with bipolar disorder.

Given that prevalence rates remained stable over time, there was no statistically significant change in DALY rates between 1990 and 2013. While there was a 49.2% increase in crude DALYs across this time period, this was fully accounted for by population growth and ageing. The age-standardized DALY rates remained stable over time (1990: 134.7, 84.5–200.4 per 100 000; 2013: 136.5, 86.2–202.3 per 100 000). There were 5.5 million (3.5–8.2 million) DALYs recorded for females and 4.4 million (2.8–6.5 million) for males. Figure 4 shows DALYs for bipolar disorder across the life span for both males and females. There were some differences in DALYs between countries, although these were not significantly different from the global mean. DALY rates and their 95% uncertainty intervals by country for 2013 are provided as Supporting Information (Table S2).

TABLE 2 Availability of epidemiological data for bipolar disorder

Location	Prevalence Number of studies	Excess mortality Number of studies
Australasia	4	–
Australia	3	–
New Zealand	1	–
High-income North America	4	1
USA	4	1
Europe, Western	11	4
Denmark	0	1
Finland	1	–
Germany	1	–
Iceland	1	1
Ireland	2	–
Israel	1	–
Italy	2	–
Netherlands	1	–
Norway	2	–
Sweden	0	2
Europe, Central	1	–
Bulgaria	1	–
Romania	1	–
Europe, Eastern	1	–
Russia	1	–
High-income Asia Pacific	5	1
Japan	4	1
South Korea	1	–
Asia, East	4	–
China	4	–
Asia, South	1	–
India	1	–
Asia, Southeast	1	–
Timor-Leste	1	–
Latin America, Southern	1	–
Chile	1	–
Latin America, Central	2	–
Colombia	1	–
Mexico	1	–
Latin America, Tropical	2	–
Brazil	2	–
North Africa/Middle East	2	–
Iraq	1	–
Lebanon	1	–
Sub-Saharan Africa, East	1	–
Ethiopia	1	–

A full list of the included data sources is provided as Supporting Information (Data S3).

3 | DISCUSSION

In GBD 2013, we examined and assembled data available on the epidemiology of bipolar disorder from 1980 onwards. Bipolar disorder was in the top 20 leading causes of disability worldwide, and one of the top five causes of mental and substance use disorder burden. Although the prevalence of bipolar disorder in 2013 was relatively low compared to the prevalence of other diseases and injuries, the high disability weight for a manic episode of bipolar disorder meant that the global rate of bipolar disorder YLDs (138.3 per 100 000) was similar to those of prevalent conditions such as asthma (147.9 per 100 000) and Alzheimer's disease (108.5 per 100 000).

Prevalence and burden rates of bipolar disorder have remained constant over the last 23 years, but demographic shifts caused by declining global mortality rates and increasing mean population age have led to a steady increase in prevalent cases and crude burden. It is important that health systems begin planning for services that have the capability to address this increase in burden. Although past GBD studies have resulted in increased global attention being paid to mental and substance use disorders as a whole, there remains few policy initiatives to address their burden.[12,29] Treatment rates remain low and relatively few resources are spent on mental health. In low-income countries, approximately 0.5% of the total health budget is assigned to mental health, compared to 2.4% in middle-income countries and 5.1% in high-income countries.[30,31] This is disproportionate to the proportion of all-cause burden due to mental and substance use disorders. When split by the Commonwealth's grouping of high-, middle- and low-income countries, 10.7% of total burden in high-income countries was due to mental and substance use disorders compared to 5% in middle-income countries and 5.2% in low-income countries in 2013.[32]

In spite of this, effective intervention strategies exist for bipolar disorder. With better coverage, these have the potential to reduce its burden to some extent. Pharmacotherapy remains the recommended first-line therapy for manic, depressive and residual states.[33] First- and second-generation antipsychotics (including haloperidol, risperidone, olanzapine, quetiapine, aripiprazole, asenapine, carbamazepine, and ziprasidone), anticonvulsants (including sodium valproate), and lithium have all demonstrated efficacy in managing acute mania.[34] Lithium, quetiapine and the anticonvulsant lamotrigine are recommended first-line treatments for acute bipolar I disorder.[35] Lithium, lamotrigine and quetiapine are also recommended first-line residual therapy.[33] The addition of psychological therapies such as psychoeducation and cognitive behaviour therapy to pharmacotherapy can further prevent and delay relapse[36] potentially via improved treatment adherence.[37]

