Screening for common mental disorders in primary care in low and middle income countries: A rational approach to address the mental health treatment gap?

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Submitted in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy
under the Executive Committee
of the Graduate School of Arts and Sciences

COLUMBIA UNIVERSITY
2020

Abstract

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The goal of this dissertation is to examine the utility of screening for common mental disorders in primary care in low and middle income countries. Screening for common mental disorders in primary care is often considered as an important step in addressing the mental health treatment gap in low and middle income countries. Nevertheless, there is insufficient evidence to support routine mental health screening in primary care in these countries. Even in high income countries, there is a lack of consensus on the effectiveness of routine mental health screening in primary care, especially screening for depression. Challenges to screening include the high rates of false positive diagnosis, poor evidence on outcomes for people identified by screening, and potential harms due to screening.

The specific aims of this dissertation are to: 1) synthesize evidence from low and middle income countries on the current practices of screening for common mental disorders in primary care and the use of screening instruments; 2) understand the significance of a positive screen for common mental disorder in primary care, specifically the distribution and the stability of ICD-10 diagnosis for screened positive patients, their clinical course over a period of one year, and the factors associated with the clinical course; 3) examine the factors associated with antidepressant prescriptions for patients screened positive for common mental disorders in primary care and evaluate the appropriateness of antidepressant prescriptions following screening.

Based on our review of literature, evidence to support routine screening for common mental disorders in primary care in low and middle-income countries is inadequate. We highlight concerns

about the fidelity with which screening is implemented, especially the flawed use of screening instruments. Introducing depression screening and physician notification in these settings seldom results in improved access to care or appropriate care. The majority of patients identified by screening in primary care have contextual, and probably non-pathological psychological distress (see page iii, for definition of key terms) which is often temporary and self-limiting. Patients with persistent distress symptoms identified by repeated screening, and those with moderate to severe depression may benefit from screening in the presence of evidence based stepped care interventions that are easily accessible and acceptable. Although, the long term effects of these interventions and the sustainability of such primary care based programs in low and middle income countries are uncertain.

Our analysis of data from a cluster randomized control trial in India confirmed that a significant proportion of patients screened positive for common mental disorders in primary care has psychological distress that is temporary and self-limiting. However, a smaller, albeit important share of patients also experienced psychological distress that persisted throughout one-year follow-up. Persistent distress was predicted by psychosocial and economic disadvantage. Thus, psychosocial support systems and structural interventions have a larger role to play in addressing psychological distress. We found poor diagnostic stability for ICD-10 based diagnoses, and the most stable and prevalent diagnosis was mixed anxiety and depressive disorder. Further, we found that antidepressants are widely prescribed following screening especially for women and older adults. While many patients with moderate to severe depression could benefit from antidepressants, it is problematic that a significant proportion of patients with less severe disorders also received anti-depressant prescription despite the availability of non-pharmacological treatment options.

In summary, there is a lack of empirical evidence to support routine screening for common mental disorders in primary care in low and middle income countries as an effective strategy to identify those in need of treatment; instead screening could lead to over diagnosis and inappropriate

antidepressant prescriptions. To address psychological distress in primary care and the unmet need for treatment in low and middle income countries, there is an urgent need to focus on locally driven and culturally relevant approaches to case finding and intervention.

Table of contents

List of figures

Definition of key terms

Common mental disorders: Common mental disorders are non-psychotic mental health conditions that include depressive, anxiety, adjustment and somatic symptom disorders that impair daily functioning (1).

Psychological distress: a state of emotional suffering represented by symptoms of depression (e.g., sadness, loss of interest, hopelessness) and/or anxiety (e.g., feeling tense, restlessness;) (2, 3) . Emotional suffering may be accompanied by somatic symptoms (e.g., insomnia; headaches; tiredness) that possibly will be different across cultures (3, 4). Typically, questionnaire based screening for common mental disorders identifies patients with psychological distress which could be pathological or a non-pathological normal response to a situational crisis.

Pathological psychological distress: Psychological distress, "when it is accompanied by other symptoms that, when added up, satisfy the diagnostic criteria for a psychiatric disorder" (3). In addition, pathological distress is often unmanageable/intolerable leading to impairment of functioning, and the distress is beyond an expectable or culturally approved response to stressors or loss (5, 6).

Non-pathological distress: Psychological distress that occurs in response to stressful life situations and the distress is not greater than what would be expected within the sociocultural context. Non-pathological distress is often transient and self-limiting but could also be chronic due to ongoing unresolved psychosocial problems. Generally, active intervention, whether psychological or pharmacological, is not needed for conditions likely to be self-limiting, although monitoring may be advisable (5)

Acknowledgments

I want to thank the members of my internal dissertation committee, Professors Sharon Schwartz, Ezra Susser, and Katherine Keyes for liberally sharing their time and ideas with me in the dissertation process and throughout my time at Columbia. I feel very fortunate for the opportunity to work with them. I owe special thanks to my dissertation sponsor Professor Sharon Schwartz for being an extremely patient and thorough mentor. The completion of my training with a fulltime job would not have been possible without the incredible support I received from Professor Anne Paxton, who not only championed my admission into the Department of Epidemiology, but facilitated my success throughout the doctoral program. She has also been a source of invaluable advice and genuine friendship. I would also like to express my thanks to Liliane Zaretsky, whose warm words and support has been a great comfort and a constant source of encouragement.

This dissertation is dedicated to my whole family, for their persistent love and support. But especially, it is dedicated to my wife Asha for the patience and support throughout all these long years and my daughter Daksha.

Chapter 1: Introduction

Screening for common mental disorders in primary care is often regarded as an important step to address the treatment gap for mental disorders in low and middle income countries. Unfortunately, the reliance on screening is founded more on intuition than evidence (7). This dissertation attempts to systematically examine the utility of screening for common mental disorders in primary care in low and middle income countries.

In recent years the field of global mental health has successfully brought attention to the heavy burden of mental disorders, exacerbated by the lack of suitable and accessible mental health care in most low and middle income countries (8, 9). A growing body of evidence shows that, it may be possible for effective treatment for common mental disorders to be delivered through primary care by lay health workers and primary care physicians (10-13). However, under recognition of common mental disorders among patients attending primary care facilities is thought to be a major barrier in providing treatment. In this context, screening is considered as an important strategy to detect mental disorders and translate the evidence of effective interventions to reduce the burden of mental disorders (14). The assumption is that screening increases the likelihood that those in need of treatment will be identified and appropriately treated (15). Further, in low middle income countries with a shortage of trained clinicians, screening helps in task sharing as lay health workers or ancillary medical personnel could be trained to screen for common mental disorders (14).

Despite these potential benefits, evidence on primary care based screening of common mental disorders, especially depression, remains inconclusive even from high income countries in which most of the studies have been conducted. As a result, the national guidelines from the United Kingdom (UK) and Canada do not recommend screening for depression in primary care, although the United States Preventive Services Task Force (USPSTF) recommends screening when adequate systems are in place to ensure accurate diagnosis, effective treatment, and appropriate follow up (16-18). The evidence on

screening from low and middle income countries is unclear and has not been systematically assessed. In this context, promoting mental health screening in primary care without clear evidence of their benefit may not only diverts scarce treatment resources, but also exposes patients misdiagnosed with mental disorders to unnecessary treatment and adverse drug effects.

The primary goal of this dissertation is to critically examine the use of screening for common mental disorders in primary care in low and middle income countries. In particular, this dissertation aims to understand the significance of psychological distress or probable mental disorders identified by screening in primary care and how screening influences the clinical management, and the course of these conditions identified by screening.

This dissertation is organized into five chapters. Following the introductory chapter, the second chapter is a systematic literature review examining the evidence base for screening for common mental disorders in primary care. Specifically, the review synthesizes evidence on the current practice of screening and the use of screening instruments for common mental disorders in primary care from low and middle income countries. In the third chapter, based on the data from a primary care based randomized control trial from India, we examine the significance of a positive screen for common mental disorder in primary care and the clinical course of screened positive primary care patients. The fourth chapter investigates factors associated with antidepressant prescription for screened positive patients, and the appropriateness of those prescriptions. The final chapter summarizes the findings from the prior chapters, highlighting implications for primary care practice in low and middle income countries, and provides recommendations for further studies.

Chapter 2: A systematic literature review of screening for common mental disorders among adults in primary care in low and middle-income countries

Introduction

Common mental disorders are non-psychotic mental health conditions that include depressive, anxiety, adjustment and somatic symptom disorders that impair daily functioning (1). A recent meta-analysis of the global prevalence of common mental disorders among adults reports a prevalence of 17.6% within the past year and 29.2% across the lifetime (19). Common mental disorders are identifiable in primary health care settings globally, contribute considerably to the global burden of mental disorders, and have been shown to adversely affect a broad range of health, social and economic outcomes (20-22). Early identification and treatment of these disorders could decrease adverse events such as suicides, and improve disease outcome and quality of life. However, in low and middle-income countries, the severe shortage of trained clinical specialists and the inequitable distribution of available specialists is a major challenge in providing adequate mental health care (23). In these resource poor settings, integrating mental health care into primary care that forms the back bone of health care delivery (i.e. government primary health care clinics and private general practitioner clinics) is considered key to addressing the substantial treatment gap for mental health. For many scholars, screening for common mental disorders in primary care is a vital step in this process (24).

But there are reasons to be cautious about this approach as primary care based screening of depression in high-income countries has raised several concerns (7). These include the high rates of false positive diagnosis, poor evidence on outcomes for people identified by screening, and potential harm due to screening (25). As a result, the United Kingdom's National Institute for Health and Clinical Excellence and the Canadian Task Force for Preventive Health Care no longer recommend routine depression screening in primary care, although the United States Preventive Services Task Force continues to recommend screening (16, 18, 26, 27). On the other hand, the effect of screening in low

and middle-income country could be different due to the extremely low recognition of and treatment for common mental disorders in these countries compared with high income countries.

Since the experience of primary care based screening of common mental disorders in high income countries gives us pause about the utility of screening in low and middle-income countries, it is worth examining whether primary care based screening of common mental disorders is sensible for these settings.

To justify integrating routine screening for mental disorders in primary care, the screening program should identify significant numbers of new cases of mental disorders, and engage patients in treatment that is ultimately beneficial to them. At present we have limited evidence on whether screening could fulfill these goals in primary care in low and middle-income countries. This matters since ineffective screening programs could divert scant resources from caring for patients already identified with mental disorders. In addition, it could also lead to unnecessary treatment, adverse drug effects, experience of stigma and social distance for patients who are incorrectly identified as having a mental disorder.

The key question that we need to address is, whether screening for common mental disorder in primary care in low and middle-income countries is ultimately beneficial to patients. To directly answer this question, a comparison between outcomes in a screened and a non-screened group of primary care patients is necessary. Ideally, the evidence should be based on high quality randomized control trials (RCT) of screening that demonstrate significant positive outcomes to justify the cost and possible harm associated with screening (28). Unfortunately, primary care based RCTs of screening for common mental disorders are not available. However, screening for common mental disorders is routinely done in primary care based observational studies and RCTs of interventions for common mental disorders. Given the absence of RCTs of screening, a lesser alternative is to synthesize evidence from such studies from primary care in low and middle income countries.

Observational studies and RCTs of interventions among screened positive patients could inform us about the prospects of primary care based mental health screening in low and middle-income countries in several ways. First, by showing how screening is carried out in these settings and whether the practice of screening conforms to the general principles of screening. For instance, screening should be done using a reliable and valid instrument appropriate for the population. Ideally the instrument should be developed for the study population using culturally relevant explanatory models and the local idioms of distress (29) or by cross-cultural adaptation of an existing instrument. Cross-cultural adaptation of a psychological screening questionnaire is a complex task involving extensive translation process, cultural adaptation and verification. In addition, the validity of the adapted questionnaire in the new environment should be evaluated through several steps including: evaluating the factorial structure, establishing content and criterion validity by comparing with a gold standard diagnosis and demonstrating adequate reliability and stability. For initial screening of a health condition the crucial parameter is the sensitivity of the screening questionnaire, however, when an instrument is used for case finding or diagnosis the key parameter is its positive predictive value (PPV), the probability that a screened positive person meets the diagnostic criteria for the psychiatric diagnosis (15). Even when a screening instrument exhibits good sensitivity and specificity, the PPV could be poor if the true prevalence of the health condition is low for the population (30). Further, screening for common mental disorders is not a standalone process, it only identifies individuals who are at increased risk for a mental disorder. In addition to the use of a screening tool that is reliable and validated for the study population, screening needs to be followed up with a diagnosis (26). Examining the presence of these critical elements and their effectiveness could inform the validity of the screening process.

Second, screening is futile unless it is followed by evidence based interventions that are accessible and acceptable. Examining how screening influences treatment receipt and the clinical course of illness for screened positive patients under the prevailing or usual care help us to appraise the utility and

pragmatic application of screening in these settings. Finally, by evaluating whether interventions lead to better outcome for patients screened positive for common mental disorders.

This review

We conducted a systematic literature review to assess the evidence for the effectiveness of primary care based screening for common mental disorders among the general population in low and middle-income countries. For this we focused on three areas of research:

I. The current practice of primary care based mental health screening and how it conforms to the general principles of screening; specifically: 1) Is screening carried out using reliable and appropriately validated screening instrument? 2) are the screening instruments used for screening or diagnosis? 3) are the parameters of the screening instruments (sensitivity/specificity, positive predictive value etc.) appropriate to meet the screening objectives?

II. The treatment and the clinical course of patients identified by screening under the prevailing or 'usual care', specifically: 1) what proportion of screened positive patients received effective treatment under usual care, and what are the factors associated with treatment receipt? 2) What are the short term and long term clinical outcomes under usual care? 3) What are the predictors of the clinical course?

III. Effectiveness of interventions for patients screened positive for common mental disorders identified by screening in primary care; specifically: 1) the types of interventions described in primary care based RCTs; 2) what is the effect of intervention for short, medium and long-term follow-up? 3) is there any evidence of harm reported from these studies?

To answer these questions, we drew together evidence from a range of primary care based studies:

1) Cross-sectional studies that screened and/or diagnosed patients for common mental disorders in primary care.

2) Cohort studies that examined the effect of introducing screening for common mental disorders in primary care practices in low and middle-income countries. In addition to describing the typical response of a primary care practice to screening, some of these studies also reported the clinical course of screened positive patients under usual care.
3) Randomized controlled trials of interventions for common mental disorders among patients identified by screening in primary care. These studies examined whether intervention following screening resulted in better outcomes for patients screened positive for common mental disorders.

We focused on studies that pertain to general adult primary care populations and excluded studies in special populations such as perinatal women, studies focusing on geriatric populations etc. While exploring the practice of screening for common mental disorders in low and middle-income countries, we need to keep in mind the reality of primary care based screening and treatment in these settings, since it influences the scope of screening and the challenges in its implementation. First, at present, routine screening for common mental disorders outside research settings is virtually nonexistent in most of these countries. Clinical diagnosis and treatment of common mental disorders in primary care is also very rare. Second, the 'usual care' for common mental disorders in primary care is 'no care' in most settings or limited to inadequate psychopharmacological treatments or referral to a mental health specialist.

Methods

Search strategy

We conducted a systematic literature search using three electronic databases: PsycINFO, EMBASE and PubMed. A combination of a broad set of search terms representing any common mental disorders, primary health care models, screening, and low- and middle-income countries was used for electronic search. The search terms were customized for each database according to the PRISMA guidelines. (see appendix A for a full list of search terms) Search results were transferred into Covidence, a reference management system for systematic reviews (31). The list of studies was screened to exclude duplicates

and further refined by appraising the study titles with the inclusion and exclusion criteria. In the next step two independent reviewers (including the author) reviewed the abstracts of retained studies to see if they meet the inclusion criteria and reviewers met to reach agreement on any conflicting decisions. The author read the full text of all articles retained following the abstract review. The references in the eligible articles were screened for additional articles not captured in the first round of search.

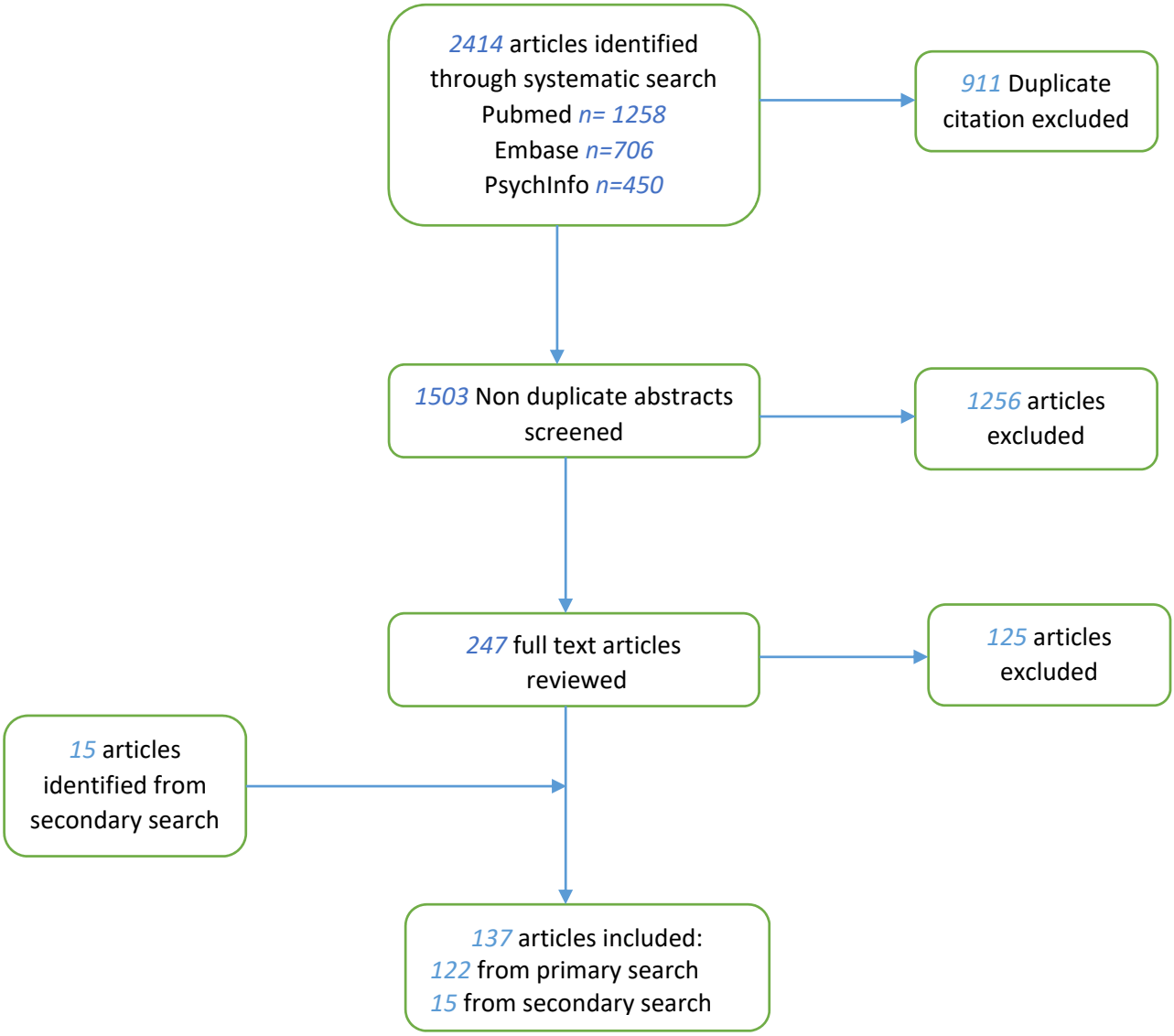
Inclusion criteria

We included original quantitative research articles published in English based on studies conducted in primary care in low and middle-income countries between 1975 and 2017. The countries were identified using the World Bank Group's analytical classification of countries based on Gross National Income (GNI) per capita threshold (32). Studies were selected if the country was classified as low or middle-income at the time of the study. Only studies among adults 18 and above conducted in a primary care clinic or a general medical outpatient clinic in a hospital that functioned as a primary care facility were included.

