Published in final edited form as:

Gen Hosp Psychiatry. 2014 ; 36(1): . doi:10.1016/j.genhosppsy.2013.09.008.

The prevalence of bipolar disorder in general primary care samples: a systematic review

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Abstract

Objective—To obtain an estimate of the prevalence of bipolar disorder in primary care.

Methods—We used the PRISMA method to conduct a systematic review in January 2013. We searched seven databases with a comprehensive list of search terms. Included articles had a sample size of 200 patients or more and assessed bipolar disorder using a structured clinical interview or bipolar screening questionnaire in random adult primary care patients. Risk of bias in each study was also assessed.

Results—We found 5595 unique records in our search. Fifteen studies met our inclusion criteria. The percentage of patients with bipolar disorder found on structured psychiatric interviews in 10 of 12 studies ranged from 0.5% to 4.3%, and a positive screen for bipolar disorder using a bipolar disorder questionnaire was found in 7.6% to 9.8% of patients.

Conclusion—In 10 of 12 studies using a structured psychiatric interview, approximately 0.5% to 4.3% of primary care patients were found to have bipolar disorder, with as many as 9.3% having bipolar spectrum illness in some settings.. Prevalence estimates from studies using screening measures which have been found to have low positive predictive value were generally higher than those found using structured interviews.

Keywords

bipolar disorder; primary care

1. Background

Understanding the prevalence of major depression and anxiety disorders in primary care patients has led to the development of clinical interventions aiming to improve recognition

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Prior presentations: None

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and treatment of these disorders in primary care. For example, the prevalence of major depression in primary care is 5–10% (1). A higher percentage of major depression is found in some subgroups of patients, such as 12–18% of patients with diabetes and 15–23% of patients with heart disease (2). With this knowledge, investigators developed population-based interventions for primary care patients with depression (3), diabetes and depression (4), and depression and diabetes and/or heart disease (5) that significantly improved quality of care of patients with depression. Other investigators showed that one or more of four anxiety disorders occurred in approximately 20% of primary care patients (6). A subsequent clinical trial showed that treating patients with anxiety disorders in primary care with a collaborative care intervention was associated with a greater reduction in anxiety symptoms, compared to usual care (7). Compared to the existing literature on major depression and anxiety disorders in primary care, less is known about the prevalence of other psychiatric disorders such as bipolar disorder.

The lifetime prevalence of bipolar disorder in community samples from the National Comorbidity Survey Replication (NCS-R) is 1.0% for bipolar I disorder, 1.1% for bipolar II disorder, and 2.4% for sub-threshold bipolar disorder symptoms (8). Despite this established prevalence in the community, the prevalence of bipolar disorder in clinical primary care populations is not as well-defined partly due to the use of a variety of methods to diagnose bipolar disorder in these studies (9). It is important to have an estimate of bipolar disorder prevalence in primary care because knowledge of disease prevalence can influence accurate disease recognition (10).

Unfortunately, in many patients with bipolar disorder, there is often a gap of 10 years between the onset of symptoms and impairment and the diagnosis of bipolar disorder, arguing for an opportunity to enhance recognition in clinical settings (11). Primary care settings offer an opportunity for earlier recognition of bipolar disorder because patients with bipolar disorder are likely to initially present to primary care for several reasons. Patients with bipolar disorder commonly experience general medical problems such as diabetes, and are seen in primary care settings for care of those illnesses (12,13). Additionally, patients with bipolar disorder have been shown to experience syndromal or subsyndromal depressive symptoms one third to one half of the time in longitudinal studies (14,15). Patients with bipolar disorder experiencing depression will likely initially present to primary care for treatment (16). Patients with bipolar illness also have high rates of anxiety and substance use disorders that often lead to seeking medical treatment for somatic symptoms (8). Furthermore, few patients with bipolar disorder receive consistent specialty psychiatric care (16), making it even more likely that patients experiencing recurrence of depressive symptoms will present to primary care.

In this paper, we aimed to obtain an estimate of the prevalence of bipolar disorder in the general primary care population by systematically reviewing the literature.