These intervention strategies have the potential to alleviate the severity (and therefore the disability weight) of bipolar disorder but full remission is rare.[1] Using data from the National Survey of Mental Health and Wellbeing in Australia, Andrews and collaborators estimated the proportion of burden due to bipolar disorder that could be averted in a hypothetical situation where everyone with bipolar disorder in the population received complete evidence-based interventions. Only 40% of the burden due to bipolar disorder could be averted using current best practices.[38] Although this identifies bipolar disorder as a condition where preventive intervention strategies could be beneficial, these are far from established. GBD 2013's capacity to estimate prevalence and burden by age, sex and country has the potential to assist in the selection, modification and delivery of

TABLE 3 Age-standardized prevalence rates [% (95% uncertainty)] of bipolar disorder by sex, year, region, and the 25 most populous countries included in the Global Burden of Disease Study 2013

	1990		2013	
Country	**Female**	**Male**	**Female**	**Male**
Global	0.8 (0.7–0.8)	0.6 (0.5–0.7)	0.8 (0.7–0.8)	0.6 (0.5–0.7)
High-income Asia Pacific	0.7 (0.6–0.8)	0.6 (0.5–0.6)	0.7 (0.6–0.8)	0.6 (0.5–0.6)
Japan	0.7 (0.6–0.8)	0.6 (0.5–0.7)	0.7 (0.6–0.8)	0.6 (0.4–0.7)
Southeast Asia	0.7 (0.6–0.8)	0.6 (0.5–0.7)	0.7 (0.6–0.8)	0.6 (0.5–0.7)
Indonesia	0.7 (0.6–0.8)	0.6 (0.5–0.7)	0.7 (0.6–0.8)	0.6 (0.5–0.7)
Philippines	0.7 (0.6–0.9)	0.6 (0.5–0.7)	0.7 (0.6–0.8)	0.6 (0.5–0.7)
Vietnam	0.7 (0.6–0.8)	0.6 (0.5–0.7)	0.7 (0.6–0.8)	0.6 (0.5–0.7)
Thailand	0.7 (0.6–0.9)	0.6 (0.5–0.7)	0.7 (0.6–0.8)	0.6 (0.5–0.7)
Myanmar	0.7 (0.6–0.8)	0.6 (0.5–0.7)	0.7 (0.6–0.8)	0.6 (0.5–0.7)
East Asia	0.6 (0.5–0.7)	0.5 (0.4–0.5)	0.6 (0.5–0.7)	0.5 (0.4–0.5)
China	0.6 (0.5–0.7)	0.5 (0.4–0.5)	0.6 (0.5–0.7)	0.5 (0.4–0.5)
Central Asia	0.8 (0.7–0.9)	0.6 (0.5–0.7)	0.8 (0.7–0.9)	0.6 (0.5–0.7)
South Asia	0.8 (0.7–0.9)	0.6 (0.6–0.7)	0.8 (0.7–0.9)	0.6 (0.5–0.7)
India	0.8 (0.7–0.9)	0.6 (0.6–0.7)	0.8 (0.7–0.9)	0.6 (0.5–0.7)
Pakistan	0.8 (0.7–0.9)	0.6 (0.6–0.7)	0.8 (0.7–0.9)	0.6 (0.5–0.7)
Bangladesh	0.8 (0.7–0.9)	0.6 (0.5–0.7)	0.8 (0.7–0.9)	0.6 (0.6–0.7)