Exclusion criteria

We excluded studies done in outpatient psychiatric clinics, other specialist clinics and among inpatients. Studies exclusively among special populations such as perinatal women, students, military personals, refugees, victims of violence or natural disaster or among patients with a diagnosis of a health condition (cancer patients, HIV patients etc.) were also excluded.

Fig 2.1. PRISMA flow diagram representing the selection of articles for this systematic review



Results

The literature search identified 137 eligible articles representing studies from 37 countries (33-169) (see appendix B for the full list and characteristics of the selected articles). The selection process is schematically represented in figure 2.1 according to the PRISMA guidelines. Briefly, we identified 1503 unique articles by systematic search of three electronic databases: PubMed, PsychINFO and Embase. Following abstract reviews, we retrieved 247 articles for full text review. Based on our inclusion and

exclusion criteria, 122 articles were included in the final list of articles selected for full text review. In addition, we identified 15 articles from the references of the originally selected articles. The final list (see appendix B) included 137 original research articles on primary care based screening for common mental disorders from low and middle-income countries.

The majority of studies (n=115) were cross-sectional and the rest were RCTs (n=14) and Cohort studies (n=8). Table 2.1 details the characteristics of the cohort studies and RCTs. We did not find any RCTs of screening that could directly evaluate the benefit or harm due to screening. However, we did identify 14 articles based on RCTs reporting the effect of interventions among patients screened positive for common mental disorders in primary care (41-54). In addition, we found 8 cohort studies that screened for common mental disorders in primary care (33-38, 40, 170). These include 6 cohort studies describing the course of common mental disorders in primary care patients identified by screening under usual care (34-38, 170). The maximum follow-up period for the cohort studies and RCTS were 12 months. Unfortunately, none of these studies performed a direct comparison between a screened and non-screened group of primary care patients to study the net effect of screening.

The current practice of screening and conformity to screening principles

Most studies screened patients attending primary care clinics with medical complaints. Consultation for mental disorders are rarely reported from primary care in low and middle-income countries, although symptoms such as insomnia, lack of appetite and nonspecific somatic symptoms are common (52, 86, 121, 134). Some studies screened all eligible patients attending the clinic on particular days and a few conducted a systematic sampling, for example screening every 3rd eligible patient.

All studies included in this review used at least one screening questionnaire to identify patients with mental disorders. As depicted in table 2.2, we identified 29 unique questionnaires including the different versions of the General Health Questionnaire (GHQ) (171) and the patient Health Questionnaire (PHQ) (172). The most commonly used screening instrument is the GHQ-12 (n=38; 28%)

(173) followed by Self-Reported Questionnaire -20 item version (SRQ-20) (n=25; 18%) (106), and PHQ-9 (n=18; 13%) (174). About 60% of studies (n=82) screened patients for general psychological distress that suggests common mental disorders using questionnaires such as the GHQ or the SRQ. The remainder used questionnaires that specifically screen for depression or anxiety such as the Patient Health Questionnaire (PHQ-9), the Becks Depression Inventory (BDI)(175), and the Generalized Anxiety Disorder questionnaire (GAD-7)(176).

Reliability and validity of screening instruments

Studies often use screening instruments developed elsewhere by adapting them to the local context as developing them specifically for the study population using culturally relevant explanatory models and the local idioms of distress is a time consuming and resource intensive process. A few studies included in this review used screening questionnaires developed specifically for the study population or for groups that share cultural and linguistic heritage. For example, some studies used the Shona Symptoms Questionnaire (SSQ) developed in Zimbabwe (59), Vietnamese Depression Scale (VDS) (177) developed for the Vietnamese refugee population in the United States (135) [21] and the Rahim Anxiety Depression Scale (RADS) developed in Sudan (178) and used in many Arabic speaking countries (144). Most studies used screening questionnaires developed in North America or Europe translated into the local language. None of them reported going through a comprehensive cross-cultural adaptation and validation process, with the exception of a few studies such as the recent validation study of PHQ-9 in Nepal by Kohrt et al. (118).

In many studies translation of questionnaires is limited to expert translation, while some studies also reported back-translation and revisions to retain linguistic or semantic equivalence. Few described extensive cultural adaptation to meet technical and conceptual equivalence. Many of these studies reported reliability of the translated screening instrument in terms of internal consistency, although there is less emphasis on its validity in the study population. Only about 20% (n=26) of the studies used

screening questionnaires that have been appropriately validated for the study population (35, 38, 40-42, 44, 53, 60, 70, 97, 101, 105, 107, 118, 123, 129, 133, 137, 140, 145, 151, 153, 156, 166, 169, 179). Fifty-eight percent (n=80) of studies mentioned using a validated screening instrument, however, upon examining the citations used to support validation claims, we found that the validation was often done in an unrelated population or the validation itself was flawed. For example, several studies used screening instruments validated among university students, adolescents, geriatric populations, perinatal women or cancer patients (36, 42, 83, 116, 120, 127). If the population being studied differ significantly from the population for which the screening instrument was developed, it could unfavorably affect the meaning, validity and reliability of the instrument (180). In most validation studies the gold standard used for diagnosis is a standardized diagnostic interview. The validity of the diagnostic instruments is seldom reported and there is no evidence supporting their accuracy in the population under study. Further, about 20% of studies used screening instruments that are not validated for the study population.

Use of screening questionnaire for screening vs. diagnosis

Out of the 137 eligible studies, 78 (57%) used a two stage case finding process, following-up screening with a diagnosis, either using a standardized diagnostic instrument or a clinical interview. The remaining studies (n=59) used screening alone for case finding and the majority of those studies (n=51) depicted a positive screen as a diagnosis. (Appendix B shows the screening process used in each study) Thus about one-third of studies (n=46) reported the prevalence of mental disorders in primary care solely based on screening.

Appropriate parameters for screening and diagnosis

When an instrument is used for case finding or diagnosis the key parameter is its positive predictive value (PPV), the probability that a screened positive person meets the diagnostic criteria for the psychiatric diagnosis (15). Sensitivity and specificity of the screening instrument are more commonly

reported than population specific parameters such as the positive and negative predictive values. In about 50% of studies reviewed, we identified the PPV of the screening instrument, either reported in the study, or calculated from the data, or from the original validation study. The PPV ranged from 0.10 to 0.86 and the average PPV of the screening instruments is about 0.62 (median 0.65). This could lead to significant proportion of false positive diagnosis especially when a screened positive patient is not followed up by a diagnostic assessment as in 43% of studies we reviewed. For example, in a recent validation study of the PHQ-9 from Nepal, 60% of positively screened patients were false positives in spite of meticulous cultural adaptation employed in the study (118).

The treatment and the clinical course of patients identified by screening under usual care

Screening is only the first step in a comprehensive treatment program. Patients identified by screening need easy access to appropriate treatments that could significant improvement the clinical course and outcomes.

Treatment receipt following screening

We found only one study that described the effect of screening on treatment receipt under the usual-care provided in primary care clinics. This was an international multi-site study across six sites, two of which were in middle-income countries (Russia, Brazil). The results of the study were published in two articles (36) (170). In this study, primary care physicians were notified of the diagnosis of major depression following a two stage screening process using the Center for Epidemiologic Studies Depression (CES-D) Scale and the Composite International Diagnostic Interview (CIDI). The decision to treat the depressive episode was left solely to the attending physician (36).

Patients were asked at 3 months and 9 months about their mental health care during the prior 3 months. Rates of treatment varied widely among study sites. Only about 3% of patients in Russia and 17% of patients in Brazil diagnosed with current depressive disorder received any treatment during the 9-month follow-up period under the usual care. The percentage who received any potentially effective

treatment was 1% in Russia and 9% in Brazil. These rates were significantly lower than those reported from some of the sites in high-income countries. For example in Seattle, about 40% of primary care patients diagnosed with a depressive disorder using the 2 stage screening process received potentially effective treatment (170). Potentially effective treatment in this study was defined as receiving at least the minimum effective dose levels of antidepressant or three or more specialist mental health visits in 3 months. The study concluded that depression screening and physician notification are not sufficient to initiate appropriate treatment for depression. Often, the attributes of the health care system, rather than the clinical features of the patient determined the likelihood of effective treatment following screening for depression (170).

In study sites in Russia and Brazil, patients reported concerns about the cost of treatment as the most common barrier to receiving treatment (36, 170). Potential adverse effects of treatment and stigma associated with mental health treatment were the other common barriers to treatment. The study did not find any association between baseline patient characteristics, including the severity of depression, with the likelihood of receiving effective treatment for depression.

Course of common mental disorders identified by screening in primary care

We identified five papers that reported the course of common mental disorders identified by screening in primary care. These include studies from Nigeria (35), Zimbabwe (38, 40) and two international multi-site studies (33, 34, 37). The multi-site studies are the WHO Collaborative Study on Psychological Problems in General Health Care with sites from seven low/middle-income countries (India, China, Chile, Brazil, Nigeria, Turkey and Greece) and the Longitudinal Investigation of Depression Outcomes (LIDO) project in which two middle-income countries (Russia and Brazil) were included. Three of these studies focused on major depression and two on any common mental disorders (35, 40). The follow-up period for all studies was one year except the LIDO project, which followed up patients for

nine months. In the following section we report the short term and long term course of mental disorders identified by screening under usual care and its predictors from these studies.

Short-term outcomes under usual care

The study from Zimbabwe reported the rates of short-term recovery (2-3 months) under usual care (38). Usual care did not involve any systematic treatment with antidepressants or psychological therapies and the authors used locally developed screening questionnaire, the Shona Symposium Questionnaire (SSQ) for case identification. In this study, at 2 months, about 62% of patients screened positive as cases at baseline were no longer identified as cases. Among the patients interviewed both at 2 months and 12 months nearly half of the patients recovered by 2 months and remained so at 12 months. The findings from this study suggest that the largest group of screened positive patients have a short remitting course.

We also considered a primary care based RCT from Chile in which 3560 women attending primary care screened positive (49% n=1731) for psychological distress (41). The women were screened again after two weeks without any treatment in the interim. Ninety-four percent of screened positive women returned for the second screening and among them only 722 (44%) scored above the case threshold. This also suggests that for a significant proportion of primary care patients who screened positive for psychological distress the symptoms could be transient and self-remitting and many of these patients who come in for a medical complaint might be distressed about their medical problem itself.

Long-term outcomes under usual care

Of the five studies that reported the course of common mental disorders identified by screening in primary care, four reported long term disease outcomes ranging from 9 to 12 months (34-36, 38, 170). In these studies evidence based psychological or psychopharmacological treatments were largely unavailable and anecdotal evidence suggests that primary health care providers sometimes prescribe non-specific treatments such as analgesics, vitamins, and hypnotics (181). Three studies reported

persistent disorder under these circumstances, defined as an ICD-10 diagnosis of depression or a symptom score suggestive of common mental disorder both at baseline and at follow-up (35, 36, 38). The prevalence of persistent disorders under usual care was 18% in Nigeria and 28% in Zimbabwe at 12 months follow-up, and 42% in Brazil at 9 months follow-up. Due to the long interval between the evaluations it is not possible to verify if the symptoms persisted throughout the follow-up period, or if it is a recurrence of symptoms. Four studies also reported full recovery at the end of follow-up period (9-12 months) which ranged from 25% to 50% for patients under usual care following screening (34-36, 38).

Predictors of the course for screened positive patients

Studies we reviewed reported baseline symptom severity and disability as key predictors of disorder persistence both in short term (2-3 months) and long term (9-12 months) follow-up (38) (34). The rate of persistence was also higher among subjects who continued to experience adverse socioeconomic events compared with those who did not. A study from Zimbabwe found that resolution of economic constraints was associated with lower rates of persistence (58). Complete remission at the LIDO study sites in Russia and Brazil was also predicted by fewer stressful life events during the follow-up period (39).

The study from Zimbabwe also found that recognition of psychiatric morbidity by traditional healers in terms of local idioms related to mental disorder was significantly related to better outcome (38). Similarly, subjects recognized as cases by GP/ PHC nurses, without screening, were more likely to become disease free at 2 months and 12 months compared to cases identified only by screening. This benefit is unlikely due to antidepressant medications as they are rarely prescribed (182). The LIDO study from Brazil also found no association between antidepressant treatment and complete remission and none of the participants from Russia reported antidepressant use [9, 13].

In primary care, patients are screened for common mental disorders while seeking medical care. Since they often have physical illnesses, it is likely that the presence of these clinical conditions also

affect disability and quality of life (36). We identified three studies from low and middle-income countries describing the course of common mental disorders and its association with disability and quality of life among primary care patients screened positive for common mental disorders. These studies from Zimbabwe, Russia and Brazil described a close association between disability and depression (34, 36, 40). They also described baseline disability as an independent predictor of persistent depression. The study from Brazil showed significant improvement in all domains of the quality of life scale (WHOQOL-BREF) and the Quality of Life Depression Scale (QLDS) during a nine-month follow-up of patients diagnosed with major depression (36). Although, at the end of this study, 42% of the individuals still had major depression, only 9% of patients were on adequate treatment with antidepressants during the study period. As discussed before, disability and poor quality of life due to coexisting physical morbidity is a major challenge in understanding the direction of the relationship between common mental disorders and disability in primary care.

To address this issue, the WHO Collaborative Study on `Psychological Problems in General Health Care' and the study by Gurejee et al. from Nigeria controlled for physician-rated severity of physical illness at baseline (35, 139). These studies described the incidence of physical and social disability among primary care patients diagnosed with depression and other common mental disorders. The WHO study found that at 3 and 12 month follow-up, among those with depressive illness at baseline 29% and 27% respectively were found to have an onset of physical disability compared with 22% and 18% onset rate among those who were not depressed at baseline (37). The adjusted odds ratio for onset of physical disability for depressed vs. non-depressed patients was 1.47 (95% CI, 0.99-2.17) at 3 month and 1.78 (95% CI, 1.15-2.73) at 12-month follow-up. The second study from Nigeria found that after adjusting for physician-rated severity of physical illness at baseline, an ICD-10 diagnosis of common mental disorders at baseline did not predict the onset of disability by 12 months (35). However, the study did find that overall psychological distress measured by GHQ-28 at baseline predicted onset of disability (Adjusted OR

3.5 95% CI 1.0-12). In this study from Nigeria only 32% subjects with psychological distress reached the threshold for ICD-10 diagnoses and those who did not nevertheless showed evidence of impairment, both cross-sectionally and 12 months later.

Effectiveness of interventions for patients screened positive for common mental disorders

Undoubtedly, the most crucial component of a primary care based screening program is interventions that lead to better outcomes for people identified by screening. We identified 11 intervention trials among patients screened positive for common mental disorders in primary care (41-54). The results from these trials are reported in 14 papers since two trials reported their findings in more than one paper, however there is no overlap in the results since the papers referred to different follow-up periods (3 months vs. 12 months) (49-51, 54). The trials were based in primary care clinics in India, Pakistan, Chile, South Africa, Zimbabwe, Kenya, Vietnam and Nigeria.

Types of intervention

The majority of the trials (n=8) evaluated multicomponent interventions that included psychoeducation and some form of psychological therapy and/or antidepressant medication (41-44, 46-48, 50, 51, 53). Other trials evaluated the benefit of a training program for health workers that included screening and treatment for common mental disorders (45), and the difference in compliance between selective serotonin reuptake inhibitor (SSRI) and tricyclic antidepressants among primary care patients identified by screening (52). Only three trials focused solely on the effect of antidepressants: two trials from India, one in which an SSRI was compared against placebo and psychological treatment and a second one that compared the compliance between SSRI and tricyclic antidepressants (48, 52). The third trial from Pakistan compared SSRI with psychosocial interventions (44).