2. Methods

Our systematic review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method (17). A protocol for this review was not registered or published before conducting the review. We decided a priori to perform a qualitative systematic review only.

2.1 Risk of bias

Part of the PRISMA method involves measuring studies' risk of bias using the Cochrane Risk of Bias Tool (18), which measures risk of bias of intervention studies. We used an alternate measure developed specifically for assessing risk of bias in prevalence studies (19).

The risk of bias tool consisted of 10 yes/no items, including 4 measures of external validity (ie whether the sample was representative of the target population) and 6 measures of internal validity (ie whether the study instrument used to define a case was reliable and valid). For example, answering “yes” to Item 6 from the measure (“*Was an acceptable case definition used in the study?*”) would indicate that the study was at low risk of bias, while answering “no” would indicate the study was at high risk of bias for that item.

The first item from the risk of bias tool asked whether the study was “a close representation of the national population”. The target population for this review (primary care population) is known to be different from the national population, and is not representative of a national sample. Therefore, we omitted the first item in our assessment of each study’s risk of bias, reducing the total number of items and highest possible score to 9.

Studies with scores of 8 or 9 (8 or 9 “yes” answers) were considered to have low risk of bias, studies with scores of 7 were considered to have moderate risk of bias, and studies with scores of 6 or less were considered to have high risk of bias. The answer to a risk of bias item was considered “no” (ie the bias occurred in that study) if the study did not comment on the presence or absence of the item (19).

2.2 Search technique

We searched PubMed, Embase, CINAHL Plus, PsychInfo and 3 sections of the Cochrane Library, Cochrane Database of Systematic Reviews, Database of Abstracts of Review of Effects and Cochrane Central Register of Controlled Trials. Databases were searched from their inception to January 15, 2013. We retrieved 6,149 total citations. To identify and remove duplicate citations, we used Endnote software. After removing 555 duplicate citations, 5,594 remained for screening. One additional citation was identified and screened after the search was completed. Abstract screening was conducted by one author.

We searched PubMed database using a combination of MeSH headings and words occurring in the title or abstracts of PubMed records. Our search was limited to English language results. Editorials, letters and comments were excluded a priori. To capture the citations relating to primary care these terms were combined with an “OR.” (“Primary Health Care” [Mesh] OR “Physicians, Primary Care” [Mesh] OR “Primary Care Nursing” [Mesh] OR “Nurse Practitioners” [Mesh] OR “Internal Medicine” [Mesh:noexp] OR “Adolescent Medicine” [Mesh] OR “General Practice” [Mesh] OR “Military Medicine” [Mesh] OR “Community Medicine” [Mesh] OR “Family Physicians” [Mesh] OR “primary care” [tiab] OR “general practice” [tiab] OR “general practitioner” [tiab] OR “general practitioners” [tiab] OR “nurse practitioner” [tiab] OR “nurse practitioners” [tiab] OR “family medicine” [tiab] OR “family practice” [tiab] OR “family physician” [tiab] OR “family physicians” [tiab]). These primary care concepts were then combined with the following terms: (“Affective Disorders, Psychotic” [Mesh] OR “Mental Disorders” [Mesh:noexp] OR bipolar [tiab] OR mania [tiab] OR manic [tiab] OR “manic depression” [tiab] OR “manic depressive” [tiab]). The PubMed strategy was then replicated in each database listed above.

2.3 Eligibility

Article titles and selected abstracts found in the search were screened for relevance to the topic. Relevant articles were then selected, and full text articles were assessed for eligibility. Eligible articles included studies in English that either diagnosed bipolar disorder using a clinical examination or standardized interview, or used a bipolar disorder screening measure, in adults 18 years and older in primary care. Selected studies’ reference lists were also scanned to find additional studies.

2.4 Exclusion

Excluded studies included those focusing on populations outside of primary care such as mental health settings or community settings. Other exclusion criteria included not assessing for the presence of bipolar disorder, examining bipolar disorder prevalence in a sample of patients with an established psychiatric disorder or complaint, samples with fewer than 200 patients (due to lack of a representative sample), or studies on children or adolescents.