Oceania	0.7 (0.5–0.8)	0.5 (0.4–0.6)	0.7 (0.5–0.8)	0.5 (0.4–0.6)
Australasia	1 (0.8–1.1)	0.8 (0.7–0.9)	1 (0.8–1.1)	0.8 (0.7–0.9)
High-income North America	0.8 (0.7–0.9)	0.7 (0.6–0.8)	0.8 (0.7–0.9)	0.7 (0.6–0.8)
USA	0.8 (0.7–0.9)	0.7 (0.6–0.8)	0.8 (0.7–0.9)	0.7 (0.6–0.8)
Andean Latin America	0.9 (0.7–1)	0.7 (0.6–0.8)	0.9 (0.7–1)	0.7 (0.6–0.8)
Central Latin America	1 (0.8–1.1)	0.8 (0.7–0.9)	1 (0.8–1.1)	0.8 (0.7–0.9)
Mexico	1 (0.8–1.1)	0.7 (0.6–0.9)	1 (0.8–1.1)	0.7 (0.6–0.9)
Southern Latin America	0.9 (0.8–1)	0.6 (0.6–0.7)	0.9 (0.8–1)	0.7 (0.6–0.7)
Tropical Latin America	0.8 (0.7–0.9)	0.7 (0.6–0.8)	0.8 (0.7–1)	0.7 (0.6–0.8)
Brazil	0.8 (0.7–1)	0.7 (0.6–0.8)	0.8 (0.7–1)	0.7 (0.6–0.8)
Caribbean	0.9 (0.7–1)	0.7 (0.6–0.8)	0.9 (0.8–1)	0.7 (0.6–0.8)
Western Europe	0.8 (0.7–0.9)	0.6 (0.5–0.6)	0.8 (0.7–0.9)	0.6 (0.5–0.6)
Germany	0.8 (0.7–0.9)	0.5 (0.4–0.6)	0.8 (0.7–1)	0.5 (0.4–0.6)
France	0.8 (0.7–1)	0.6 (0.5–0.7)	0.8 (0.7–1)	0.6 (0.5–0.7)
UK	0.8 (0.7–1)	0.6 (0.5–0.7)	0.8 (0.7–0.9)	0.6 (0.5–0.7)
Italy	0.9 (0.7–1)	0.6 (0.5–0.7)	0.8 (0.7–1)	0.6 (0.5–0.7)
Central Europe	0.8 (0.7–0.9)	0.6 (0.5–0.7)	0.8 (0.7–0.9)	0.6 (0.5–0.7)
Eastern Europe	0.8 (0.7–0.9)	0.6 (0.5–0.7)	0.8 (0.7–0.9)	0.6 (0.5–0.7)
Russia	0.8 (0.7–0.9)	0.6 (0.5–0.7)	0.8 (0.7–0.9)	0.6 (0.5–0.7)
North Africa and Middle East	0.9 (0.8–1)	0.7 (0.6–0.8)	0.9 (0.8–1)	0.7 (0.6–0.8)
Egypt	0.9 (0.8–1)	0.7 (0.6–0.8)	0.9 (0.8–1)	0.7 (0.6–0.8)
Iran	0.9 (0.8–1)	0.7 (0.6–0.8)	0.9 (0.8–1)	0.7 (0.6–0.8)
Turkey	0.9 (0.8–1)	0.7 (0.6–0.8)	0.9 (0.8–1)	0.7 (0.6–0.8)
Central Sub-Saharan Africa	0.8 (0.7–0.9)	0.6 (0.6–0.7)	0.8 (0.7–0.9)	0.6 (0.6–0.7)
Democratic Republic of the Congo	0.8 (0.7–0.9)	0.6 (0.6–0.7)	0.8 (0.7–0.9)	0.6 (0.5–0.7)
Eastern Sub-Saharan Africa	0.8 (0.7–0.9)	0.6 (0.6–0.7)	0.8 (0.7–0.9)	0.6 (0.6–0.7)
Ethiopia	0.8 (0.7–0.9)	0.6 (0.5–0.7)	0.8 (0.7–0.9)	0.6 (0.6–0.7)
Southern Sub-Saharan Africa	0.8 (0.7–0.9)	0.6 (0.6–0.7)	0.8 (0.7–0.9)	0.6 (0.5–0.7)
South Africa	0.8 (0.7–0.9)	0.6 (0.6–0.7)	0.8 (0.7–0.9)	0.6 (0.5–0.7)
Western Sub-Saharan Africa	0.8 (0.7–0.9)	0.6 (0.6–0.7)	0.8 (0.7–0.9)	0.6 (0.6–0.7)
Niger	0.8 (0.7–0.9)	0.6 (0.5–0.7)	0.8 (0.7–0.9)	0.6 (0.5–0.7)

The table is formulated based on data presented elsewhere[7]; past-year prevalence estimates are presented.