There are several challenges to understanding the effectiveness of interventions from these trials due to the following reasons. First, with the exception of one placebo controlled trial from India, none of the trials had 'true' controls as the result of screening was shared with health care providers in

the control arm, and they were free to provide the usual care of choice. As discussed before, for the majority of primary care clinics in in low and middle-income countries the 'usual care' for mental disorders involves neither screening nor any interventions. Hence the control arms in most trials were 'enhanced usual care' in which providers could offer pharmacological treatment after screening and those in the intervention arm received a multicomponent package of care. Second, the majority of the trials (n=8) evaluated multicomponent interventions that included psychoeducation and some form of psychological therapy or anti-depressant medications, hence it is difficult to pinpoint the most effective intervention component. Finally, out of 11 trials only 4 used an ICD or DSM based clinical diagnosis following screening while the rest of the trials enrolled patients based on symptoms of psychological measured by screening questionnaires such as the PHQ-9 or GHQ-12 (41, 46, 48-50, 52). With these caveats in mind, we describe how interventions influenced the outcomes for psychological distress at short-term (2-3 months), medium-term 6 months and long-term 9-12 months

Short-term outcomes of intervention.

Eight trials reported short term (2-3 months) outcomes of intervention (41, 44-46, 48, 51-53). Only two of them used a clinical diagnosis of depression (41, 46) to enroll patients while the rest used screening instruments to identify patients with significant psychological distress that suggests depression. In all studies that reported short term outcomes following intervention, results favored interventions in terms of improvement in mean depressive symptom score over 2-3 months. Out of the three studies that compared rates of remission at 2-3 months, two showed significantly better remission in the treatment arm (41, 46). In the third study, while more than one-third of patients reported remission, the difference between the intervention and the control arm was not statistically significant (43). A comparison trial from Pakistan comparing antidepressants with psychosocial interventions also found that slightly more than one third of patients in both arms experienced remission at 3 months (44). Five studies that looked at short term (2-3 months) improvement in disability associated with common

mental disorders also found significantly better improvement in disability measures in the treatment arm following intervention (41, 44, 45, 48, 51).

Medium-term outcomes of intervention (6 months).

Seven trials followed up patients up to six months or more, out of which 5 reported the effect of interventions at 6 months (41, 42, 44, 47, 48). Compared with considerable improvements in the intervention arm during the first 2-3 months, by six months the effect of interventions was less conspicuous. For example, in a large cluster randomized trial from India, by six months the effect of intervention on recovery from any common mental disorder was modest and there was no significant difference in recovery between the multicomponent intervention and the usual care for patients with a diagnosis of depression (50). In this study the modest improvement with intervention was only for patients attending public primary care clinics; for those attending private GP clinics there was no difference between the intervention and usual care for any outcome measures. In a study comparing antidepressants with group psychosocial intervention among socially disadvantaged women with low literacy in Pakistan, depression symptom scores plateaued after 3 months and the substantial improvement in disability scores during the first 3 month showed a retrogressive trend by six months in both groups (44). In this trial while the antidepressant fluoxetine was given out free for six months, the group psychosocial intervention was provided only for the first three months. In contrast, the RCT from Chile that we referred earlier that enrolled women with persistent depression had booster sessions between 9 and 12 weeks and showed persistent improvement in depressive symptoms and functional improvement over six months (41). Similarly, a cluster RCT of psychological intervention for symptoms of common mental disorders from Zimbabwe also reported significantly fewer symptoms of depression among the intervention group at six months(42).

Long-term outcomes of intervention (9-12 months).

Only three trials followed up patients for more than six months. All three trials were based in India and followed up primary care patients for 12 months (48, 49, 54). Only one trial used formal diagnosis at recruitment while the rest used symptom scales to measure common mental disorder (49). The first trial was a three-arm RCT comparing psychological treatment, antidepressant and placebo for patients with psychological distress indicated by a score of 15 or more on Revised Clinical Interview Schedule (CIS-R)(48). The trial showed modest improvement in the antidepressant arm at 2 months but not over 2-12 months. Psychological intervention was not more effective than placebo for any outcome during either period. After a short-lived improvement in disability during 1-2 months both treatment groups had an increase in disability between 3 and 12 months compared with the placebo group.

The second study (2007-2009) was a cluster randomized trial examining the effectiveness of a stepped-care intervention led by lay health counsellors to address common mental disorders in primary care identified by screening (49). The study found modest effects of intervention over 12 months for those with an ICD-10 diagnosis in public primary care clinics but not in private GP clinics. For those with a subthreshold diagnosis there was no effect of intervention in public or private primary care settings. The results from this trial are influenced by poor compliance to interpersonal psychotherapy, a key component of intervention.

The third trial (54) was an RCT of the sustained effect of a brief behavioral intervention (for 3 months) based on behavioral activation and problem solving for primary care patients with moderate to severe depression indicated by a PHQ-9 score >14. At 12 months, the mean severity of the depression (BDI) and rate of remission was better for those in the intervention arm. However, there was significantly more relapse in the intervention arm and intervention had no effect on disability or mean days unable to work.

Adverse effects of intervention

Few trials reported harms or adverse effects associated with screening or interventions for common mental disorders in primary care (54). These were mostly related to adverse effect of anti-depressants which was a major reason for non-compliance to psychopharmacological treatments (52, 170).

Discussion

We reviewed the literature on primary care based screening for common mental disorders in low and middle-income countries. To the best of our knowledge, this review, which includes primary care based studies from 37 low and middle-income countries, is one of the largest to investigate this topic.

We examined whether there is enough evidence to justify integrating routine screening for mental disorder in primary care in low and middle-income countries. We focused on understanding the screening process and the use of screening instruments, in particular how it conforms to the general principles of screening, how screening influences treatment receipt and clinical course of illness under usual care, and the effectiveness of interventions for patients screened. We identified several challenges to successful screening of mental disorders in primary care in low and middle-income countries. These include major deficiencies in the screening process that could lead to significant proportion of false positive diagnosis, misrepresentation of short and self-remitting psychological distress as mental disorder that require treatment, and inadequate evidence on sustained and long term benefits of interventions, especially for antidepressants among screened positive primary care patients. A major caveat in these studies though is the absence of information on a non-screened group to compare the effect of screening. In the following sections we discuss these important findings in detail.

The practice of mental health screening in primary care based studies

First, only a small proportion of studies used screening instruments that are appropriately validated for the study population and the validity of the 'gold standard' diagnostic instruments used in validation studies are seldom reported. Second, contrary to screening guidelines, screening instruments are frequently used for diagnosing mental disorders, often misrepresenting screened positive as a diagnosis of mental disorders. The prevalence of mental disorders reported from such studies are misleading and the average false positive rate using a single stage screening could be close to 40%. The findings question the benefit of universal screening in primary care and echoes disputes about screening's utility in high income countries (25, 183). Compared with studies that follow screening with a diagnostic interview, studies that used screening alone often report inflated estimates of prevalence and their finding are less reliable.

Treatment and the clinical course of patients identified by screening under usual care.

The usual care (routine care) for common mental disorders in primary care in low and middle-income countries is very limited. Introducing depression screening and physician notification in these settings seldom results in appropriate treatment or improved access to care. Cost of treatment, cost of travel to the clinics, time lost from work, potential adverse effects of medications and stigma are important barriers to seeking treatment.

The largest group of patients who screened positive for common mental disorders in primary care have a short remitting course (38). A positive screening result is often transitory and about 56 to 62 percent of patients who originally screened positive for psychological distress, screened negative between 2 and 8 weeks without any systematic intervention (38, 41). However, a significant percentage of patients also experience persistent psychological distress ranging from 18% in Nigeria, 28% in Zimbabwe to 42% in Brazil. Compared with patients who are identified as cases exclusively by screening, those with a clinical diagnosis of depression following screening are more likely to meet the diagnostic

criteria at 12 months follow-up (184). Debilitating physical illness and disability are important risk factors for persistence of illness over 12 months. Persistence of distress symptoms are also associated with ongoing adverse life experience and resolution of adverse life situation favors lower rates of persistence.

In primary care patients the relationship between depression and disability is complex and coexisting physical morbidity is a major challenge in understanding this relationship. While disability is consistently found to be a risk factor for persistent depression, the evidence about major depression as a predictor of disability is unclear from the studies that we reviewed. This is comparable to few recent studies from high income countries that describe disability as a more robust predictor of depressive symptoms than depressive symptoms are of disability (185, 186).

Effectiveness of interventions for common mental disorders for patients identified by screening

Randomized control trials of interventions for common mental disorders in primary care in low and middle-income countries are few. Many trials are weak in terms of allocation concealment, blinding of intervention and outcome assessment and minimizing loss to follow-up. In addition, only few of them have used a clinical diagnosis of mental disorder to enroll eligible patients. In general, comprehensive benefits of intervention are most evident in short term (2-3 months) follow-up, while it is less so in long term follow-up. This could be due to the gradual improvement of patients in the control arm and poor treatment compliance over time. A lack of sustained improvement and remission in treated patients could also be explained in the light of the nature of life circumstances and difficulties many patients face in resource poor settings. The role of adverse life circumstances as a risk factor for the onset and persistence of common mental disorders is described in several studies that we reviewed (60, 170, 187). Some researchers suggest that for many patients in these resource poor settings, stressors in life are so severe and persistent that diagnosis and biomedical interventions are unlikely to be of any value unless combined with a community-based social interventions (48, 188).

It is difficult to identify specific interventions that benefited patients since most studies used a package of interventions including psychoeducation, various psychological treatments and antidepressants in a stepped care model. Moreover, poor compliance to antidepressants and psychological treatment is frequently reported in many larger trials. Some authors argue that it is the psychosocial aspects of the enhanced health worker-client interactions in trials that contributed to significant client recovery despite the paucity of medicines and poor compliance to psychological treatments (45). For example, a qualitative study nested within a primary care based RCT of stepped care intervention from India found that the positive therapeutic relationship with the health counsellor employed in the trial is the key factor that benefited patients even though adherence to interpersonal therapy and anti-depressants was limited (189). Interestingly, in this study, the effect of intervention (attributed to health counsellor) was only significant in busy government primary care clinics where consultation with physicians is commonly reported as unsatisfactory. In private clinics where physicians typically establish good rapport with patients and give personal attention to patients the effect of the stepped care intervention was not appreciable.

Evidence from newer high quality trials suggest that psychological interventions based on problem solving approaches are useful in providing sustained improvement over one year (51, 54). It may be that the problem solving approaches are more likely to address psychosocial factors associated with the causes and persistence of psychological distress. Unfortunately, there is limited evidence to support antidepressant use among primary care patients in these settings and compliance to antidepressants including newer SSRIs are generally poor.

While studies highlight the critical need to integrate screening and detection of depression with affordable, appropriate, and sustainable interventions (170), treatment compliance is relatively poor even in well-endowed study settings were treatments such as anti-depressants and psychological therapies are provided at no cost. This alludes to a major sticking point for opportunistic screening of

common mental disorders in primary care, that is, what is acceptable to patients in terms of diagnosis and treatment of common mental disorders? Limited evidence from the few qualitative studies in low and middle-income countries suggests that, while patients attribute some of their symptoms to life stressors they seldom associate their symptoms to a 'mental disorder' (190). They found it more acceptable to describe psychological distresses in terms of the local idioms of distress, without any diagnostic labels. A qualitative study nested in an RCT of primary care based mental health care in India found that, patients often doubted the role of health care intervention in addressing one's life's difficulty, which was a key reason for non-adherence (191). This has important implications for treatment and management of common mental disorders in primary care. The low compliance to anti-depressant and psychological treatment even in controlled study settings, challenges the notion that improving access to treatment for common mental disorders in primary care would address the treatment gap for these conditions.

The main challenge in primary care treatment of common mental disorders is to identify patients who are most likely to benefit from interventions. Although patients with a history of mental disorders, chronic illness and disability are more likely to have persistent psychological distress, at present there is a lack of evidence to show that primary care based screening and interventions are ultimately beneficial to these patients. Nonetheless, the few higher quality studies suggest that interventions focused on patients with severe depression(11) or persistent depressive symptoms (41) is more likely to demonstrate sustained benefit. Future studies should focus on developing methods to improve identification of patients who could benefit from medical interventions. Further, it is critical to develop and evaluate locally informed and culturally sensitive interventions based on psychosocial approaches and problem solving.

Limitations

The results of this review are influenced by the shortcomings of the literature search and of the studies that were selected. A major limitation of this reviews is the absence of studies comparing screened and a non-screened group of primary care attendees to evaluate the net effect of screening. The review was also restricted to study results published in English, hence we may have missed studies published in other languages. Further there is a risk of publication bias across studies due to the increased likelihood to report positive results associated with interventions for mental disorders in primary care.

Conclusion

At present evidence to support routine screening for common mental disorders in primary care in low and middle-income countries is limited. Most patients identified by screening in primary care have contextual, transitory and self-limiting psychological distress. Patients with persistent distress symptoms identified by repeated screening and those with moderate to severe depression may benefit from screening in the presence of easily accessible, and sustainable evidence based interventions, although long term effects of such interventions are uncertain. Available evidence on treatment for common mental disorders in primary care support culturally suitable psychological interventions focused on problem solving and psychosocial approaches

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Table 2.1 Features of clinical trials and cohort studies

Paper	Primary screener	Screening + Diagnosis	Intervention trial	Cohort study	Follow-up			Trial		Incidence-screened negative	Clinical Course
					2-3 months	6 months	9-12 months	Stepped care &/ Psychological Intervention	Anti-depressant trial		
Araya, Ricardo, et al. (41)	GHQ-12	X	X		X			X			
Barkow, Katrin, et al. (33)	GHQ-12	X		x			X			X	
Chibanda, Dixon, et al.(42)	SSQ		X			X		X			
Chowdhary, Neerja, et al.(43)	PHQ-9		X		X			X			
Fleck, Almeida, et al.(34)	CES-D	X		x			X				X
Gureje, Oye. (35)	GHQ-12	X		x			X				X
Husain, Nusrat, et al. (44)	SRQ-20	X	X		X	X			X		
Jenkins, Rachel, et al. (45)	GHQ-12		X		X						
Lima, Ana da Silva et al. (36)	CES-D	X		x			X				X
Niemi, Maria, et al.(46)	PHQ-9	X	X		X			X			
Oladeji, Bibilola D., et al. (47)	PHQ-9		X		X	X		X			
Ormel, J., et al. (37)	GHQ-12	X		x	X		X				X
Patel, Vikram, et al. (50)	GHQ-12	X	X			X		X			
Patel, Vikram, et al. (48)	GHQ-5		X		X	X	x	X	X		
Patel, Vikram, et al. (49)	GHQ-12	X	X				X	X			
Patel, Vikram, et al. (38)	SSQ			x	X		X				X
Patel, Vikram, et al. (51)	PHQ-9	X	X		X			X			
Pereira et al.(52)	GHQ-5	X	x		X				X		
Petersen, I., et al. (53)	SRQ-20		X		X	X					
Simon, Gregory E., et al. (170)	CES-D	X		x			X				X
Todd, C., et al. (40)	SSQ			x	X		x			X	
Weobong, B et al. (54)	PHQ-9		X				X	X			

Table 2.2 Mental health screeners used:

Screening questionnaire	Number of studies
BDI (Beck's depression inventory)	6
CES-D (Center for Epidemiologic Studies Depression Scale)	7
GAD-7 (Generalized anxiety disorder- 7 items)	2
GHQ-12 (General health questionnaire -12 items)	38
GHQ-28 (General health questionnaire-28 items)	4
GHQ-30 (General health questionnaire-30 items)	2
GHQ-5 (General health questionnaire-5 items)	2
HADS (Hospital anxiety depression scale)	1
IDSS (International depression symptom scale)	1
K-10 (Kessler psychological distress Scale 10 item)	1
MDQ (Mood disorder questionnaire)	1
MHIS (mental health item sheet)	1
Unnamed study specific screener	5
NSRQ-20 (Nigerian Self-reported questionnaire)	1
PGI-HQ (Post graduate inst. health questionnaire- India)	2
PHQ (Patient health questionnaire)	3
PHQ-15 (Patient health questionnaire 15 item)	1
PHQ-4 (Patient health questionnaire 4 item)	1
PHQ-9 (Patient health questionnaire 9 item)	18
RAD (Rahim anxiety depression scale)	1
SDQ-9 (Screening for depression questionnaire)	1
SDS (Zung- Self rating depression scale))	3
SRQ-20 (Self-reported questionnaire)	25
SRQ-24 (Self-reported questionnaire)	1
SSC (Somatic symptom checklist)	1
SSQ (Shona Symptom questionnaire)	6
SWB (Subjective well-being subscale)	1
VDS (Vietnamese Depression scale)	1

Chapter 3: What does mental health screening identify in primary care? A study of the clinical course of screened positive patients from India

Introduction

Common mental disorders are non-psychotic mental health conditions that include depressive, anxiety, adjustment and somatic symptom disorders that impair daily functioning (1, 192). They have a high prevalence in primary health care settings globally, contribute to the global burden of mental disorders, and adversely affect a broad range of health, social and economic outcomes (60, 123, 139, 181, 193, 194). Early identification and treatment of common mental disorders could decrease adverse events such as suicides, and improve disease outcome and quality of life. Therefore, routine mental health screening of adults attending primary care clinics, along with accessible mental health care at primary care, is often presumed to improve outcomes for common mental disorders (18, 195, 196).

Even though screening for mental disorders for early detection and treatment is 'intuitively appealing' (7), the evidence for the effectiveness of mental health screening in primary care is insufficient. There are two main reasons for the lack of consensus regarding primary care-based screening for common mental disorders, particularly related to screening for depression. First, questionnaire-based screening typically used to identify people at risk of common mental disorders is often unreliable when used in the general population or primary care, and results in high false positive rates (25, 197). This is because most questionnaire based screening for common mental disorders identifies patients with psychological distress which could be pathological needing treatment or non-pathological. Although clinical diagnosis following screening helps to discern pathological from non-pathological distress, follow-up diagnosis and evidence based treatments are the weak links in many screening programs. For instance, a recent study from primary care offices in multiple centers in the United States found that the use of short depression screening measures in these settings was associated with increased depression diagnosis and increased antidepressant recommendations and/or

prescriptions in patients with few or no depression symptoms (198). False positive screenings may expose individuals to stigmatization, additional psychologic testing, as well as needless psychologic and pharmacologic treatment regimes. Second, the majority of patients identified by screening in primary care have symptoms of mental disorders that are more likely to reflect physical illness, and psychosocial problems (188, 199). They are typically diagnosed with milder forms of depression or subthreshold conditions that are often short-lived (200). Meta-analyses have found that antidepressants are generally not effective for milder forms of depression and report poor risk benefit ratio for treating these individuals (201-203).