2.5 Data abstraction

Information on each study was abstracted independently by one author onto a data collection tool. Abstracted information included how the primary care sample was obtained, population studied, sample size, age and sex characteristics of the population, method of diagnosing bipolar disorder or screening tool used, and prevalence measurement. The main summary measure was estimated prevalence of bipolar disorder.

3. Results

3.1 Search results

The results of our search are shown in the PRISMA flow diagram (Figure 1). We obtained 6149 results, which included 5594 unique records. One additional record was found after the search was conducted. Therefore we screened the titles and abstracts of 5595 records. The full text of 280 studies was assessed for eligibility. Fourteen studies met our inclusion criteria, and one additional study was identified in one study's reference list, leaving 15 studies (19–33) for inclusion in the qualitative synthesis. The studies' findings are summarized in Table 1. Risk of bias in each study is described below.

3.2 Studies using structured interviews

Twelve studies (20–31) used a structured interview to diagnose bipolar disorder, bipolar spectrum illness or prior history of mania in primary care patients. Four studies used the MINI International Neuropsychiatric Interview (MINI) (20, 25, 30, 31), three used the PRIME-MD (26–28), two used the Diagnostic Interview Schedule (DIS) (21, 22), and one study each used the Clinical Interview Schedule (23), Present State Examination 9th Version (24) and a 79 question structure questionnaire plus clinical examination by a psychiatrist (29). The percentage of patients with bipolar disorder found on structured interviews ranged from 0.5% to 11.4%. Of the twelve studies, ten found a prevalence of bipolar disorder between 0.5 to 4.3%. Two studies found higher percentages of 9.3% (when including “bipolar spectrum”) and 11.4% (in a setting with a higher than usual prevalence of psychiatric disorders) respectively.

Olfson, et al. (20) used the MINI to study a random group of primary care patients (n=1001) with scheduled appointments in a large health maintenance organization and found bipolar disorder in 1.2% of patients. Notably, 75% of the patients with bipolar disorder were also found to have a co-occurring psychiatric or substance use disorder, and among patients with psychiatric illness, those with bipolar disorder had the highest odds of recent loss of work time (OR 7.1, 95% CI 1.4–34.8, $p<.05$). No evidence of bias was found across the 9 items from the bias tool in this study.

Szadoczky, et al. conducted two studies in Hungary (21, 22). Using the Diagnostic Interview Schedule, the investigators found that 1.3% of randomly selected primary care patients (n=301) attending an appointment had bipolar disorder (21). One measure of bias of external validity was present (response rate <75% and no comparison of responders to non-responders). In a follow-up study (22) of all patients visiting 12 primary care practices during one week (n=1815), a 12-month bipolar disorder prevalence of 0.5% was found. The

follow-up study had no measures of bias found based on external validity but had two measures of bias found based on internal validity (unacceptable case definition, inappropriate prevalence period).

Liu, et al. (23) used the Clinical Interview Schedule to assess the prevalence of psychiatric disorders among consecutive primary care patients (n=200) attending a clinic appointment and found that 0.5% of patients had a semi-structured interview consistent with bipolar disorder. Information on two measures of bias of external validity was not reported and therefore the bias items were considered present (sampling frame was not representative of target population, and response rate <75% and no comparison of responders to non-responders). This study also had one measure of bias found based on internal validity (inappropriate denominator of interest).

Investigators in Finland (24) found that the 12-month prevalence of bipolar disorder was 2.1% among patients who had previously attended a primary care appointment (n=437). This study had one measure of bias found based on external validity (response rate <75% and no comparison of responders to non-responders), and two measures of bias found based on internal validity (inappropriate prevalence period, and lack of reporting on study denominator). Serrano-Blanco, et al. (25) randomly selected patients of 74 primary care physicians in Spain and administered the MINI to patients (n=5402) to detect the 12-month prevalence of mania or hypomania. Less than 1% (0.8%) of patients were found to have experienced mania or hypomania over the preceding 12-months based on the MINI. One measure of bias was found based on external validity (response rate <75% and no comparison of responders to non-responders), and two measures of bias were observed based on internal validity (unacceptable case definition and prevalence period).