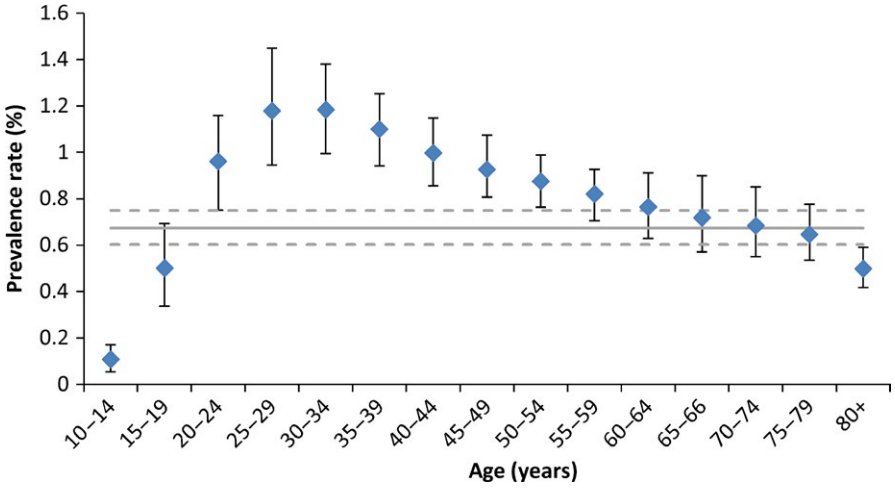

FIGURE 2 Global prevalence rates of bipolar disorder in 2013, by age. Past-year prevalence is estimated from 10 years onwards. Solid grey line: age-standardized prevalence rate; broken grey lines: 95% uncertainty around age-standardized prevalence rate