These issues are particularly pertinent in low and middle-income countries where a significant proportion of people face poverty, injustice, inequality, violence and lack of opportunities without sufficient economic or social safety nets or access to any social welfare services. In these settings, many screened positive individuals may be experiencing non-pathological distress. Although these patients could have screened positive for common mental disorders and met criteria for a diagnosis in primary care clinics, their symptoms are more likely to reflect situational distress and not diseases or disorders that might benefit from medical interventions such as antidepressants (204, 205). Examining the course of mental disorders identified by screening in primary care could help us to understand the clinical significance of a positive screen, and may provide useful insight to distinguish non-pathological distress from pathological distress that requires medical interventions (3). Unfortunately, at present, we have little information regarding the course of psychological distress or the clinical significance of a positive screen for common mental disorders in primary care in low and middle-income countries.

In an attempt to address this knowledge gap, we studied the clinical course of psychological distress and common mental disorders identified by screening in primary care clinics in India. The overarching goal of this study was to understand the significance and progression of common mental

disorders identified by screening in primary care. Specifically, we aimed to answer the following questions:

1. What proportion of patients screened positive for common mental disorders have a mental disorder diagnosable by a fully structured ICD-10 diagnostic instrument and what is the distribution of the diagnoses? What are the patient characteristics associated with a diagnosable mental disorder among screened positive patients?
2. How stable are the baseline ICD-10 diagnoses and what is the trajectory of overall psychological distress over a period of one year?
3. Based on the distress scores during one year follow up, what are the proportions of patients with mild and short distress, a fluctuating course and persistent distress? and what are the factors associated with persistent distress?

Methods

Study design and sample

A study of the course of common mental disorders identified by screening in primary care is required to answer our questions. Typically, what we observe in study settings is the 'clinical course' that is the disease course that would include the influence of usual care in a particular setting, since once screened positive, few patients could intentionally be excluded from any intervention for mental health conditions such as depression as it is unethical not to offer well accepted treatments (206). However in many resource poor settings, the usual care for screened positive patients is 'no care' and thus the clinical course may very well be similar to the natural course. For this study we used data from a cluster randomized control trial (RCT), the MANAS trial from Goa, India to examine the course of screened positive patients.

MANAS is one of the largest community trials in mental health in primary care in a low or middle income country. Details of the study's sample and design are described extensively elsewhere, and the summary that follows draws on those descriptions (207). The aim of the trial was to assess the effectiveness of a collaborative stepped care intervention led by a lay health counsellor in the recovery of primary care patients from common mental disorders. The trial was designed as a cluster randomized control trial with the primary care clinic as the unit of randomization. Each study arm included 12 clinics; half were free public primary health clinics (PHC) and the rest were private general practitioner (GP) clinics. Eligible adult primary care attendees screened positive for common mental disorders from the 24 study clinics were identified and followed up for a for a period of one year. The recruitment and follow-up were completed from April, 2007, to September, 2009 (50).

The collaborative stepped care model involved a lay health counsellor leading the screening for common mental disorders and managing interventions in collaboration with the primary care physician and a visiting psychiatrist. The intervention included psychoeducation, antidepressants and interpersonal psychotherapy delivered in 'steps' depending on the severity of the illness and the patients' response to treatment. Patients in the control clinics - the usual care group, received usual care, which is the primary care physician starting the treatment of their choice. In this trial the usual care in the control group is enhanced by screening for common mental disorders by a lay health counsellor and providing screening results to physicians. Physicians in the control clinics were allowed to start treatments of their choice. Antidepressants were prescribed by physicians in both control and intervention arms, while other components of the intervention such as psychoeducation, interpersonal psychotherapy and collaborative case management were only available in the intervention clinics. The original study found a modest benefit for the collaborative stepped care intervention in public primary care clinics, but not in private GP clinics (50, 184).

We used baseline data from all trial participants in the MANAS trial to answer our questions related to screening and diagnosis. We then focused primarily on participants in the control group of the trial to understand the clinical course of patients screened positive for common mental disorders under usual care. A limitation of this database though, is the absence of follow-up data of a sample of primary care patients who screened negative as a comparison.

Recruitment

Patients visiting the primary health clinic were invited to participate in the mental health screening while waiting to see the physician. A health counsellor administered the screening questionnaire to those who consented. The result of the screening interview was shared with the primary care physician during the medical consultation. Only those patients who were expected to be resident in the study communities for the following 12 months were considered as eligible for recruitment. See figure 3.1 for the number of patients consented and eligible for recruitment. Eligible patients who screened positive and agreed to join the trial were also accessed for any mental disorder using a structured diagnostic interview schedule during the same visit. The ICD-10 diagnosis was generated later using a computer algorithm but was not available to the primary care physician during the consultation.

Figure 3.1 depicts the progress of participants through the trial. Altogether 20,352 patients were screened for common mental disorders using the GHQ-12 of whom 3816 (18.8%) screened positive. Among the screened positive, 382 were not eligible and 638 refused, yielding a final sample of 2796 participants. The number of patients enrolled in the collaborative stepped-care clinics and in the enhanced usual care clinics were 1360 and 1436 respectively. Outcome assessments were done at two, six, and twelve months using a structured diagnostic interview at the home of study participants by interviewers from an institution not related to the implementation of the intervention program and blind to the study arm status. The completion rates were 89% (n=2491) at two months, 87% at six

months and 85% at twelve months. Overall, 2181 (78%) of all screen-positive participants were seen at all three follow-up visits.

Measures

Screening scale and diagnostic interview

The MANAS trial used the 12-item General Health Questionnaire (GHQ-12) to screen for psychological distress and recruit patients into the trial. The Clinical Interview Schedule-Revised (CIS-R) was used to assess symptom severity and generate ICD-10 diagnoses of common mental disorders.

The 12-item General Health Questionnaire (GHQ-12)

The GHQ was designed to measure psychological distress in population surveys and epidemiological studies, and to screen for non-psychotic mental disorders in clinical settings (208). Originally developed in the UK, the GHQ is one of the most widely used screening questionnaires internationally, including in India. The short 12-item version of the GHQ has been used previously in studies at the study site in Goa, India (209). GHQ-12 is designed as a unidimensional scale for the assessment of mental distress or a minor psychiatric morbidity with a main focus on depressive symptomatology (210). The 12 items assess the respondent's current state and focus on the inability to carry out normal functions and the appearance of new and distressing symptoms (208). Each item is scored as 0 ('less or no more than usual') or 1 ('rather or much more than usual'), giving a maximum total score of 12. In this study GHQ-12 was used at the baseline for screening primary care patients. A recent systematic review of validated screening tools for common mental disorders in low and middle income countries calculated a diagnostic odd ratio (DOR) of 22.59 for GHQ-12 based on its psychometric properties (211). DOR is a measure of a screening tool's effectiveness and is defined as the 'ratio of the odds of disease in test positives relative to the odds of disease in test negatives' (212). DOR>20 is considered to indicate strong validity (211). A cut-off score of 5/6 was used for screening primary care patients in the MANAS trial. A validation study of GHQ with cut-off score of 5/6 in this study population

found sensitivity of 73%, specificity of 90%, and a positive predictive value of 61% (56). Even though GHQ is designed to measure the risk of non-psychotic psychiatric illness, a positive result on GHQ-12 is not a diagnosis of mental disorder, but it helps to inform further evaluation and intervention.

The Clinical Interview Schedule- Revised (CIS-R)

The revised version of the Clinical Interview Schedule is a standardized psychiatric interview that can be administered by interviewers without clinical training in psychiatry (213). The CIS-R interview asks about symptoms of ICD-10 common mental disorders, and the questions focus on 14 symptom domains (Table 3.1). For each of these symptom domains, a screening question is asked to decide if that specific symptom was experienced by the respondent in the previous month. If the respondent experienced the symptom, a detailed evaluation of their experiences of that symptom in the previous seven days is covered by a sequence of questions. Based on the response, a score signifying the severity of the symptom domain ranging from 0-4 (or 0-5 for the depressive ideas 'symptom') is assigned for each of the 14 domains (213). A significant symptom is indicated by a score ≥ 2. A score of 0 is given for those who did not experience a particular symptom in that week. The total scores for the 14 symptom domains range from 0-57; a higher score is considered as an indication of the severity of overall psychological distress. A multi country study of lay interviewer administered CIS-R found that an overall scores of 12 or more would indicate the level of morbidity that would raise concern in a physician of a psychiatric disorder (213). Further, by applying a diagnostic algorithm to the CIS-R responses, a set of ICD-10 disorders, including generalized anxiety disorder, depressive disorders, obsessive compulsive disorder, and phobias can be diagnosed. See table 3.2 for the list of diagnoses generated using the algorithm.

The CIS-R is widely used for the diagnosis of mental disorders in epidemiological studies globally. The CIS-R has been used on every wave of the UK national mental health survey series (*The Adult Psychiatric Morbidity Survey*) to diagnose six types of common mental disorders including

depression, generalized anxiety disorder, panic disorder, phobias, obsessive compulsive disorder, and common mental disorders not otherwise specified (214). While the CIS-R has been extensively used in India, translated and field tested in the study population, we are not aware of any validation studies of CISR-R against a gold standard psychiatric interview in India. However, a cross-cultural factorial validation of the CIS-R among ethnic minority population in the UK including Indian immigrants found that underlying "depression-anxiety" construct maintains measurement invariance across ethnic groups, even though there is inconsistency in the reporting of somatic symptoms across cultures (215). CIS-R has also been successfully validated among people of Indian origin in Malaysia and that study reports a sensitivity of 88%, specificity of 96% and a positive predictive value of 97% for a cut off score of 12 (216). Further, a recent validation study of CIS-R based on the Hong Kong mental morbidity survey showed good criterion validity in diagnosing common mental disorders against the diagnoses made by the Structured Clinical Interview for the DSM-IV (217).

Focusing on symptoms from the week prior to the interview avoids recall bias, and helps to distinguish between co-occurring symptoms and symptoms which occur weeks, months apart (218). However, there is also the possibility of missing a disorder with a fluctuating course if the patient was symptom free during the week before the interview.

Sociodemographic factors

Self-reported age and gender were recorded for each participant during recruitment. Detailed sociodemographic information including ethnicity, marital status and education was compiled during the first follow-up interview within two months of recruitment. We used the responses for sociodemographic variables in their original form or recoded as described in table 3.3.

Life stressors

Patients were also asked about two major life stressors commonly reported among primary care patients: 1) presence of long standing physical illness, 2) financial difficulties, i.e. finding it difficult to

make ends meet. We recoded response to question on financial difficulty into binary form as described in table 3.3

Analysis

Data processing

Data were processed, cleaned and organized by the four interview phases (baseline, 2 months, 6 months and 12 months) by Sangath, the institution that conducted the study in India. Sangath provided de-identified data for analysis including participant characteristics, symptoms of psychological distress, diagnosis, intervention offered and outcomes measured at 2 months, 6 months and 12 months.

Missing data

The proportion of patients lost to follow-up was 11% at two months, 13% at six months, and 15% at twelve months. Overall, 2181 (78%) of all screened positive participants were seen at all three follow-up visits. Missing patients were more likely to be younger and male. The original investigators conducted a sensitivity analysis to examine the effect of the missing data by using multivariate imputation by chained equation (MICE) (50). This procedure created multiple datasets which were analyzed with an individual level Poisson regression model, allowing for within-cluster correlation using generalized estimating equations (50). Separate models by age group and sex were fitted, which showed no evidence of differential recovery rates by sex or age and there was no evidence that the missing data were associated with outcomes measured at follow-up. Under the assumption that data were missing at random after conditioning on age and gender, for the published analyses data were not imputed. The investigators of the original study thus concluded that analyses excluding missing data, but adjusted for age and gender should be unbiased (49). We followed a similar approach to follow-up analyses, excluding individuals who were lost to follow-up and adjusting for age and gender.

Clustering

In the MANAS study, the primary health clinic or a GP clinic formed a cluster and the study enrolled 2796 patients in the trial from the 24 clinics (clusters). Since individual-level regression methods are not robust when there are few clusters per group, the original analyses were based on cluster-level summary measures and the sample provided more than 90% power to detect a difference in recovery rates of 70% in the intervention group versus 50% in the control group (50). To address constraints in estimating parameters and variances with a small number of clusters (219), we used cluster wild bootstrap implemented using the user-written *'cgmwildboot*' command for linear regression models (available from https://sites.google.com/site/judsoncaskey/data) in Stata 14.2. For logistic regression models we used score bootstraps for regression analyses implemented through the '*boottest'* package in Stata 14.2 (220). For more information on cluster analyses decisions and bootstrapping method see appendix C.

Specific analysis plans

Our specific analysis plans were as follows:

To describe the proportion screened positive patients with a mental disorder diagnosable by a fully structured ICD-10 diagnostic instrument, the distribution of diagnoses, and the patient characteristics associated with mental disorders:

We first describe the key characteristics of all study participants. Since we expected differences in these characteristics by gender, we also present them separately for men and women. Then we report the prevalence of ICD-10 diagnoses and the distribution of specific diagnoses. We used bootstrapped confidence intervals to report distribution of diagnoses to account for clustering. We considered sociodemographic factors (age, gender, marital status, ethnicity and education) and two life stressors (financial difficulty and longstanding illness/disability) as predictors of baseline ICD-10 diagnosis. To model these predictors of any ICD-10 diagnosis, we used logistic regression with the score bootstrap

method. Similarly, we also examined the predictors associated with specific diagnoses. We used data from both arms of the trial for these analyses.

To examine the stability of ICD-10 diagnoses and the trajectory of overall psychological distress over a period of one year:

Since our aim is to study the clinical course of screened positive patients under usual care, we included only patients in the control group. To examine stability of the ICD-10 diagnoses we first describe the diagnosis for those screened positive at baseline, 2 months, 6 months and 12 months. Using descriptive tables, we describe the change in diagnosis at follow-up and the percentage of patients who recovered at each follow-up point. We defined recovery as not meeting an ICD-10 diagnostic criteria for any mental disorders using the structured psychiatric interview. To quantify the diagnostic stability of ICD-10 diagnosis among screened positive patient we used "prospective consistency" described by Schwartz et al. (221). Prospective consistency refers to the proportion of individuals in a category at the first evaluation who retain the same diagnosis at their follow-up evaluation.

Often the measures of diagnostic stability in epidemiological studies identify methodological unreliability rather than genuine changes in clinical states, therefore a better indicator of the changing disease picture would be the course of overall psychological distress based on the CIS-R score over time. Hence we also describe the changes in overall psychological distress measured by the diagnostic instrument CIS-R during the three follow-up interviews. We also describe the trajectory of mean scores for all participants in the control group using an appropriate graph.

To examine the proportions of patients with mild and short distress, a fluctuating course and persistent distress based on the distress scores and identifying the factors associated with persistent distress

Further, based on the CIS-R scores we identify the proportion of three clinically important groups of patients: 1) patients with mild or no psychological distress during follow-up, defined as those whose CIS-R score remained below 12 at all three follow-up; 2) patients with persistent psychological distress indicated by a CIS-R score of 12 or more at all three follow-up interviews; 3) patients with a fluctuating course indicated by a CIS-R score that varies across the threshold (score of 12) at the follow-up interviews. In our final analysis we look for patient characteristics that predict persistent psychological distress using a score bootstrapped logistic regression model.

Under the usual care model physicians are free to prescribe antidepressants in primary care. We also examined whether antidepressant prescription and use is associated with two outcomes, namely rapid recovery i.e., mild or no psychological distress during follow-up, and persistent distress.

Results

Participant characteristics

As described in table 3.4, about 82% (n=2305) of the trial participants were women. Close to half of the participant were 50 years or older and the age distribution for men and women were similar. The majority of participants were currently married (61% of women and 81% men), but a larger percentage of women were widowed or separated (34% of women and 5% of men). Only about one-third of women and half of the men had education above the primary school level. A substantial proportion of patients were poor with 47% of women and 39% of men found it difficult to make ends meet. Long standing physical illness including chronic diseases or disability was reported by 47% of women and 46% of men.

Prevalence of Common mental disorders

From the 24 study clinics, 20352 patients were screened, of whom 3816 (18.8%) screened positive for common mental disorders. Among the 2796 eligible screened positive patients who consented to participate, fifty-five percent scored between 5 and 7 on the screening instrument GHQ-12, which indicates mild psychological distress while the remaining patients scored >7 indicating

moderate to severe psychological distress. CIS-R, the diagnostic instrument used in this study generated an ICD-10 diagnosis as well as an overall score to indicate severity of psychological distress. About 80% of patients who screened positive for mental disorders using GHQ-12 also scored ≥ 12 on CIS-R, generally considered as 'case level' psychological distress.

Although most screened positive patients were diagnosed with a common mental disorder using the CIS-R, a fifth did not meet any diagnostic criteria. As depicted in table 3.5, the most prevalent diagnosis was mixed anxiety depressive disorder (37%) followed by mild to moderate depressive disorder (16%). About 11% of screened positive patients had a diagnosis of severe depressive disorder. The least prevalent diagnosis was panic disorder (4%; n= 102) followed by phobias (5%).

In a logistic regression model examining the predictors of ICD-10 diagnosis (see table 3.6), female gender (1.34 95%CI 1.08-1.66), being separated or widowed (1.31 95%CI 1.01-1.72) and extreme financial distress (1.38 95%CI 1.08-1.75) predicted the receipt of an ICD-10 diagnosis. We also examined patient characteristics that predicted specific ICD-10 diagnosis and found increased risk for generalized anxiety disorder among women compared with men (OR 2.19 95%CI 1.23-3.92), and among those who were separated or widowed (OR 1.5 95% CI 1.11-2.03). Further, the risk for mixed anxiety depressive disorder was lower among migrants from other states 0.58 (0.39-0.85). While the risk for mild to moderate depression was lower among those with long standing physical illness or disability, they were more likely to have severe depression (OR 1.4; 95%CI 0.97-2.03). We found that education and long standing physical illness did not predict the risk for any ICD-10 diagnoses. Similarly, gender did not predict any depressive diagnoses.