Three studies used the PRIME-MD structured interview (26–28) which classified patients as “rule-out bipolar disorder” rather than as having bipolar disorder, which was a bias regarding internal validity for all three studies (ie unacceptable case definition). “Rule-out” bipolar disorder means that the patient has a high likelihood of having bipolar disorder but that the diagnosis needs confirmation by a clinical examination. The initial PRIME-MD study (26) showed that 1% of primary care patients (n=1000) had a “rule-out” bipolar disorder result on the structured interview. In addition to the case definition bias, this study also had one measure of bias of external validity (lack of random sampling).

A subsequent study (27) focusing on rural primary care patients (n=396) showed that 0.9% of primary care patients had “rule-out” bipolar disorder on the PRIME-MD. This study had two measures of bias found based on internal validity (lack of random sampling, and response rate <75% and no comparison of responders to non-responders) in addition to the case definition bias. The third study using the PRIME-MD was completed in Belgium in randomly selected primary care patients (n=2316) either attending clinic appointments or receiving homecare (28). The investigators found that 1.9% of patients had a “rule-out” bipolar disorder diagnosis on the PRIME-MD. They also compared patients who attended a clinic appointment to those receiving homecare and found that 1.4% of the patients attending the clinic (N=1635) and 3.2% of the homecare patients (N=681) had the “rule-out” bipolar disorder diagnosis. In addition to the case definition bias, this study also had one measure of bias based on external validity (response rate <75% and no comparison of responders to non-responders).

Three studies found a bipolar disorder prevalence greater than 4%. Ghuloum, et al. (29) developed a 79-item structured questionnaire to screen primary care patients (n=1660) for numerous psychiatric disorders. A psychiatrist then examined the patients. Reported diagnoses (including bipolar disorder diagnosis) were based on the findings from the clinical

exams by the psychiatrist. The investigators found a bipolar disorder prevalence of 4.3%. One measure of bias was found based on external validity (lack of random sampling), and two measures of internal validity (use of unvalidated measure, and different modes of data collection used) were present.

Gaynes, et al. (30) administered the MINI to patients (n=647) attending appointments of each primary care physician at an academic center clinic. Although the authors' main aim was to determine the screening thresholds of a new psychiatric illness-screening instrument (M-3 Checklist), the gold standard MINI was used to determine disease prevalence and establish diagnoses. They found that "bipolar spectrum", a broader definition of bipolar disorder that generally includes sub-threshold bipolar disorder symptoms and cyclothymia, occurred in 9.3% of patients. This study had two measures of bias found based on external validity (lack of random sampling, and response rate <75% and no comparison of responders to non-responders). Vermani, et al. (31) administered the MINI to waiting room patients (n=840) at seven primary care clinics, and 11% of patients had a MINI consistent with bipolar disorder. This study also showed that an unusually high estimate (51.7%) of primary care patients had a psychiatric illness diagnosed using the MINI. Three measures of bias were found based on external validity (sampling frame was not representative of target population, lack of random sampling, and response rate <75% and no comparison of responders to non-responders).

3.3 Studies using screening measure

Three studies (32–34) used a screening measure to identify patients potentially having bipolar disorder. All three studies used the Mood Disorder Questionnaire (MDQ) screening measure (32–34). The percentage of patients with a positive bipolar disorder screen ranged from 7.6 to 9.8%. Because the positive predictive value of the MDQ for bipolar disorder is low compared to a structured interview (35), all three studies using the MDQ were considered to have two biases based on internal validity (unacceptable case definition, and unreliable study instrument).

The first study, by Das, et al. (32) was conducted in an academic primary care clinic and included primarily low-income Hispanic women. They found that 9.8% of patients (n=1157) had a positive screen for bipolar disorder on the MDQ and that having a positive screen was significantly associated with greater impairment and reduced health functioning compared to those with a negative screen. No biases other than the case definition and study instrument biases were present in this study.