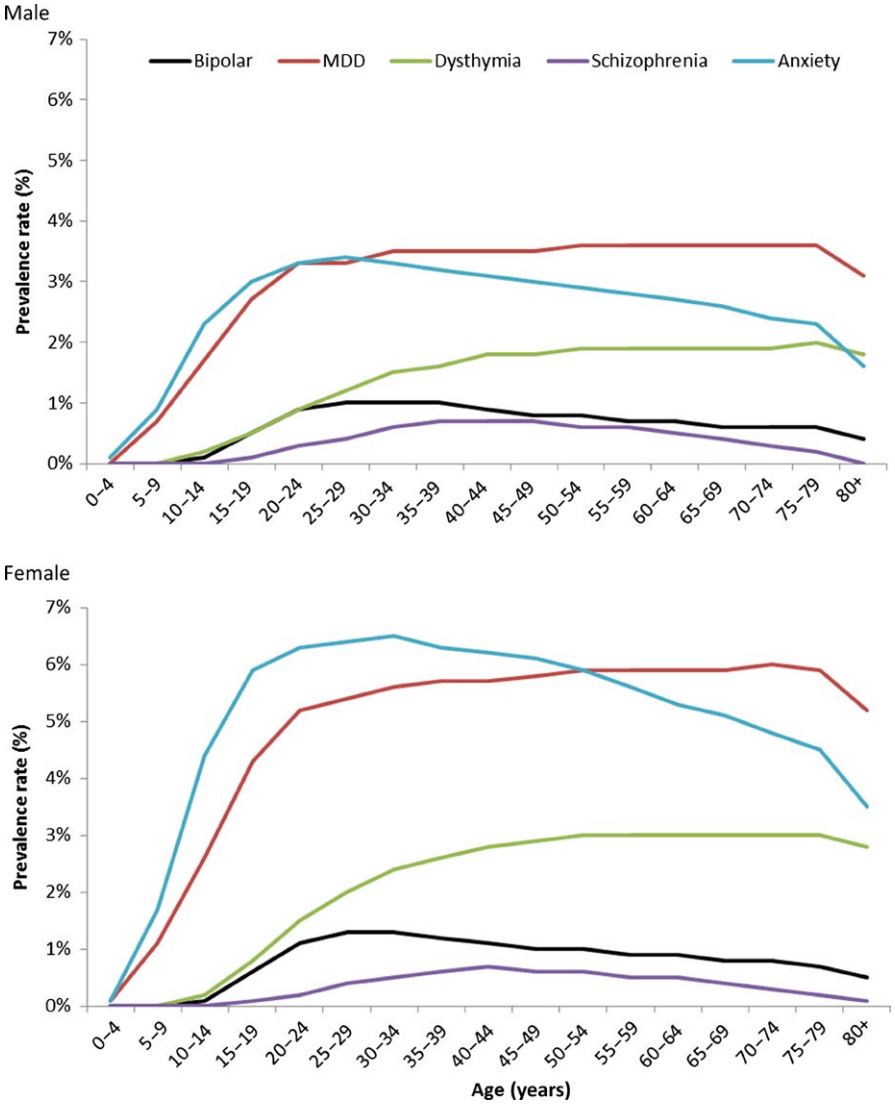

FIGURE 3 Prevalence rates of bipolar disorder in 2013, by age and sex, compared to other Global Burden of Disease Study 2013 (GBD 2013) mental disorders common in adulthood. MDD = major depressive disorder. Current prevalence is presented for all disorders except for bipolar disorder, where past-year prevance is presented

such intervention strategies. Accurate early detection and intervention during the prodromal stages of bipolar disorder may help avert burden by decreasing symptom severity and preventing progression to full disorder status.[39] Although initial detection of bipolar disorder is often difficult, there is some emerging evidence that screening for subthreshold symptoms, certain illness and course phenomena, behavioural regulation, temperament and family history of bipolar may improve early detection.[40]

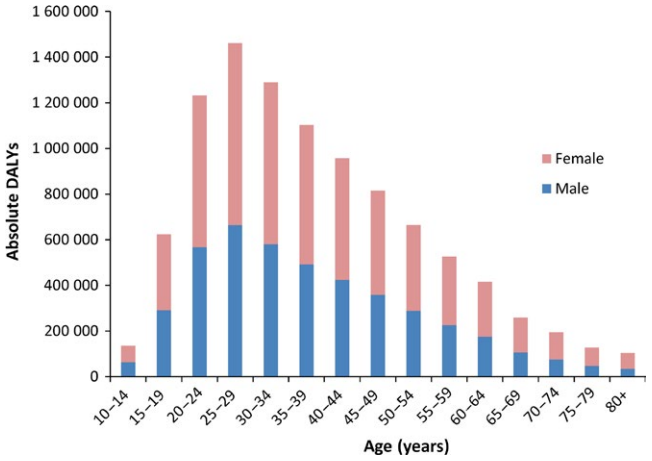

FIGURE 4 Bipolar disorder disability-adjusted life years (DALYs) in 2013, by age and sex

3.1 | Limitations

A number of methodological limitations need to be considered when interpreting our findings. There was an overall paucity of epidemiological data for bipolar disorder. Raw epidemiological data meeting our inclusion criteria were available for prevalence and to a lesser extent excess mortality, where we turned to studies using clinical samples or incomplete bipolar spectrum diagnoses. Expert prior settings on remission and a minimum age of onset were used to further inform our DisMod-MR 2.0 model. For remission, because there were no studies available reporting on complete remission, we made use of a very low remission rate in our DisMod-MR 2.0 modelling derived from expert consensus. For burden estimation purposes, a residual state of bipolar disorder was defined as milder symptoms of bipolar disorder which still imposed disability. Remission, on the other hand, referred to cases no longer meeting diagnostic criteria for the disorder and hence making no contribution to disability.[25] Unfortunately, boundaries between a residual state and complete remission are not clearly stipulated in the bipolar disorder literature. Given that individuals with bipolar disorder typically spend more time in a residual state,[25] their long-term prognosis is often between that of acute symptomatology and complete recovery.[20,21] We found only two studies investigating the incidence of bipolar disorder, both of which reported estimates that were very low when compared to reported prevalence estimates. Both these studies estimated the incidence of bipolar disorder within an adolescent school sample aged between 14 and 18 years which may not be representative of incidence across the entire lifespan.[27,28]

The epidemiological data available were also unevenly distributed between world regions. Even for prevalence (the epidemiological parameter for which we had the most data) there was a paucity of data from low- and middle-income countries. Using DisMod-MR 2.0 we also estimated prevalence for countries with no data. This strategy is by no means preferable to generation of high-quality raw data, but it enabled us to include countries with no prevalence data in burden of disease analyses. Excluding such countries from GBD 2013 would be equivalent to ignoring the existence of diseases for which we currently have no data. More representative epidemiological data are slowly emerging from low- and middle-income countries. The findings of the current study demonstrate the need for statistical authorities in countries with poor data coverage to promote more and better quality data collection on the epidemiology of bipolar disorder. Until then, it is important to consider the uncertainty ranges around our final estimates when interpreting findings.