In the following section we discuss the distribution and the stability of baseline diagnoses at 2, 6 and 12-month follow-up of participants attending the 12 control clinics.

Follow up diagnosis

About 46% (n=601), 42% (n=541) and 34% (n=427) of screened positive patients met the criteria for an ICD-10 diagnosis at 2, 6 and 12 months respectively under usual care. Table 3.7 shows the proportion of patients diagnosed at the baseline and each follow up interviews. The most prevalent diagnosis was mixed anxiety and depressive disorder diagnosed in 33% of patients at baseline, 25% at 2 months, 24% at 6 months and 19% at 12 months. This was followed by mild to moderate depression diagnosed in about 20% of patients at baseline, 8% at 2 and 6 months and 7% of patients at 12 months. About 12% of patients were diagnosed with severe depression at baseline, 4% at 2 and 6 months and 3% at 12 months. The proportion for most disorders decreased over time, and by 12 months 66% of those who screened positive at baseline did not qualify for any diagnosis.

Changes in meeting an ICD-10 diagnosis

As shown in table 3.8, about half of the followed-up patients who had a baseline ICD-10 diagnosis did not meet the criteria for a diagnosis by 2 months. The rate increased to 54% by 6 months and by 12 months 63% of patients with baseline diagnosis did not have any ICD-10 diagnosis. The maximum recovery from an ICD-10 diagnosis was for patients with a baseline diagnosis of mixed anxiety and depressive disorder (59% at 2 months; 60% at 6 months and 72% at 12 months) and the minimum was for patients with a diagnosis of panic disorder (41% at 2 months, 46% at 6 months and 54% at 12 months).

Diagnostic stability

Table 3.9 shows the prospective consistency of baseline diagnoses at 2 months, 6 months and 12 months, defined as the percentage of individuals in a diagnostic category at baseline who retain the same diagnosis at follow-up. At two-month follow-up, the prospective consistency was less than 15% for all diagnoses except mixed anxiety and depressive disorder. Among patients with an initial diagnosis of mixed anxiety and depressive disorders 24%, 22% and 17% maintained the same diagnosis at 2, 6 and 12

months respectively. For patients with a diagnosis of severe depressive episode at baseline, about 7% maintained the same diagnosis at 2, 6 and 12 months although they were not the same patients. The lowest rate of prospective consistency was for phobias diagnosed during the baseline interview at the primary care clinics.

Generally, prospective consistency is affected by switching to a new diagnosis as well as not meeting the criteria for any ICD-10 diagnosis. Table 3.10 depicts the percentage of patients switching to a new diagnosis, those who did not meet the ICD-10 diagnostic criteria for any mental disorder and those who maintained the same diagnosis at two-month follow-up. Switching to a new diagnosis was more common than maintaining the same diagnosis at 2 months for all categories except mixed anxiety and depressive disorders. As depicted in table 3.10 among patients who completed the follow-up interview at 2 months, only 17% with a baseline diagnosis of mixed anxiety and depressive disorder switched to a new diagnosis while 24% continued with their original diagnosis and about 59% no longer met any diagnostic criteria. With regard to severe depression 52% of patients switched to a new diagnosis, 42% did not meet any diagnostic criteria and 7% maintained their baseline diagnosis of severe depression. For the other baseline diagnoses, by two months, between 41 and 56 percent of patients switched to a new diagnosis, while less than 15% maintained their original diagnosis, and between 41 and 47 percent did not meet the criteria for any diagnosis.

Table 3.11 shows the diagnoses and loss to follow-up at two months for all baseline diagnostic categories in detail. For all baseline diagnostic categories, the most common outcome at 2 months was recovery from the ICD-10 diagnosis. The next common outcome was switching to a new diagnosis. Mixed anxiety and depressive disorder was the most frequent new diagnosis that patients switched into at 2 months. For example, about 23% of patients with severe depressive disorders and 21% of patients with generalized anxiety disorders switched to mixed anxiety and depressive disorder. Overall, at two-

month follow-up there were 217 new cases of mixed anxiety and depressive disorder, 83 new cases of mild to moderate depression and 46 new cases of severe depression.

As shown in table 3.11, at baseline, about 20% (n=292) of screened positive patients did not have any ICD-10 diagnosis. Among them, after subtracting lost to follow up (n=30; 11%) at two months, 70% of patients (n=183) continued without any diagnosis, while 30% received a new diagnosis (see table 3.10). The most common diagnosis was mixed anxiety and depression (15% n=45) followed by mild/moderate depressive disorder (5%). Further, 70% and 76% of patients without any ICD-10 diagnosis at baseline and who were follow-up maintained their disorder free status at 6 months and 12 months respectively.

Overall psychological distress

Since the ICD-10 clinical diagnosis of the majority of screened positive patients changed within two months, we examined the overall psychological distress measure reported from the CIS-R diagnostic interview. A scores of twelve (≥12) was used as the cut-off to suggest psychological distress indicative of common mental disorder. We found that the CIS-R cut-off (≥12) score was nearly in perfect agreement with the presence of any ICD-10 diagnoses, thus 99% of patients with an ICD-10 diagnosis scored ≥12 on CIS-R. At baseline, about 79% of screened positive patients (n=1131) in the control group scored ≥12 on CIS-R and by 2 months more than half of them scored less than 12. The mean CIS-R score for the control group at baseline interview was 19.4 (95% CI:17.6 -21.2). The mean score improved from 19.4 to 9.5 during the one year follow up. As shown in figure 3.2, the maximum improvement in score, i.e., about 40% reduction in distress score (decreased from 19.4 to 11.7) occurred within the first two months of baseline diagnosis. Between 2 months and 12 months the improvement was less pronounced and the mean distress score decreased only by about 2 points.

Pattern of distress scores

We classified screened positive patients into three clinically important groups based on the course of psychological distress: 1) patients with distress of short duration i.e., patients whose overall distress score remained below threshold (<12) throughout the follow up period; 2) patients with persistent distress i.e., those whose score remained above threshold (≥12) in all three follow-up interview; 3) patients with a fluctuating course i.e., those whose score was not consistently above or below the threshold. Overall, about 19% of patients (n=218) experienced persistent distress throughout the follow up period while for 42% (n=483) of patients the distress experienced was uneven. For 39% (n=448) of screened positive patients the distress was of short duration and they did not report any case level distress during follow-up interviews.

Predictors of persistent distress

To examine patient characteristic that could predict persistent distress among patients, we investigated important sociodemographic factors and life stressors. As reported in table 3.12, in a score bootstrapped logistic regression mode we found female gender (OR 1.51; 95%CI 1.01-2.26), severe financial distress (OR 2.13; 95%CI 1.65-2.75), and higher baseline distress score (OR 1.08; 95%CI 1.03-1.12) on the CIS-R scale predicted persistent distress during one-year follow-up. Those with lower education (OR1.59; 95% CI 0.97-2.58) and long standing illnesses (OR 1.43 0.98-2.08) were also more likely to have persistent distress, although the relationship was not statistically significant at the conventional level of confidence.

Role of antidepressants in the clinical course under usual care

Following screening, about 50% (n=717) of patients in the control group received a prescription for an antidepressant from the primary care physician and 447 (31%) of patients reported using an antidepressant medication for more than 15 days. We examined whether antidepressant prescription or antidepressant treatment (for more than 15 days) predicted two clinically important outcomes i.e.,

distress of short duration and persistent distress. As depicted in table 3.13, we did not find any association between the clinical outcomes and prescription for antidepressant or antidepressant use in a bivariate model as well as in multivariable models that adjusted for severity of symptoms at baseline. Further a subgroup analysis including only patients with a baseline diagnosis of depression did not find any association between use of antidepressant for more than 15 days and psychological distress of short duration (distress that lasted for less than two months).

Discussion

Summary of key findings

In routine screening of adult primary care patients, close to one-fifth (19%) of the patients screened positive for common mental disorders and about 80% of screened positive patients received an ICD-10 diagnosis of a mental disorder. The most common diagnoses were mixed anxiety depressive disorder (37%), mild to moderate depression (16%) and severe depression (11%). However, by two months, 50% of patients with a baseline ICD-10 diagnosis in the control group no longer met the diagnostic criteria for any diagnosis. In addition, about three-fourth of the baseline diagnoses changed within two months. The overall psychological distress score (CIS-R score) markedly improved for more than half of the patients in the control group to below case threshold level by two months, and the mean distress score for the cohort remained below the case threshold level at 2, 6 and 12-month follow-up. A significant percentage of screened positive patients (39%) experienced a relatively short period of psychological distress and did not report any 'case level' psychological distress during one-year follow-up. Nevertheless, nineteen percent of screened positive patients reported persistent distress throughout the follow-up period and 42% experienced a fluctuating course. We found increased risk for persistent distress among women, those with lower education, those experiencing long standing physical illness or disability and those who faced severe economic difficulties. Higher baseline psychological distress scores also predicted

persistent distress. However, perhaps due to poor compliance, we did not find any association between antidepressant use and the clinical outcomes that we examined.

Significance of the findings

According to the 2018 Lancet Commission report on global mental health, screening for common mental disorders is an active component of the integrated and collaborative care model for the integration of mental health in primary health-care platforms (222). However, the results from our study demonstrate that screening and treatment for common mental disorders in primary care is more complicated than often assumed. Casey et al. in 2001 suggested that psychiatric disorders in primary care could be divided into three broad categories: distress requiring no specific interventions, distress that need intervention and major psychiatric disorders (223). Based on our examination of the clinical course of screened positive patients from primary care in India, we report that a significant proportion of screened positive patients have self-limiting psychological distress that might require no specific interventions.

Self-limiting psychological disorders in primary care

We found that the duration of probable mental disorder identified by screening was relatively short for the majority of patients. About 39% of them did not report any 'case level' psychological distress during follow-up. This is not an unexpected finding as some researchers have argued that much of the cases that is picked up by screening in for depression in general population is non-pathological distress, that remits without treatment (224). However, the clinical course of major (225) depression reported from outpatient care settings in high income countries appear less favorable (226). Only one-fourth of the patients remit within 6 months and more than half of the patients still have major depressive disorder after 24 months (227, 228). There could be several reasons for this dramatic improvement within two months that we found in our study population. In this study, baseline screening and diagnosis was conducted at the primary care clinics or the private GP clinics when patients were waiting to see a physician whereas follow-up interviews were at the patient's home. In these clinics, medical consultations

are almost exclusively for acute illness or for chronic health conditions while annual physical exams or 'well visits' for adults are virtually nonexistent. For many patients, stress related to their physical illness, long waiting periods, vying for attention in a busy and overcrowded primary care clinic and the looming health care expenses could all contribute to psychological distress. In addition, a significant percentage of people in these settings face challenging life circumstances without any economic or social safety nets or access to social services. Some patients may also over-endorse symptoms asked during screening and diagnosis to communicate the urgency of their needs in busy clinics. Thus, misdiagnosis of situational distress at the primary care clinic as a mental disorder is a strong possibility especially when using standardized questionnaires without clinical judgment. While self-limiting psychological distress 'formally' could have met criteria for screening and diagnosis at baseline, it is more likely to be a reflection of the situational distress. In effect, opportunistic screening in primary care occurs at an inopportune moment for the patient, whereas the follow-up interview at home in few weeks is more likely to reflect their typical mental state. A similar study from primary care clinics in Chile also found that more than half of the women who screened positive for common mental disorder screened negative during a follow-up screening within two weeks (41). Regression to the mean is another possible cause for lower score for some patients at follow up.

Further, we found that less than 15% of patients retained their original diagnosis at two-month follow-up. The only exception was those with a baseline diagnosis of mixed anxiety and depressive disorder as 24% of them had the same diagnosis at 2 months. A rapid switch in psychiatric diagnosis within two months is more likely due to methodological issues in diagnosis rather than any actual change in psychopathology (229). As discussed above, for many patients screening in primary care happens at a stressful moment and in a stressful environment, possibly leading to misinterpretation of non-pathological distress as mental disorder.

Persistent distress and its predictors

Close to one-fifth (19%) of the screened positive patients experienced high levels of psychological distress at all follow-up interviews. Women, socioeconomically disadvantaged and those with long standing physical illness and disabilities were the most likely to experience persistent distress.

The burden of chronic diseases and associated disability is increasing in countries like India, and we found close association between persistent psychological distress and long standing physical illness and disability similar to prior studies. Studies have reported increasing late-life depression in India and its association with chronic physical disorders (230). A recent qualitative study from our study site in Goa, India also report that chronic health problems and increasing physical limitations leading to psychological distress especially in older population (231).

As expected, we found severe economic distress as an important predictor of persistent distress. A qualitative study among this primary care population in Goa examining the explanatory models of common mental disorders found patients attributing economic problems as one of the most important factors causing psychological distress in adults (190). In the past two decades the interaction between poverty and mental ill health has been well documented in low and middle income countries and our findings add further evidence to this (232).

Finally, we found increased risk for persistent distress among women which may be partially explained by structural gender inequality and violence against women that are particularly important in our study setting and in many other low and middle-income countries (233). Unequal distribution of socio-economic resources and unfavorable opportunities in patriarchal societies are frequently reported as contributors to psychological distress in women (234, 235).

Effects of interventions

In our secondary analysis of MANAS data examining the clinical course of common mental disorders under usual care, we examined only the follow-up data from the control arm. While

antidepressants were prescribed to about half of the screened positive patients in the control arm, only 60% of those who received the prescription reported them taking the medication for more than 2 weeks. Similar rates of antidepressant discontinuation has been reported from India; for example, a primary care based study from a rural community in South India found that within four weeks 35%, and by 12 weeks 56% of patients have discontinued antidepressants (236). These rates are higher than 24% noncompliance reported at two weeks from general practice clinics in the UK (237). After adjusting for baseline symptoms severity, we did not find any significant effect of antidepressant in clinical outcomes for patients with any ICD-10 diagnosis or those with a diagnosis of depression. One possibility for this muted response could be the dilution of antidepressant effect due to a significant proportion of patients with non-pathological distress, or milder depression or adjustment disorders for which antidepressants have no proven effectiveness (201, 203) . Also, the published results from the RCT based on the MANAS trial comparing the intervention and control arms showed only a modest benefit of the collaborative stepped care model of care for (49, 50, 189, 191). There was no effect for intervention in private GP clinics, the type of clinic that provides nearly 80% of outpatient care in India (238). The study also found relatively poor acceptance for the diagnosis of a mental disorder and weak adherence to brief interpersonal psychotherapy (190), and for anti-depressant medication offered free of cost through the trial. These results could be a reflection of the challenges related to the primary care based screening and diagnosis we discussed above. For instance, the dilutions of the effect of interventions could be due to the spontaneous improvement in patients with self-limiting psychological distress in the control arms of the trial. Similarly, poor adherence to treatment offered may partly be due to the lack of acceptance of the diagnosis of mental disorders and perceived usefulness of biomedical treatment among patients experiencing situational distress. In fact, a qualitative study among patients from this study reported that while patients linked their symptoms to psychosocial difficulties in their life, they were reluctant to consider their distress as a mental disorder (190).

There are three important messages that emerge from these results: first, for a significant proportion of primary care patients a positive mental health screening result indicates self-limiting non-pathological distress. This finding is consistent with the serious false positive problem with mental health screening reported from high income countries. The high false positive rate is one of the main reasons that the Canadian Task Force for Prevention and UK's National Institute for Clinical Excellence does not recommend routine screening for depression in primary care. Even though the circumstances in countries such as UK and Canada are different, our results suggest that screening in primary care in low and middle income countries face similar challenges. This is also demonstrated in a recent study from Nepal that found that, despite extensive cross cultural adaptation, questionnaire based primary care screening for depression had a 55% false positive rate (118).

Second, our study supports the concern raised by many psychiatric researchers from low and middle income countries that current classifications (e.g. DSM-IV/5 and ICD-10/11) and their scaled down versions for primary care are inoperable in primary care setting in these countries (239). We found poor diagnostic stability for ICD-10 based diagnoses, and the most stable and prevalent diagnosis was mixed anxiety and depressive disorder. Unfortunately, mixed anxiety and depression is not included in the DSM-5 or in the current WHO guidelines designed for primary care. Overall, psychological distress scores based on CIS-R was more useful in our study to track the trajectory of distress, suggesting that dimensional approaches to psychological distress could be more useful in primary care than current diagnostic classifications.

Third, psychosocial support systems and structural interventions have a larger role to play in addressing psychological distress. Though the significance of the social drivers of poor mental health such as poverty, social and gender inequality and injustice are well recognized, global mental health programs have largely relegated these factors as secondary to individual level medical interventions (199). While individual level interventions may help in temporary relief of symptoms, structural solutions are critical

to address increased risk for persistent distress among women, those with lower education, and those related to long standing physical illnesses and disability, and severe economic hardships. This calls for a central role for programs to address issues of access to quality health care, disability support, and recovery from economic shocks in addressing psychological distress. Further, gender-based violence and discrimination needs evidence-based primary and secondary prevention practices at various levels (240, 241).

Future directions

While we highlighted problems with routine screening of common mental disorders among primary care patients, it simply means that there is insufficient evidence to recommend routine screening and does not minimize the significance of these disorders. Thus, there is an undeniable role for interventions for psychological distress in primary care, however a critical factor is to identify individuals who will benefit from these interventions. Identifying those with persistent distress by repeated assessments and setting up higher threshold for interventions are some of the strategies that need further evaluation. For example, the study by Arya et al. found strong effect of primary care based intervention for mental disorders by recruiting only women with persistent distress identified by repeated follow-up evaluation (41). Similarly, a recent study by Patel et al. demonstrated effectiveness of psychological treatments by recruiting patients with moderately severe to severe depression in primary care while excluding those with less severe conditions (11).

Limitations

Due to the absence of primary care based data on the natural course of common mental disorders from low and middle-income countries, we relied on data from a cluster RCT for this study. The original RCT was designed for group level comparison between the intervention and control arm while our analyses examined the clinical course of psychological distress among screened-positive patients.

Although bootstrap models help to minimize some of the limitation of the data due to clustering, the sample may not offer enough power for all the analyses.