Rouillon, et al. (33) used the MDQ as a screening measure in primary care clinics in France. They found that 8.3% of patients attending appointments (n=9220) had a positive MDQ screen. The investigators used a slightly higher cutoff score on the MDQ (8 or more) than the other MDQ studies which used a score of 7 or more. This study had two measures of bias found based on external validity (lack of random sampling, response rate <75% and no comparison of responders to non-responders) in addition to the case definition and study instrument biases. Castelo, et al (34) found that 7.6% of patients (n=720) in three primary care clinics in Brazil had a positive screen on the MDQ. No biases other than the case definition and study instrument biases were present in this study.

3.4 Risk of bias in studies

The risk of bias scores for the studies included in this systematic review ranged from 5 to 9 out of 9 possible points. The two studies with 9 out of 9 (20) and 8 out of 9 (21) were considered to have low risk of bias. Six studies (22, 26, 28, 30, 32, 34) had 7 out of 9 points, and were considered to have moderate risk of bias. Six studies (23, 24, 25, 27, 29, 31) had 6

out of 9 points and one study (33) had 5 out of 9 points; these seven studies and were considered to have high risk of bias.

4. Discussion

Bipolar disorder was diagnosed using a structured interview in 0.5 to 4.3% of primary care patients in 10 of 12 studies. Two studies found much higher percentages of 9.3 to 11.4%. It is likely that the differences in case identification techniques and populations used in these studies included in this review partly account for the variance in prevalence estimates. Also almost one-half of the studies had high risk of bias based on problems with external and internal validity.

Gaynes, et al. (30) found that 9.3% of patients had a MINI consistent with “bipolar spectrum” rather than a diagnosis of bipolar disorder. The broader outcome of “bipolar spectrum” differed from the other structured interview studies that used bipolar disorder as the outcome. This difference may have accounted for the higher observed prevalence since “bipolar spectrum” generally includes people with sub-threshold bipolar disorder symptoms and cyclothymia. The study by Vermani, et al. (31) found that 11.4% of patients had bipolar disorder based on the MINI. This study also found that 51.7% of primary care patients had any psychiatric disorder diagnosed with the MINI, suggesting either that the clinic sites used for the study had an unusually high number of patients with psychiatric illness or that psychiatric illness was over-detected. Most primary care based studies have found that approximately 20 to 25% of primary care patients have psychiatric illness (26).

A previous systematic review (36) on the prevalence of bipolar disorder among primary care patients with psychiatric complaints showed that bipolar disorder screening measures overestimated the occurrence of bipolar disorder. Approximately 3 to 9% of patients with depression or another psychiatric complaint had bipolar disorder based on the results of a structured clinical interview, while 20 to 30% of patients had a positive result on a bipolar disorder screening measure.

Similarly, our results show that in general primary care patients, bipolar screening measures find higher percentages of patients with positive screens for bipolar disorder compared to studies that diagnose bipolar disorder using structured interviews. The three screening measure studies using the MDQ (32–34) found that 7–10% of patients had a positive screen for bipolar disorder. Ten of the structured interview studies found bipolar disorder in 0.5–4.3% of patients, while two studies found higher percentages for reasons described above. The higher percentages found in screening studies is likely due to the low positive predictive value of the MDQ in primary care, which translates into a high number of false positive results (35, 37).

The NCS-R showed that approximately 4.5% of the general population had either bipolar I disorder (1.0%), bipolar II disorder (1.1%) or sub-threshold bipolar disorder (2.4%) (8). None of the studies included in our results differentiated among bipolar I disorder, bipolar II disorder and sub-threshold bipolar disorder symptoms, as done in the NCS-R. Therefore, we are unable to firmly conclude whether bipolar I disorder, bipolar II disorder or sub-threshold bipolar disorder symptoms occur as often or more often in primary care samples compared to the general population. However, the structured interview study from an academic family medicine clinic (30) that used a “bipolar spectrum” definition found a prevalence of 9.3% which is twice as high as the overall prevalence found in the NCS-R. The definition of “bipolar spectrum” was not defined in that study, though likely included patients with sub-threshold bipolar disorder. The ten structured interview studies that found a prevalence between 0.5–4.3% likely considered bipolar I disorder or bipolar II disorder only in their case definitions, though this point was not mentioned in any study. The NCS-R prevalence

for bipolar I disorder and bipolar II disorder (2.1%) falls within the observations from these ten structured interview studies.