The accuracy of burden estimates also depends on the representativeness of disability weights estimated for bipolar disorder. It is unclear whether brief lay descriptions such as those presented in Table 1 can accurately capture the complexity of the disability due to bipolar disorder. Although GBD 2013 replicated the disability weights survey in Hungary, Italy, Sweden, and the Netherlands, only the lay description for a depressive episode was included in these surveys. Disability weights for manic and residual states of bipolar disorder were informed by the GBD 2010 disability weights surveys. Replication of the disability weights survey to further test the different lay descriptions used in GBD 2013 is required for more definite conclusions. It is also important to note that GBD disability weights were designed to capture "within-the-skin" health loss; broader welfare and psychosocial losses, although important, were not captured. Narrowing the definition of disability weights to within-the-skin health loss likely explains why health state valuations were very similar between survey sites in both GBD 2010 and GBD 2013, which in turn facilitated the comparability of burden estimates between settings.[22,23] Nevertheless, as bipolar disorder is often accompanied by significant losses to economic, social, and academic functioning,[41,42] the exclusion of welfare loss leads to an underestimate of the true burden attributable to this disorder and could mask differences between countries in the non-health component of welfare loss.

Finally, despite evidence to show an increased risk of mortality in those with bipolar disorder,[43–45] GBD 2013 found no deaths directly attributable to bipolar disorder and therefore no YLLs. This was because GBD 2013 made use of ICD-10 cause of death classifications which can only assign a death to its direct, rather than underlying, cause.[2] Deaths due to other causes occurring as a result of bipolar disorder were represented elsewhere in the GBD 2013 list of causes. The lack of YLLs is contrasted by literature demonstrating a significantly increased risk of death and decreased life expectancy in those with bipolar disorder compared to the general population.[46,47] All-cause mortality from bipolar disorder and cause-specific mortality from cardiovascular disease, diabetes mellitus, chronic obstructive pulmonary disease, influenza or pneumonia, unintentional injuries, and suicide are increased in those with bipolar disorder compared to the general population.[48] For instance, a supplementary comparative risk assessment analysis of GBD 2010 data showed that, when bipolar disorder was assessed as a risk factor for suicide, 5.4% of deaths and YLLs allocated to suicide in the study (falling under the injuries cause group in GBD 2013) could be attributed back to bipolar disorder. The inclusion of attributable suicide DALYs would have increased the overall burden due to bipolar disorder from 0.5% (0.3%–0.8%) to 0.6% (0.4%–0.8%) and would have changed the global ranking from 46th to 44th leading cause of burden.[49]

4 | CONCLUSIONS

GBD 2013 estimated the prevalence and burden of bipolar disorder by country, region, age, sex, and year. We sought to improve on findings from previous burden of disease studies by expanding the epidemiological data set and improving the methodology used to estimate burden. Although some limitations and areas for further improvement have been highlighted, the implications of our findings are far from trivial. Results show that, despite being relatively rare, bipolar disorder is a disabling illness due to its early onset, severity and chronicity. Current trends in growth and aging are leading to an increase in the burden of bipolar disorder over time. It is important that resources be directed towards not only improving the coverage of evidence-based intervention strategies for bipolar disorder but also establishing preventive strategies to prevent new cases of the disorder from occurring.

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DISCLOSURES

The authors of this paper do not have any commercial associations that might pose a conflict of interest in connection with this manuscript.

AUTHOR CONTRIBUTIONS

AJF, with guidance from TV, HAW, and other members of the GBD group, assembled the input data and conducted analyses to generate burden estimates for bipolar disorder. AJF wrote the first draft of this manuscript and all other co-authors contributed to subsequent drafts. All authors contributed to and approved the final manuscript.