We described the clinical course of psychological distress in screened-positive patients under usual care. However, adherence to the intervention was relatively poor, although this might be an indication of the acceptance of a psychiatric diagnosis in the study settings. The study explored a limited number of predictors and some important predictors such as spousal alcohol use, domestic abuse/violence, and traditional support systems were not included. Despite these limitations our study offers some important points to review screening for common mental disorders in primary care.

Our findings on the stability of psychiatric diagnoses lean on the validity of the revised Clinical Interview Schedule (CIS-R) used in this study. We are not aware of any validation studies of CISR-R against a gold standard psychiatric interview in India. However, CIS-R has been validated among Indian immigrants elsewhere, routinely used in India, and translated and field tested in the study population.

Finally, the absence of information on patients screened negative for common mental disorders precludes us from drawing conclusions about the effectiveness of screening, although the clinical course of screened positive patients indicate critical issues related to the utility of screening in primary care.

Conclusion

Our study provides important evidence to improve the detection and management of mental disorders in low and middle income countries. We found that screening for common mental disorders in primary care identifies a significant proportion of patient with non-pathological distress. At the same time a smaller but important share of patients experience intermittent and persistent psychological distress often predicted by psychosocial and economic disadvantage. This suggests a larger role for psychosocial and economic interventions to help those patients who are most affected by mental health issues in primary care. The laudable achievement of including mental health in the Sustainable Development Goals

(SDG) is an opportunity to integrate psychosocial and economic interventions to mental health treatment models in locally informed ways (242).

Figure 3.1 Trial profile

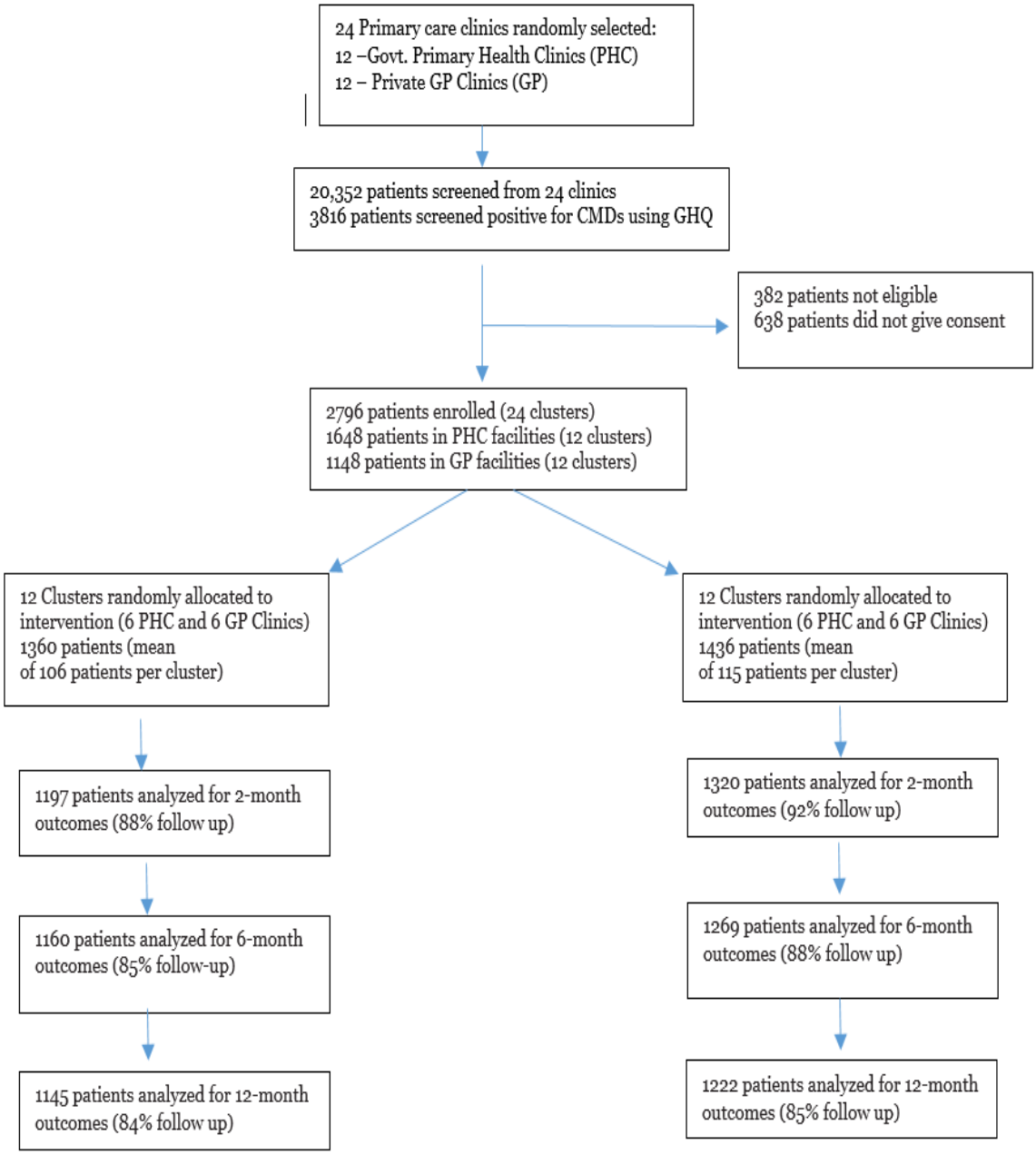

Figure 3.2 Trajectory of psychological distress

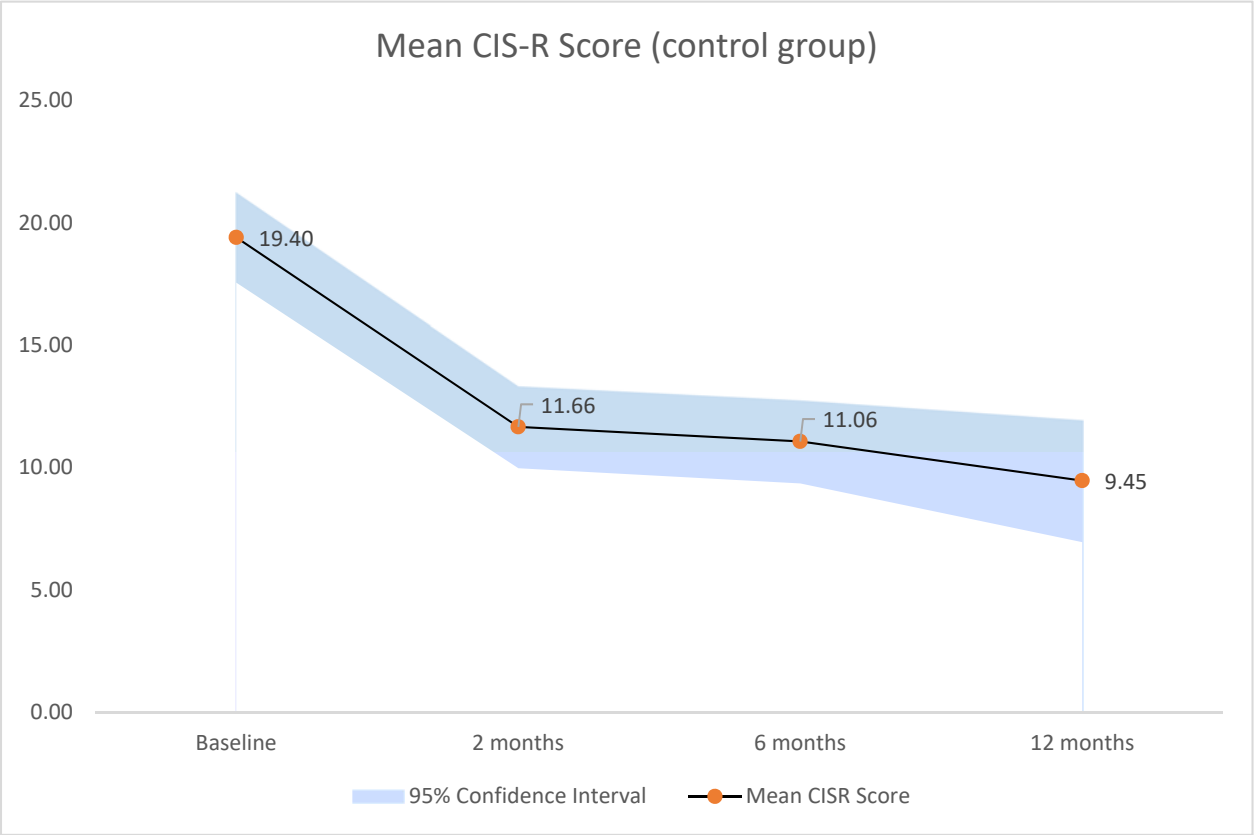

Table 3.1. Symptoms represented in the 14 sections of the CIS-R interview (213)

Defining Symptoms	Symptom description
Somatic symptoms	Aches, pains or any sort of discomfort that was brought on or made worse because you were feeling low, anxious or stressed.
Concentration/ forgetfulness	Problems with concentrating on what you were doing or forgetting things.
Sleep Problems	Problems with trying to get to sleep or with getting back to sleep, or sleeping more than usual.
Irritability	Feeling irritable or short tempered with those around you (over things that seem trivial looking back on them).
Worry about physical health	Worrying about your own physical health (all respondents) or worrying that you might have a serious physical illness (only respondents who didn't report a long-standing illness, disability or infirmity).
Depression	Feeling sad, miserable or depressed, or not being able to enjoy or take an interest in things as much as usual.
Depressive ideas	Feeling guilty, feeling hopeless, feeling not as good as others and thoughts of suicide (only respondents who scored 1 or more in the previous Depression section.)
Worry	Worrying about anything other than your own physical health.
Anxiety	Feeling anxious or nervous, or finding your muscles tense or that you couldn't relax.
Phobias	Feeling anxious, nervous or tense about any specific things or situations when there was no real danger, or avoiding any situation or thing because it would have made you feel nervous or anxious, even though there was no real danger.
Panic	Anxiety or tension getting so bad that you got in a panic (for example, feeling that you might collapse or lose control unless you did something about it).
Compulsions	Finding that you kept on doing things again and again when you knew you had already done them (for example, checking things like taps or washing yourself when you had already done so).
Obsessions	Having thoughts or ideas over and over again that you found unpleasant and that you would have preferred not to think about, that still kept on coming into your mind.

Table 3.2. Possible ICD-10 diagnosis derived from CIS-R algorithm (213)

- PANIC: (D) panic disorder (f41.0)
- GAD: (D) generalised anxiety disorder (f41.1)
- MADD: (D) mixed anxiety/depressive disorder (f41.2)
- OCD: (D) obsessive compulsive disorder (f42)
- PHOB: (D) any phobia - combined category
- DEP: (D) depressive episode - combined category
- NEUROTIC: (D) Any neurotic disorder - CIS-R
    - F3200: (D) mildep w/o somsym - ICD-10 diagnosis f32.00
    - F3201: (D) mildep with somsym - ICD-10 diagnosis f32.01
    - F3210: (D) moddep w/o somsym - ICD-10 diagnosis f32.10
    - F3211: (D) moddep with somsym - ICD-10 diagnosis f32.11
    - F4000: (D) agora w/o panic - ICD-10 diagnosis f40.00
    - F4001: (D) agora with panic - ICD-10 diagnosis f40.01
- SEVDEP: (D) severe depression - ICD-10 diagnosis f32.2
- MILDDEP: (D) mild depression
- MODDEP: (D) moderate depression
- SOCPHOB: (D) social phobia - ICD-10 diagnosis f40.1
- SPECPHOB: (D) specific (isol) phobia - ICD-10
- AGORA: (D) any agoraphobia

Table 3.3 list of recoded predictors

Mean age	• Age in completed years
Gender	0. Male 1. Female
Marital status	0. Single or married 1. Widowed or separated
Education	0. Above primary (elementary) school 1. Primary school or below
Ethnicity	0. Goan 1. Immigrant
Financial situation	0. Comfortable or Just about getting by 1. Finding it difficult to make ends meet (extreme difficulty)
Long standing physical illness/disability	0. No 1. Yes

Table 3.4 Characteristics of study participants

	All participants (n=2796)	**Women** n=2305 (82%)	**Men** n=491 (18%)
	N (%)	N (%)	N (%)
Age *(n=2796)*			
18-29	294 (10.5)	239 (10.4)	55 (11.2)
30-39	571 (20.4)	466 (20.2)	105 (21.4)
40-49	733 (26.2)	628 (27.3)	105 (21.4)
50-59	534 (19.1)	438 (19)	96 (19.6)
60 & above	664 (23.8)	534 (23.2)	130 (26.5)
Marital Status *(n=2511)*			
Never married	159 (6.3)	100 (4.8)	59 (14.1)
Married	1618 (64.4)	1278 (61.1)	340 (81.3)
Widowed/separated	734 (29.2)	725 (34.2)	19 (4.6)
Ethnic group *(n=2510)*			
Goan	2401 (95.7)	2013 (96.2)	388 (92.8)
Migrant	109 (4.3)	79 (3.8)	30 (7.2)
Education *(n=2508)*			
Above primary school	929 (37.0)	710 (34.0)	219 (52.5)
Primary school or below	1579 (63.0)	1381 (66.0)	198 (47.5)
Financial situation *(n=2506)*			
Comfortable or Just about getting by	1361 (54.3)	1105 (52.9)	256 (61.4)
Finding it difficult	1145 (45.7)	984 (47.1)	161 (38.6)
Long standing physical illness/ disability *(n=2425)*			
No	1280 (52.8)	1066 (52.6)	214 (53.8)
Yes	1145 (47.2)	961 (47.4)	184 (46.2)

Table 3.5. Baseline CIS-R* diagnoses

Diagnosis	**Women** N (%)	**Men** N (%)	**Total** N (%)	**95% CI for the total**
Mixed anxiety depressive disorder	852 (37)	180 (36.7)	1032 (36.9)	(32-42.1)
Mild-moderate depression	368 (16)	79 (16)	447 (16)	(12.4-20.4)
Severe depression	273 (11.9)	46 (9.4)	319 (11.4)	(9-14.3)
Generalized Anxiety disorder	149 (6.5)	15 (3.1)	164 (5.9)	(4.3-7.9)
Phobias	124 (5.4)	22 (4.5)	146 (5.2)	(3.4-7.9)
Panic disorder	102 (4.4)	32 (6.5)	134 (4.8)	(3-7.7)
No disorder	437 (19)	117 (23.9)	554 (20)	(16.5-23.5)

*The Clinical Interview Schedule-Revised (CIS-R)

Table 3.6. Predictors of baseline diagnoses from score bootstrapped logistic regression model

	Any ICD 10 diagnosis OR (95% CI)	Generalized Anxiety disorder OR (95% CI)	Mixed anxiety depressive disorder OR (95% CI)	Mild-moderate depression OR (95% CI)	Severe depression OR (95% CI)	Phobias OR (95% CI)
Gender *(n=2796)*						
Male						
Female	1.34 (1.08-1.66)	2.19 (1.23-3.92)	1.01 (0.80-1.28)	0.99 (0.77-1.28)	1.30 (0.88-1.92)	1.21 (0.80-1.83)
Age *(n=2796)*	1.00 (0.99-1.01)	1.01 (0.99-1.02)	1.00 (1.00-1.01)	0.99 (0.98-1.00)	1.01 (1.00-1.02)	0.98 (0.96-1.00)
Marital Status *(n=2511)*						
single/married (ref)						
Separated/Divorced	1.31 (1.01-1.72)	1.6 (1.21-2.1)	1.07 (0.93-1.25)	0.83 (0.64-1.09)	1.33 (0.89-2.00)	0.79 (0.49-1.28)
Ethnic group *(n=2510)*						
Goan (ref)						
Migrant	1.24 (0.82-1.88)	1.3 (0.58-2.92)	0.58 (0.39-0.85)	1.41 (0.67-2.97)	1.13 (0.55-2.34)	1.94 (0.81-4.65)
Education *(n=2508)*						
Above primary school (ref)						
Primary school or below	0.81 (0.65-1.03)	1.11 (0.73-1.68)	0.95 (0.78-1.15)	0.97 (0.71-1.34)	0.79 (0.55-1.14)	1.08 (0.83-1.41)
Financial situation						
Comfortable/getting by (ref)						
Extremely difficulty	1.38 (1.08-1.75)	0.86 (0.61-1.21)	0.98 (0.79-1.22)	1.36 (0.97-1.90)	1.14 (0.82-1.59)	1.10 (0.78-1.55)
Long standing physical illness/ disability	1.15 (0.87-1.53)	1.56 (0.97-2.52)	0.94 (0.78-1.12)	0.73 (0.57-0.95)	1.40 (0.97-2.03)	1.25 (0.85-1.81)

Table. 3.7 Proportion of patients with a diagnosis at baseline, 2 months, 6 months and 12 months

	Baseline diagnosis		Diagnosis at 2 months		Diagnosis at 6 months		Diagnosis at 12 months	
	N	%	N	%	N	%	N	%
Mixed anxiety and depressive disorder	471	32.8	321	24.6	304	24.0	241	19.4
Mild/moderate depression	290	20.2	109	8.4	101	8.0	86	6.9
Severe depression	175	12.2	57	4.4	48	3.8	41	3.3
Gen Anxiety disorder	77	5.4	63	4.8	45	3.6	38	3.1
Panic disorder	78	5.4	26	2.0	20	1.6	16	1.3
Phobias	53	3.7	25	1.9	23	1.8	5	0.4
No ICD -10 Diagnosis	292	20.3	704	54.0	728	57.4	817	65.7
Total	1,436	100.0	1,305	100.0	1,269	100.0	1,244	100.0