Three of the twelve studies (22, 24, 25) using a structured interview measured 12-month, rather than lifetime, prevalence. Because the bipolar disorder-defining episodes (hypomania and mania) occur less often than depressive episodes in bipolar disorder (14,15), it is likely that studies using 12-month prevalence measurements underestimated the lifetime prevalence of bipolar disorder. The estimates of 0.5% (22), 2.1% (24) and 0.8% (25) are likely lower than the actual percentages of patients with lifetime bipolar disorder.

Limitations of our study include the relatively small number of studies using structured interviews or clinical examinations to diagnose bipolar disorder. Additionally, we found significant heterogeneity across the studies in the case definition of bipolar disorder, study population characteristics, study quality and study setting. No studies commented on whether the researchers conducting the structured interviews were blinded to the study's aims, which could have biased the results of the structured interviews.

5. Conclusions

Based on the structured interview studies, it is likely that bipolar disorder occurs in 0.5%–4.3% of primary care patients, with as many as 9.3% of patients having a “bipolar spectrum” illness in some settings. Prevalence estimates from studies using screening measures were higher than the estimates obtained in most structured interview studies.

Acknowledgments

Grant funding: 2T32MH020021-16

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Figure 1.
Study identification method

Table 1
Characteristics and results from studies measuring bipolar disorder prevalence in primary care samples

Study	Diagnostic or screening measure	Population and sampling method	Age [mean (SD when available)] and sex (%) of study population	Sample size	Prevalence ^a	Risk of Bias ^b , scored based on 9 items	Miscellaneous study characteristics (including location if not conducted in United States)
Studies using structured interview (n=12)							
Olsson, et al ²⁰ , 1997	MINI	Randomly selected waiting room patients with appointments scheduled at least 3 days in advance from one urban academic clinic	No mean age reported, though approximately 61% of sample over age 45 63.1 Female 37.0 Male	N=1001	1.2% (MINI consistent with bipolar disorder)	Low 9/9	Note – diagnosed as “Rule out bipolar disorder”
Szadoczky, et al ²¹ , 1997	Diagnostic Interview Schedule	Random patients attending appointments with 15 primary care physicians in 5 sites from different parts of Hungary.	38 years 57.1 Female 42.9 Male	N=301	1.3%	Low 8/9	Hungary
Szadoczky, et al ²² , 2004	Diagnostic Interview Schedule	All patients attending appointments with 12 physician from 12 primary care practices (ie one physician at each practice) during a 1 week period	40.2 years 64.1 Female 35.9 Male	N=1815	0.5% 12 month prevalence	Moderate 7/9	Hungary
Liu, et al ²³ , 2004	Clinical Interview Schedule	Every other new patient from one primary care clinic until target sample (n=200) number was reached	37.3 (16.9) years 55 Female 45 Male	N=200	0.5%	High 6/9	Taiwan
Sorvaniemi, et al ²⁴ , 2005	Present State Examination 9 th version	Randomly selected primary care patients who had previously attended one of three community health centers between September 1991 and May 1992	18–64 years old No other demographic information reported	N=437	2.1% 12 month prevalence	High 6/9	Finland
Serrano-Blanco, et al ²⁵ , 2009	MINI	Randomly selected patients attending clinic appointments of primary care physicians working at 78 randomly selected clinics	54.3 (17.3) years 63.0 Female 37.0 Male	N=5402	0.8% (MINI consistent with “mania or hypomania” over previous 12 months) 12 month prevalence	High 6/9	Spain
Spitzer, et al ²⁶ , 1994	PRIME-MD	Patients from four primary care clinics. 1/3 of patients were selected as a convenience sample. The remaining 2/3 of patients were selected using site-	55 (16.5) years 60.0 Female 40.0 Male	N=1000	1%	Moderate 7/9	