REFERENCES

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)*. Fourth Edition, Text Revision ed. Washington DC: American Psychiatric Association; 2000.
2. World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders. Clinical Descriptions and Diagnostic Guidelines*. Geneva: World Health Organization; 1992.
3. Hirschfeld RM. The efficacy of atypical antipsychotics in bipolar disorders. *J Clin Psychiatry*. 2003;64(Suppl 8):15–21.
4. Lish JD, Dime-Meenan S, Whybrow PC, Price RA, Hirschfeld RM. The National Depressive and Manic-depressive Association (DMDA) survey of bipolar members. *J Affect Disord*. 1994;31:281–294.
5. Chisholm D, van Ommeren M, Ayuso-Mateos JL, Saxena S. Cost-effectiveness of clinical interventions for reducing the global burden of bipolar disorder. *Br J Psychiatry*. 2005;187:559–567.
6. Andrews G. Reducing the burden of depression. *Can J Psychiatry*. 2008;53:420–427.
7. Global Burden of Disease Study Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2015;386:743–800.
8. GBD Mortality Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2015;385:117–171.
9. GBD DALYs Hale Collaborators. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990-2013: quantifying the epidemiological transition. *Lancet*. 2015;386:2145–2191.
10. World Bank. *World Development Report 1993. Investing in Health: World Development Indicators*. New York: World Bank; 1993.
11. Murray CJL, Vos T, Lozano R et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2197–2223.
12. Whiteford HA, Degenhardt L, Rehm J et al. The global burden of mental and substance use disorders, 2010. *Lancet*. 2013;382:1575–1586.
13. Ferrari AJ, Baxter AJ, Whiteford HA. A systematic review of the global distribution and availability of prevalence data for bipolar disorder. *J Affect Disord*. 2010;34(1–3):1–13.
14. Moher D, Liberati A, Tetzlaff J, Altman DG, The PG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. *PLoS Med*. 2009;6:e1000097.
15. Kruijshaar ME, Barendregt J, Vos T, de Graaf R, Spijker J, Andrews G. Lifetime prevalence estimates of major depression: an indirect estimation method and a quantification of recall bias. *Eur J Epidemiol*. 2005;20:103–111.
16. Moffitt TE, Caspi A, Taylor AJ et al. How common are common mental disorders? Evidence that lifetime prevalence rates are doubled by prospective versus retrospective ascertainment. *Psychol Med*. 2010;40:899–909.
17. Simon GE, VonKorff M. Recall of psychiatric history in cross-sectional surveys: implications for epidemiologic research. *Epidemiol Rev*. 1995;17:221–227.
18. Susser E, Shrout PE. Two plus two equals three? Do we need to rethink lifetime prevalence? A commentary on 'How common are common mental disorders? Evidence that lifetime prevalence rates are doubled by prospective versus retrospective ascertainment' by Moffitt et al. (2009). *Psychol Med*. 2010;40:895–897.
19. Flaxman A, Murray C, Vos T, eds. *Integrated Meta-regression Framework for Descriptive Epidemiology*. Seattle, WA: University of Washington Press; 2015.
20. Angst J, Sellaro R. Historical perspectives and natural history of bipolar disorder. *Biol Psychiatry*. 2000;48:445–457.
21. Colom F, Vieta E. The road to DSM-V. Bipolar disorder episode and course specifiers. *Psychopathology*. 2009;42:209–218.
22. Salomon JA, Vos T, Hogan DR et al. Common values in assessing health outcomes from disease and injury: disability weights mea-