Table 3.8 Patients overcoming baseline diagnostic category at 2, 6 and 12 months

Baseline diagnosis	No ICD-10 diagnosis at 2 months		No ICD-10 diagnosis at 6 months		No ICD-10 diagnosis at 12 months	
	N	%*	N	%*	N	%*
Any ICD 10 *(n=1144)*	521	50.0	553	54.4	628	63.2
Mixed anxiety and depressive disorder *(n=471)*	251	58.6	251	60.5	292	71.6
Mild/moderate depression *(n=290)*	120	45.5	138	52.9	151	58.8
Severe depression *(n=175)*	66	41.5	75	49.7	84	56.0
Gen Anxiety disorder *(n=77)*	31	44.3	31	45.6	38	58.5
Panic disorder *(n=78)*	30	41.1	33	45.8	37	54.4
Phobias *(n=49)*	23	46.9	25	50.0	26	56.5
No ICD -10 Diagnosis *(n=292)*	183	69.9	175	69.4	189	75.6

* Percentage of all those who had the diagnosis at baseline and were still in the study at the follow-up point. Percentage may not match to baseline 'n' due to loss to follow-up

Table 3.9. Prospective consistency- percentage of patients retaining their original baseline diagnoses at 2, 6 and 12 months

Baseline diagnosis	**Prospective consistency at 2 months % (N)**	**Prospective consistency at 6 months % (N)**	**Prospective consistency at 12 months % (N)**
Mixed anxiety and depressive disorder	24.3 (104)	21.9 (91)	16.9 (69)
Mild/moderate depression	9.9 (26)	9.2 (24)	7.8 (20)
Severe depression	6.9 (11)	7.3 (11)	7.3 (11)
Gen Anxiety disorder	14.3 (10)	5.9 (4)	3.1 (2)
Panic disorder	2.7 (2)	1.5 (1)	1.5 (1)
Phobias	2 (1)	4 (2)	-
No ICD -10 Diagnosis	69.9 (183)	69.4 (175)	75.6 (189)

Table 3.10 Patients who switched to a new diagnoses and those who retained their original diagnosis at 2 months

Baseline diagnosis *(n=1305)**	**% of patients who switched to a new diagnosis at 2 months** N (%)	**%* of patients who retained their original diagnosis at 2 months** N (%)	**% of patients who did not meet any diagnostic criteria** N (%)
Mixed anxiety and depressive disorder *(n=428)*	73 (17.1)	104 (24.3)	251 (58.6)
Mild/moderate depression *(n=264)*	118 (44.7)	26 (9.9)	120 (45.5)
Severe depression *(n=159)*	82 (51.6)	11 (6.9)	66 (41.5)
Gen Anxiety disorder *(n=70)*	29 (41.4)	10 (14.3)	31 (44.3)
Panic disorder *(n=73)*	41 (56.1)	2 (2.7)	30 (41.1)
Phobias *(n=49)*	25 (53)	1 (2)	23 (47)
No ICD -10 Diagnosis *(n=262)*	79 (30.1)	183 (69.9)	183 (69.9)

*Include only those patients who completed the follow-up interview at 2 months

Table 3.11. Diagnosis of each baseline diagnoses at 2 months

	Diagnosis at two months															
Baseline diagnostic categories ↓	Mixed anxiety & depressive disorder		Mild/ moderate depression		Severe depression		Gen Anxiety disorder		Panic disorder		Phobias		No ICD -10 Diagnosis		Missing/lost to follow-up	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Mixed anxiety and depressive disorder (n=471; 32.80%)	104	22.08	29	6.16	13	2.76	18	3.82	7	1.49	6	1.27	251	53.29	43	9.13
Mild/moderate depression (n=290; 20.19%)	72	24.83	26	8.97	15	5.17	13	4.48	9	3.1	9	3.1	120	41.38	26	8.97
Severe depression (n=175; 12.19%)	41	23.43	24	13.71	11	6.29	9	5.14	5	2.86	3	1.71	66	37.71	16	9.14
Gen Anxiety disorder (n=77; 5.36%)	16	20.78	6	7.79	3	3.9	10	12.99	1	1.3	3	3.9	31	40.26	7	9.09
Panic disorder (n=78; 5.43%)	28	35.9	6	7.69	5	6.41	2	2.56	2	2.56			30	38.46	5	6.41
Phobias (n=53; 3.69%)	15	28.3	5	9.43	2	3.77	3	5.66			1	1.89	23	43.4	4	7.55
No ICD -10 Diagnosis (n=292; 20.33%)	45	15.41	13	4.45	8	2.74	8	2.74	2	0.68	3	1.03	183	62.67	30	10.27
Total 1436	321	22.35	109	7.59	57	3.97	63	4.39	26	1.81	25	1.74	704	49.03	131	9.12

Table 3.12. Predictors of persistent psychological distress in control group (n= 1149)

	Persistent distress		Adjusted odds ratio*
	No	**Yes**	
Mean Age	47.1	48.8	1.01 (0.99-1.03)
Sex			
Male	147 85.47%	25 14.53%	
Female	784 80.25%	193 19.75%	1.51 (1.01-2.26)
Marital Status			
Single/Married	659 82.48%	140 17.52%	
Separated/widowed	272 77.71%	78 22.29%	1.16 (0.88-1.52)
Ethnic group			
Goan	894 80.83%	212 19.17%	
Migrant	37 86.05%	6 13.95%	0.79 (0.4-1.57)
Education			
Above primary school	330 86.16%	53 13.84%	
Primary school or below	601 78.46%	165 21.54%	1.59 (0.97-2.58)
Severe financial distress			
No	482 86.69%	74 13.31%	
Yes	449 75.72%	144 24.28%	2.13 (1.65-2.75)
Long standing illness			
No	497 84.09%	94 15.91%	
Yes	411 77.84%	117 22.16%	1.43 (0.98-2.08)
Baseline distress score (CIS-R)	18.5	24.1	1.08 (1.03-1.12)

*OR adjusted for age and gender to account for loss to follow-up (see analysis –missing data for details)

Table 3.13. Prescription and use of antidepressants among patients with short and persistent distress

	Short distress			Persistent distress		
	No N (%)	**Yes N (%)**	**Adj. OR***	**No N (%)**	**Yes N (%)**	**Adj. OR***
Antidepressant prescription						
No	341 (58.5)	242 (41.5)		481 (82.5)	102 (17.5)	
Yes	360 (63.6)	206 (36.4)	0.98 (0.6-1.58)	450 (79.5)	116 (20.5)	1.01 (0.54-1.89)
Use of antidepressant						
None/less than 15 days	469 (59.3)	322 (40.7)		635 (80.3)	156 (19.7)	
More than 15 days	232 (64.8)	126 (35.2)	0.92 (0.57-1.48)	296 (82.7)	62 (17.3)	0.72 (0.38-1.34)

*Odds ratio adjusted for age, gender and baseline symptom severity

Chapter 4: Antidepressant prescriptions in primary care in India: insights from a cluster randomized control trial

Introduction

According to the World Health Organization's latest 'Global Health Estimates', in low and middle income countries, depressive disorders are the second leading cause of years lost due to disability (243). There is increasing recognition that depressive disorders are common among primary care patients in these countries, but often undetected, and that when it is detected, it is frequently untreated. Early identification and treatment of depression could decrease adverse events such as suicide, and improve disease outcome and quality of life. Hence there is a growing call for routine screening and treatment for depression at the primary care level (196).

At present, the World Health Organization, and advocacy groups such as the Movement for Global Mental Health support a collaborative stepped care model to integrate mental health care into primary care in low and middle income countries (244, 245). The collaborative stepped care is a systematic approach to delivering and monitoring treatments involving various levels of care providers ranging from lay health workers to clinical specialist in a staged system comprising grades of interventions. Thus the most effective yet least resource intensive evidence based treatment is delivered to the patient based on severity and 'stepping up' services only as needed. Antidepressants are a critical component of this model of care, particularly for patients with moderate to severe depression (244). Meanwhile, the use of antidepressants in primary care is now under scrutiny in many high income countries as described below.

There has been a dramatic increase in antidepressant use in high income countries since the 1990s (246-248). For example, in England, the number of antidepressants prescriptions has nearly doubled in the past decade and in the United States between 1999 and 2014 the number of adults who reported taking antidepressant medication over the past month has increased by 65 percent (249) (250).

But the lack of a clear relationship between depression prevalence and antidepressant prescribing rates has led many researchers to question the clinical basis for increased prescriptions (251). A major reason for the surge in antidepressant prescription is a rapid rise in prescription by non-psychiatrist providers compared with psychiatrists, especially in primary care (252, 253). At present in many high income countries, the majority of antidepressants are prescribed in primary care (252). The increased incidence and duration of antidepressant prescription in primary care is partially driven by the popularity of newer antidepressants such as the Selective Serotonin Reuptake Inhibitors (SSRIs) that are better tolerated by patients (254).

Studies from-high income countries have described several factors that influence antidepressant prescription (255). Patient characteristics such as female gender, older age, white race, higher education and severity of symptoms are often associated with increased antidepressant prescribing (256-258). Similarly, physicians' attitude, experience and comfort with anti-depressant prescription, insurance coverage for treatment, lack of non-pharmacological treatment options are some of the health system related factors associated with increased prescriptions (255, 259, 260). In addition, recent studies have found that factors such as direct-to-consumer advertising of antidepressants has led to increased patient demand and prescription of antidepressants for milder conditions such as adjustment disorders (261, 262). Unfortunately, we have limited information on factors associated with antidepressant prescribing in low and middle-income countries. Although, an international multicenter study that included five low/middle income countries described severity of symptoms, older age, and female gender as important factors associated with psychotropic medication prescriptions in primary care (263).

A fundamental issue related to providing treatment for common mental disorders is the difficulty in setting up a valid diagnostic boundary between common mental disorders such as major depressive disorder and intense normal sadness or distress that usually does not require biomedical

intervention (264). These are non-pathological normal response to environmental stressors, and often dissipates over time or with improvements in the stressful situation. In this paper we label such conditions as non-pathological sadness or non-pathological distress. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM versions III to 5), symptoms of mental disorders "must not be merely an expectable and culturally sanctioned response to a particular event" and DSM's descriptive diagnostic criteria frequently depend on contextual information to decide whether symptoms are caused by normal processes or suggest an internal dysfunction that points to a mental disorder (265). It is expected that clinical judgment will help to exclude non-pathological distress and reduce false positive diagnoses. However, in situations where the diagnostic criteria tend to be applied algorithmically as in screening, and when clinician rely on screening results without a detailed clinical examination, the safeguard of the contextual criteria is lost (265). In 2009, a meta-analysis of the clinical diagnosis of depression in primary care found that in general, false positives diagnosis of depression significantly outstrips true positives (266). This increased risk for false positive diagnosis combined with over-reliance on antidepressants could possibly result in patients with non-pathological distress, adjustment disorders and mild depression receiving antidepressant prescriptions, especially when access to non-pharmacological interventions are limited.

In general, evidence from meta-analyses of placebo-controlled trials only support the use of antidepressant drugs for a small proportion of patients, particularly those with severe depression, for which the evidence of benefit is strongest (267). However, the clinical course of depressive disorders found in primary care is often less severe and less complicated than those seen in specialist settings, and spontaneous remission is common (268, 269). In this context an exponential increase in the use of antidepressants in primary care in some high-income countries is leading to the reevaluation of antidepressant prescriptions. There is a growing concern that over prescription of antidepressants and medicalization of patients with non-pathological distress is as important as under recognition and under

treatment of severe depression (260, 270, 271). Recent studies from the US support this view, showing that over prescription of antidepressants is common in community settings in the US (272). Further, more than half of the US physicians and psychiatrists who participated in a nationally representative survey believed that physicians too often treat non-pathological sadness and worry as a medical illness (273). This could possibly be due to the misdiagnosis of non-pathological sadness as depression in primary care and the overestimation of the effectiveness of antidepressants in treating mild to moderate depression (273), while at the same time, access to specialist mental health care for people with severe mental disorders remains poor (274).

In most low and middle income countries, antidepressants are more commonly prescribed by mental health specialists and in mental health clinics than in primary care (275, 276). Recently, under new initiatives access to antidepressants in primary care is slowly improving in many of these countries, for example, antidepressants, commonly SSRIs, are now available for prescription, free of charge to patients in public primary care clinics in several states in India (277-279). Yet, little is known about the antidepressant prescription practices in primary care in these countries. The few trials of interventions for common mental disorders in primary care from low and middle income countries were primarily focused on non-pharmacological intervention (51, 280). Trials that included psychotropic medications often have antidepressants as part of a care package, and it is difficult to parse out the effect of antidepressants from other components of the care package such as psychoeducation and psychotherapy (41, 50). Evidence, mostly from high income countries, suggests that antidepressants are effective for treating depressive disorders in the primary care, but the effect size is relatively small compared with placebo (281). A recent update on a Cochrane review also provides some evidence of the effectiveness of antidepressants in primary care, but the authors urged caution due to evidence of publication bias, high rate of withdrawal from studies and the high level of pharmaceutical industry involvement (269). Further, studies from low and middle income countries suggest that compliance with

antidepressants, including newer SSRIs is generally poor among primary care patients (50, 52). A major reason for suboptimal effectiveness and the lack of compliance could be poorly targeted antidepressant treatment in primary care.

Given that that the proposed screening for depression in primary care could lead to an increase in antidepressant treatment in low and middle income countries, there is an urgent need to better understand the use of antidepressants in these settings. Hence this study aims to examine the use antidepressants in primary care in low and middle income countries. Specifically, we aim to study the patient characteristics, clinical features and clinic related factors associated with primary care physician's decision to prescribe antidepressants for a patient screened positive for common mental disorder. Further, we will examine the congruity between physician's decision to prescribe antidepressants and the psychiatric diagnosis. Thus the focus of this study is the prescription behavior of primary care physicians, regardless of whether patients were compliant to the prescription recommendations.

Methods

Study design and sample

We used data from a cluster randomized control trial (RCT), the MANAS trial from Goa, India. MANAS is one of the largest community trials in mental health in primary care in a low or middle income country. Details of the study's sample and design are described extensively elsewhere, and the summary that follows draws on those descriptions (207). The aim of the trial was to assess the effectiveness of a collaborative stepped care intervention led by a lay health counsellor in the recovery of primary care patients from common mental disorders. The trial was designed as a cluster randomized control trial with the primary care clinic as the unit of randomization. Each study arm included 12 clinics; half were free public primary health clinics (PHC) and the rest were private general practitioner (GP) clinics. Eligible adult primary care attendees screened positive for common mental disorders from the 24 study

clinics were recruited. Study participants went through baseline assessment and follow-up evaluation at 2 months, 6 months and 12 months. The recruitment and follow-up were completed from April, 2007, to September, 2009 (50).

The collaborative stepped care model involved a lay health counsellor leading the screening for common mental disorders and managing interventions in collaboration with the primary care physician and a visiting psychiatrist. The intervention included psychoeducation, antidepressants and interpersonal psychotherapy delivered in 'steps' depending on the severity of the illness and the patients' response to treatment. Patients in the control clinics were screened for common mental disorders by a lay health counsellor and the screening results were provided to the primary care physician. Physicians in the control clinics were allowed to start treatments of their choice. Antidepressants were prescribed by physicians in both control and intervention arms, while other components of the intervention such as psychoeducation, interpersonal psychotherapy and collaborative case management were only available in the intervention clinics. The original study found a modest benefit for the collaborative stepped care intervention in public primary care clinics, but not in private GP clinics (50, 184).

Recruitment

Patients visiting the primary health clinic were invited to participate in the mental health screening while waiting to see the physician. A health counsellor administered the screening questionnaire to those who consented. Only those patients who were expected to be resident in the study communities for the following 12 months were considered as eligible for recruitment. Eligible patients who screened positive and agreed to join the trial were also accessed for any mental disorder using a structured diagnostic interview schedule during the same visit. The ICD-10 diagnosis was generated later using a computer algorithm but was not available to the primary care physician during the consultation. Figure 4.1 depicts the progress of participants through the trial. Altogether 20,352

patients were screened for common mental disorders using the GHQ-12 of whom 3816 (18.8%) screened positive. Among the screened positive, 382 were not eligible and 638 refused, yielding a final sample of 2796 participants. The number of patients recruited from the collaborative stepped-care clinics and in the enhanced usual care clinics were 1360 and 1436 respectively. For this study we used baseline data from all trial participants (n=2796) to examine factors associated with antidepressant prescription in primary care.

Measures

Screening scale and diagnostic interview

The MANAS trial used the 12-item General Health Questionnaire (GHQ-12) to screen for psychological distress and recruit patients into the trial (173). The Clinical Interview Schedule-Revised (CIS-R) was used to assess symptom severity and generate ICD-10 diagnoses of common mental disorders (213).

The 12-item General Health Questionnaire (GHQ-12)

The GHQ was designed to measure psychological distress in population surveys and epidemiological studies, and to screen for non-psychotic mental disorders in clinical settings (208). Originally developed in the UK, the GHQ is one of the most widely used screening questionnaires internationally, including in India. The short 12-item version of the GHQ has been used previously in studies at the study site in Goa, India (209). GHQ-12 is designed as a unidimensional scale for the assessment of mental distress with a main focus on depressive symptomatology. The 12 items assess the respondent's state during the past two weeks and focuses on the appearance of new and distressing symptoms and the inability to carry out normal functions (see appendix D) (208). Thus the GHQ is sensitive to short-term psychiatric disorders but not to long-standing attributes of the respondent (282). Each item is scored as 1 or 0 based on the presence or absence of a feature of psychological distress, giving a maximum total score of 12. In this study GHQ-12 was used at the baseline for screening primary

care patients with cutoff score of 5/6. Even though GHQ is designed to measure the risk of non-psychotic mental disorders, a positive result on GHQ-12 is not a diagnosis of mental disorder, but it helps to inform further evaluation and intervention. In the study population in Goa, India, using a cut-off of 5/6 the GHQ-12 showed sensitivity of 73%, specificity of 90%, and a positive predictive value of 61% (56).