Study	Diagnostic or screening measure	Population and sampling method	Age [mean (SD when available)] and sex (%) of study population	Sample size	Prevalence ^d	Risk of Bias ^b , scored based on 9 items	Miscellaneous study characteristics (including location if not conducted in United States)
		specific methods aiming to avoid sampling bias					
Philbrick, et al ²⁷ , 1996	PRIME-MD	Consecutive scheduled and walk-in patients attending appointments at two rural primary care clinics between June 16 th and August 4 th , 1993.	55.5 years 65.9 Female 34.1 Male	N=396	0.9%	High 6/9	Note – diagnosed as “Rule out bipolar disorder”
Anseau, et al ²⁸ , 2004	PRIME-MD	Randomly selected patients attending appointments or receiving home visit with 90 randomly selected primary care physicians with at least 7 years of clinical practice and 20 daily patient contacts.	No mean age reported, though approximately 43% of sample age 50 years or older 58.7 Female 41.3 Male	N=2316	1.9%	Moderate 7/9	Belgium Note – diagnosed as “Rule out bipolar disorder”
Ghuloum, et al ²⁹ , 2011	79 question diagnostic questionnaire and clinical examination by a psychiatrist	Patients attending appointments at 12 primary care clinics (9 urban and 3 semi- urban)	38 (12.1) years 53.8 Female 46.2 Male	N=1660	4.3% (questionnaire consistent with bipolar disorder; diagnosis confirmed by psychiatrist)	High 6/9	Qatar
Gaynes, et al ³⁰ , 2010	MINI	Three consecutive patients of each primary care physician in one academic clinic examined within 1 month after attending the clinic appointment	45.2 (15.4) years 70.9 Female 29.1 Male	N=647	9.3% (MINI consistent with “bipolar spectrum”)	Moderate 7/9	
Vermani, et al ³¹ , 2011	MINI	All waiting room patients presenting for clinic appointment on days that research assistants were in clinic to recruit subjects from 7 clinics over 6 months	37 (16) years 72.7 Female 27.3 Male	N=840	11.4% (MINI consistent with bipolar disorder)	High 6/9	Canada
Studies using screener (n=3)							
Das, et al ³² , 2005	MDQ	Waiting room patients, one urban, academic clinic, randomly sampled based on the position of the seat the patients selected in the waiting room	51 (12.2) years 69.5% Female 30.5% Male	N=1157	9.8% (MDQ 7 with 2 or more concurrent symptoms resulting in moderate or severe impairment)	Moderate 7/9	
Rouillon, et al ³³ , 2011	MDQ	All patients attending a clinic appointment during 1 week of 95 randomly selected primary care physicians from 95 practices. Patients seen more than one time	47.2 (17.9) years 60% Female 40% Male	N=9220	8.3% (MDQ 7, with 2 or more concurrent symptoms resulting in moderate or severe impairment)	High 5/9	France, Included patients age 15 and older

Study	Diagnostic or screening measure	Population and sampling method	Age [mean (SD when available)] and sex (%) of study population	Sample size	Prevalence ^a	Risk of Bias ^b , scored based on 9 items	Miscellaneous study characteristics (including location if not conducted in United States)
Castelo, et al ³⁴ , 2012	MDQ	Consecutive patients in 3 urban clinics. Patients were selected based on their numeric order of arrival for scheduled appointments, with a different number assigned for selection each day.	44.4 (14.7) years 71.9% Female 28.1% Male	N=720	7.6% (MDQ 8, with 2 or more concurrent symptoms resulting in moderate or severe impairment)	Moderate 7/9	Brazil

^a Lifetime prevalence except where noted

^b Measured using the Risk of Bias in Prevalence Studies tool by Hoy, et al (19). We considered 8 or 9 out of 9 as low risk of bias, 7 out of 9 as moderate risk of bias, and 6 or less out of 9 as high risk of bias. **Low risk** of bias suggests that further research is *very unlikely* to change the confidence in prevalence estimate. **Moderate risk** of bias suggests that further research is *likely* to impact our confidence in the estimate and *may* change the estimate. **High risk** of bias suggests that further research is *very likely* to have an important impact on the confidence of the estimate and *likely* to change the estimate.