surement study for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2129–2143.
23. Salomon JA, Haagsma JA, Davis A et al. Disability weights for the Global Burden of Disease 2013 study. *Lancet Glob Health*. 2015;3:e712–e723.
24. Haagsma JA, Noordhout C, Polinder S et al. Assessing disability weights based on the responses of 30 660 people from four European countries. *Popul Health Metr*. 2015;13:10.
25. Ferrari AJ, Saha S, McGrath JJ et al. Health states for schizophrenia and bipolar disorder within the Global Burden of Disease 2010 Study. *Popul Health Metr*. 2012;10:16.
26. Vos T, Flaxman AD, Naghavi M et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2163–2196.
27. Lewinsohn PM, Hops H, Roberts RE, Seeley JR, Andrews JA. Adolescent psychopathology: I. Prevalence and incidence of depression and other DSM-III-R disorders in high school students. *J Abnorm Psychol*. 1993;102:133–144.
28. Lewinsohn PM, Klein DN, Seeley JR. Bipolar disorders in a community sample of older adolescents: prevalence, phenomenology, comorbidity, and course. *J Am Acad Child Adolesc Psychiatry*. 1995;34:454–463.
29. Murray CJL, Lopez AD, eds. *The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability From Diseases, Injuries, and Risk Factors in 1990 and Projected to 2020*. Cambridge: Harvard University Press; 1996.
30. Tomlinson M. Global mental health: a sustainable post Millennium Development Goal? *Int Health*. 2013;5:1–3.
31. World Health Organization. Mental Health Atlas. 2011. Available from: http://www.who.int/mental_health/publications/mental_health_atlas_2011/en/. Accessed January 12, 2016.
32. Institute for Health Metrics and Evaluation. GBD compare. 2015. Available from: http://vizhub.healthdata.org/gbd-compare/. Accessed January 5, 2016.
33. Yatham LN, Kennedy SH, Parikh SV et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) collaborative update of CANMAT guidelines for the management of patients with bipolar disorder: update 2013. *Bipolar Disord*. 2013;15:1–44.
34. Cipriani A, Barbui C, Salanti G et al. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. *Lancet*. 2011;378:1306–1315.
35. Vieta E, Locklear J, Gunther O et al. Treatment options for bipolar depression: a systematic review of randomized, controlled trials. *J Clin Psychopharmacol*. 2010;30:579–590.
36. Lam DH, Burbeck R, Wright K, Pilling S. Psychological therapies in bipolar disorder: the effect of illness history on relapse prevention—a systematic review. *Bipolar Disord*. 2009;11:474–482.
37. Miklowitz DJ, Scott J. Psychosocial treatments for bipolar disorder: cost-effectiveness, mediating mechanisms, and future directions. *Bipolar Disord*. 2009;11(Suppl. 2):110–122.
38. Andrews G, Issakidis C, Sanderson K, Corry J, Lapsley H. Utilising survey data to inform public policy: comparison of the cost-effectiveness of treatment of ten mental disorders. *Br J Psychiatry*. 2004;184:526–533.
39. Salvatore P, Baldessarini RJ, Tohen M et al. The McLean-Harvard First Episode Project: two-year stability of DSM-IV diagnoses in 500 first-episode psychotic disorder patients. *J Clin Psychiatry*. 2009;70:458–466.
40. Ratheesh A, Berk M, Davey CG, McGorry PD, Cotton SM. Instruments that prospectively predict bipolar disorder—A systematic review. *J Affect Disord*. 2015;179:65–73.
41. Fajutrao L, Locklear J, Priaulx J, Heyes A. A systematic review of the evidence of the burden of bipolar disorder in Europe. *Clin Pract Epidemiol Ment Health*. 2009;5:3.
42. Woods SW. The economic burden of bipolar disease. *J Clin Psychiatry*. 2000;61(Supp 13):38–41.
43. Harris EC, Barraclough B. Suicide as an outcome for mental disorders: a meta-analysis. *Br J Psychiatry*. 1997;170:205–228.
44. Harris EC, Barraclough B. Excess mortality of mental disorder. *Br J Psychiatry*. 1998;173(JULY):11–53.
45. Ramsey CM, Spira AP, Mojtabai R, Eaton WW, Roth K, Lee HB. Lifetime manic spectrum episodes and all-cause mortality: 26-year follow-up of the NIMH Epidemiologic Catchment Area Study. *J Affect Disord*. 2013;151:337–342.
46. Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. *JAMA Psychiatry*. 2015;72:334–341.
47. Charlson FJ, Baxter AJ, Dua T, Degenhardt L, Whiteford HA, Vos T. Excess mortality from mental, neurological and substance use disorders in the Global Burden of Disease Study 2010. *Epidemiol Psychiatr Sci*. 2015;24:121–140.
48. Crump C, Sundquist K, Winkleby MA, Sundquist J. Comorbidities and mortality in bipolar disorder: a Swedish national cohort study. *JAMA Psychiatry*. 2013;70:931–939.
49. Ferrari AJ, Norman RE, Freedman G et al. The burden attributable to mental and substance use disorders as risk factors for suicide: findings from the Global Burden of Disease Study 2010. *PLoS ONE*. 2014;9:e91936.

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