The Clinical Interview Schedule- Revised (CIS-R)

The revised version of the Clinical Interview Schedule is a standardized psychiatric interview that can be administered by interviewers without clinical training in psychiatry (213). The CIS-R interview asks about symptoms of ICD-10 common mental disorders, and the questions focus on 14 symptom domains (Table 4.1). For each of these symptom domains, a screening question is asked to decide if that specific symptom was experienced by the respondent in the previous month. If the respondent experienced the symptom, a detailed evaluation of their experiences of that symptom in the previous seven days is covered by a sequence of questions. Based on the response, a score signifying the severity of the symptom domain ranging from 0-4 (or 0-5 for the depressive ideas 'symptom') is assigned for each of the 14 domains (213). A significant symptom is indicated by a score ≥ 2. A score of 0 is given for those who did not experience a particular symptom in that week. The total scores for the 14 symptom domains range from 0-57; scores of 12 or more indicate a psychiatric disorder (213). Further, by applying a diagnostic algorithm to the CIS-R responses, patients can be assigned to a set of ICD-10 diagnostic categories, including generalized anxiety disorder, depressive disorders, obsessive compulsive disorder, and phobias. See table 4.2 for the list of diagnoses generated using the algorithm.

The CIS-R is widely used for the diagnosis of mental disorders in epidemiological studies globally. The CIS-R has been used on every wave of the UK national mental health survey series (*The Adult Psychiatric Morbidity Survey*) to diagnose six types of common mental disorders including depression, generalized anxiety disorder, panic disorder, phobias, obsessive compulsive disorder, and common

mental disorders not otherwise specified (214). While the CIS-R has been extensively used in India, translated and field tested in the study population, we are not aware of any validation studies of CISR-R against a gold standard psychiatric interview in India. However, a cross-cultural factorial validation of the CIS-R among ethnic minority population in the UK including Indian immigrants found that underlying "depression-anxiety" construct maintains measurement invariance across ethnic groups, even though there is inconsistency in the reporting of somatic symptoms across cultures (215). CIS-R has also been successfully validated among people of Indian origin in Malaysia and that study reports a sensitivity of 88%, specificity of 96% and a positive predictive value of 97% for a cut off score of 12 (216). Further, a recent validation study of CIS-R based on the Hong Kong mental morbidity survey showed good criterion validity in diagnosing common mental disorders against the diagnoses made by the Structured Clinical Interview for the DSM-IV (217).

Sociodemographic factors

Self-reported age and gender were recorded for each participant during recruitment. Detailed sociodemographic information including ethnicity, marital status and education was compiled during the first follow-up interview within two months of recruitment. The coding of the variables is provided in table 4.3.

Life stressors

Patients were also asked about two major life stressors commonly reported among primary care patients: 1) presence of long standing physical illness and 2) financial difficulties, i.e. finding it difficult to make ends meet. (variable coding in table 4.3)

Clinic level factors (level 2 variables)

The study included only two clinic level variables, namely, the type of clinic (private GP clinic and free public clinic) and the study arm/mental health care model (collaborative stepped care and usual

care). Other important level-two factors such as the qualification and training of primary care physician, availability of support staff or other unique features of the clinic were not examined in this study.

Analysis

Data processing

Data were processed, cleaned and organized by the four interview phases (baseline, 2 months, 6 months and 12 months) by Sangath, the institution that conducted the study in India. Sangath provided de-identified data for analysis including participant characteristics, symptoms of psychological distress, diagnosis, intervention offered and outcomes measured at 2 months, 6 months and 12 months.

Specific analysis plans

To identity factors associated with primary care physician's decision to prescribe antidepressants for a patient screened positive for common mental disorder:

We first describe the key characteristics of all screened positive study participants. Based on prior studies (283, 284) we expected difference in these characteristics by gender, hence we also present them separately for men and women. Then, we report the incidence of antidepressant prescription by the primary care physician. The data was clustered by clinics with an intraclass correlation coefficient (ICC) of 0.17 for the outcome antidepressant prescription. Hence, we used a two-level hierarchical logistic regression model (level one for patients and level two for clinics) with bootstrapped confidence intervals to examine factors associated with primary care physician's decision to prescribe antidepressants.

We examined two main categories of individual level (level one) factors as follows: 1) sociodemographic factors (age, gender, marital status, ethnicity and education) and two life stressors (financial difficulty and longstanding illness/disability); 2) clinical factors including screening score, symptoms elicited during the standardized diagnostic interview and the psychiatric diagnosis.

In our analyses, we examined two level-two factors that could be associated with antidepressant prescription, namely, the type of clinic (private GP clinic and free public clinic) and the mental health care model or study arm, i.e. collaborative stepped care vs. usual care.

To examine congruity between physician's decision to prescribe antidepressants and the CIS-R based diagnosis:

We examined the relationship between psychiatric diagnoses based on the standardized diagnostic interview (CIS-R) and the odds of receiving an antidepressant prescription. A two-level hierarchical logistic regression model with bootstrapped confidence intervals was used to assess this relationship. While the physicians in this study were not told the psychiatric diagnosis, they received the results of screening score (GHQ score) categorized as no distress (GHQ score 0-5), mild distress (GHQ score 6-7) and moderate to severe distress (GHQ score >7). We examined the proportion of antidepressant prescriptions given for moderate to severe depression, mild depression and for patients who did not meet criteria for a psychiatric diagnosis according to the CIS-R based diagnostic interview.

Results

Participant characteristics

As described in table 4.4, about 82% (n=2305) of the trial participants were women. Close to half of the participants were 50 years or older and the age distributions for men and women were similar. With regard to those who refused to participate, there was no significant difference in gender distributions, although participants who did not consent tended to be younger than those who did consent. The majority of participants were currently married (61% of women and 81% men), but a larger percentage of women were widowed or separated (34% of women and 5% of men). Only about one-third of women and half of the men had education above the primary school level. A substantial proportion of patients were poor with 47% of women and 39% of men finding it difficult to make ends

meet. Long standing physical illness including chronic diseases or disability was reported by 47% of women and 46% of men.

Based on the GHQ screening score, 55% (n=1524) of patients scored in the 'mild' range for psychological distress, while the remaining patients (45%; n=1272) scored in the 'moderate to severe' range. Table 4.5 shows the distribution of psychiatric diagnoses at baseline derived from CIS-R based standardized the diagnostic interview. The most common diagnosis was mixed anxiety depressive disorder (36.9%; n=1032) followed by moderate to severe depression (21.1%; n=589). The distribution of diagnoses were similar for men and women.

Antidepressant prescription

About 47% of screened positive patients (n= 1320) received a prescription for an antidepressant after consulting the primary care physician.

Predictors of antidepressant prescription

As depicted in table 4.6, women were more likely to receive a prescription for antidepressant than men (48% vs. 42%) and prescription receipt increased with age. After adjusting for age and gender, we did not find any clear association between antidepressant prescription and marital status, education, ethnicity, economic situation, or the presence of a long standing physical illness.

Clinical factors associated with antidepressant prescription

The screening result that the primary care physician received rated psychological distress in screened positive patients as '*mild*' or *'moderate to severe'*. As described in table 4.7, about 55% of screened positive patients (n=1524) scored in the 'mild' range for psychological distress and the remaining patients scored in the 'moderate to severe' range. Among those patients in the 'mild' range 29% received an antidepressant prescription compared with about 70% of patients in the 'moderate to severe' range.

Although the psychiatric diagnosis based on the standardized diagnostic interview (CIS-R) at recruitment was not available to the primary care physician, we examined the relationship between the odds of receiving an antidepressant prescription and overall CIS-R score, any ICD-10 diagnosis, and specific psychiatric diagnosis. As depicted in table 4.7, patients who scored ≥12 on the CIS-R scale which indicate a possible psychiatric disorder, were 2.63 times more likely to receive an antidepressant prescription. Slightly more than half of the patients (51.5%) who qualified for an ICD-10 diagnosis received an antidepressant prescription and they were 2.55 times more likely to receive the prescription than those without a diagnosis. Further, about 20% of the screened positive patients did not qualify for any psychiatric diagnosis, yet, close to one-third of those patients also received an antidepressant prescription. With regard to specific diagnosis, nearly 60% of patients with a diagnosis of moderate to severe depression received a prescription for antidepressant followed by 53% of those with phobias and 50% of those with generalized anxiety disorder. Compared with those without any diagnosis, those with moderate to severe depression were four times more (OR 3.97 95% CI 3.01-5.25) likely to receive a prescription. However, close to half of the patients with milder forms of disorder such as mixed anxious depressive disorder and mild depression also received an antidepressant prescription.

We examined the relationship between specific symptoms elicited during the CIS-R based diagnostic interview administered by the health counsellor and the propensity for an antidepressant prescription. As shown in table 4.8, we found that the presence of any of the symptoms of psychological distress increased the odds of receiving a prescription, although symptoms of depression (OR 2.00 95%CI 1.67-2.35) and depressive ideas (OR 2.03 95%CI 1.69-2.44) were the strongest factors. As described in table 4.9, in a multivariable model that included all the symptoms, age, and gender, we found that patients reporting forgetfulness/concentration problems (OR 1.36; 95% CI 1.13-1.65), sleep problems (OR 1.59; 95% CI 1.3-1.9), depressive feelings (OR 1.36 95% CI 1.12-1.65), depressive ideas (OR 1.38

95%CI 1.12-1.71) and anxiety (OR 1.28 95% CI 1.01-1.64) were more likely to receive a prescription for an antidepressant compared to individual who did not report those specific symptoms.

Clinic related factors (level 2 factors) associated with antidepressant prescription

About half of the study clinics (n=12) were public primary care clinics that offered free services and medication. The remaining clinics (n=12) were private GP clinics that required out of pocket payment at the point of service. As part of the trial, half of the both public clinics (n=6) and private GP clinics (n=6) provided collaborative stepped care services for mental health care while the rest provided usual care.

We examined whether there is any difference in antidepressant prescription between primary care clinics enrolled in the collaborative stepped care treatment arm of the trial and the control clinics with usual care. Overall 44% of screened positive patients who attended a clinic with stepped care treatment model received an antidepressant prescription compared with 50% who attended a usual care clinic (OR 1.15; 95%CI. 0.46-1.29). As depicted in table 4.10, about 38% of screened positive patients who did not meet any diagnosis received an antidepressant prescription in usual care clinic compared with 23% in the collaborative stepped care clinic (OR 2.20; 95% CI 1.01-4.79). For some diagnoses such as moderate to severe depression and panic attack, a higher proportion of patients in the collaborative stepped care clinics received an antidepressant prescription while for other diagnoses such as mild depression and mixed anxiety and depression patients in the usual care clinics were more likely to get a prescription.

As shown in table 4.11, We also found some variations between antidepressant prescriptions in public primary care and private GP clinics. Overall, patients attending private GP clinics were slightly more likely (53%; n=613) to receive an antidepressant prescription compared with public primary care clinics (43%; n=707), although the confidence interval for this association was imprecise (OR. 1.63; 95%CI 0.77-3.42).

We could only analyze the above two level-two factors associated with antidepressant prescription, namely, the type of clinic and the study arm, while other important level-two factors such as the qualification and training of primary care physician, availability of support staff etc. were not measured in this study. Yet, we found that overall 29% (95% CI 8%-43%) of the variance in antidepressant prescription is explained by measured and unmeasured level-two factors.

Appropriate prescriptions

According to World Health Organization's MH-Gap treatment guidelines an antidepressant prescription is appropriate for adults with a moderate to severe depressive episode/disorder(244). In this study, about 60% of patients with a diagnosis of moderate to severe depression received a prescription for an antidepressant. Referring back to table 4.7, across all diagnoses, patients with moderate to severe depression were the most likely to receive an antidepressant prescription. Compared with screened positive patients who did not qualify for a diagnosis those with a diagnosis of moderate to severe depression were about four times (OR 3.97; 95%CI 3.01-5.25) as likely to receive an antidepressant prescription. As discussed earlier, the prescription was solely based on screening results and the clinical encounter as the primary care physician did not receive the CIS-R based standardized diagnosis.

About 46% to 52% of patients with a diagnosis other than moderate to severe depression also received a prescription for antidepressant. These include patients diagnosed with panic disorder (49%), mild depression (46%), phobias (53%), generalized anxiety disorder (50%) and mixed anxiety-depression (47%). Finally, about 31% of screened positive patients who did not qualify for a diagnosis also received a prescription for an antidepressant.

Discussion

Summary of main findings

Following screening for common mental disorders in primary care clinics in India, nearly half of all screened positive patients received a prescription for an antidepressant. Although patients with

moderate to severe depression were the most likely to receive an antidepressant prescription, close to half of the patients with less severe diagnoses such as mild depression and mixed anxiety depressive disorder also received antidepressant prescription. Further, about one-third of patients without any psychiatric diagnoses received an antidepressant prescription.

Women and older adults were more likely to receive a prescription; other factors such as education, socioeconomic situation or presence of chronic illnesses were not associated with the prescription of antidepressants. Patients with screening scores in the moderate to severe range were six times as likely to receive a prescription than those in the mild range. Similarly, patients who found it difficult to concentrate, those with sleep problems, depressive feelings and depressive ideas, and symptoms of anxiety were more likely to get a prescription.

The rate of prescription was slightly higher in private GP clinics than in free public primary care clinics although the confidence interval for this association was imprecise. Finally, there was no major difference between the rates of prescription in clinics with a collaborative stepped care treatment model that offered non-pharmacological interventions and those clinics that only offered antidepressants.

Indications for antidepressant prescriptions

This study represents a scenario that would become common if screening for mental disorders becomes a routine practice in primary care clinics and private GP clinics in low and middle income countries. Following screening, the physician recommends an intervention based on the screening result and a brief clinical encounter. Usually a standardized psychiatric diagnosis is not included in this process, however this study had access to the CIS-R based psychiatric diagnosis that was not available to the physician during the clinical consultation.

In general, treatment guidelines recommend limiting antidepressants to patients with moderate to severe depression (244, 285). Yet, we found that antidepressants are widely prescribed, and almost half of the patients screened positive for a common mental disorder received a prescription for

antidepressants. Even though physicians were unaware of the CIS-R based psychiatric diagnosis, patients with moderate to severe depression were the most likely diagnostic group to receive an antidepressant prescription, and 60% of them received a prescription. Further, 47% to 53% of patients with generalized anxiety disorder, phobias, panic disorders and mixed anxiety depressive disorder also received a prescription. Unfortunately, we do not have enough information to determine the clinical basis for these prescriptions and some of these prescriptions for conditions such as insomnia could be appropriate (286). However, antidepressant prescriptions received by 46% of patients with mild depression and 31% percent of patients with no mental disorder suggest over-prescription following screening in primary care. Our findings are similar to reports from primary care in high income countries that a significant proportion of antidepressant prescriptions are given to patients without depression or mild depression that do not indicate pharmacotherapy (287). While physicians sometime prescribe antidepressants for off label indications, there is no evidence that this is beneficial to patients (287, 288). On the other hand, about 40% of patients with moderate to severe depression did not receive any antidepressant prescription, although it is possible that some of these patients might have received non-pharmaceutical interventions. But a subgroup analysis of prescription by the study arms showed that, in usual care clinics without any non-pharmaceutical treatment options, 45% of patients with moderate to severe depression did not receive any antidepressant prescription compared with 35% without a prescription in the collaborative stepped care clinics. Primary care physicians' misinterpretation of the severity of depression is a possible reason that patients with subthreshold symptoms receive an antidepressant prescription (289) while those with moderate to severe depression do not receive one.

Factors associated with antidepressant prescription

On examining factors related to antidepressant prescription, we found slightly higher percentage of prescription for women than men and a steady increase in the prescription with increasing age. Though there is limited information on antidepressant prescription in relation to gender

and age distribution from low and middle income countries, a recent study comparing antidepressant use in five European countries reported a similar increase in prescription with increasing age and among women (248). In our study population the prevalence of depression was similar across age bands (ref: chapter 4), but those in the older age groups were still more likely to receive a prescription. Data from high income countries show that despite the fact that major depression is less prevalent in older age groups (290), they are more likely to receive antidepressant prescriptions and have longer treatment duration than younger patients (291, 292). This is a reason for concern as older patients are more sensitive to adverse effects of antidepressant medications and drug interactions, as they frequently have comorbidities and multiple medications (291, 293). A study of 60,746 primary care patients aged 65 years and older from the UK found significant associations between use of antidepressant drugs and a number of adverse events in people with depression (294). Therefore, it is critically important to prescribe antidepressants strictly for evidence based indications and also explore non pharmacological treatment options (295).

Role of collaborative stepped care

An important element of this study is the collaborative stepped care program for the management of common mental disorders implemented in half of the study clinics. The program had psychoeducation and interpersonal psychotherapy as non-pharmacological treatment options freely available to all patients. We expected lower rates of antidepressant prescription in these clinics due to availability of non-drug treatment options, yet, antidepressant prescriptions rates in these clinics were not appreciably different from those clinics without these treatment options. However, we found that patients with mild depression and those who didn't qualify for any diagnosis were less likely to get antidepressant prescriptions in these clinics with non-pharmacological treatment options. A plausible reason for the high rates antidepressant prescription in these clinics, despite the availability of non-pharmacological treatment options could be the lack of demand for interpersonal psychotherapy that

required regular follow-up. A qualitative study based on this trial reported that patients were reluctant to return to clinic for regular follow-ups due to a number of reasons (190).

Limitations

We acknowledge some of the limitations of this study. First, the lack of information on screened negative patients limit us from a full understanding of antidepressant prescriptions in primary care. Second, about 17% of eligible patients refused to participate and those who refused were younger. We attempted to address this selection bias by adjusting for age in our analyses. Third, we have limited information on physician related factors such as training, years of experience etc. related to the prescription of antidepressants. Fourth, the interpretation of the results is somewhat vulnerable to the validity of the diagnosis based on the revised Clinical Interview Schedule (CIS-R). We are not aware of any validation studies of CISR-R against a gold standard psychiatric interview in India. Although CIS-R has been validated among Indian immigrants elsewhere, is routinely used in India, and translated and field tested in the study population. Finally, we are unable to draw definite conclusions on the appropriateness of antidepressant prescriptions as we lack of information on the physicians' diagnosis of the patients and the decision making process that contributed to prescribing. Despite these limitation, to the best of our knowledge this is the first study that focuses on antidepressant prescriptions following screening in primary care in a low or middle income country.

Conclusion

In this study on treatment for common mental disorders in primary care from a middle income country, we found that antidepressants are widely prescribed following screening. While many patients with moderate to severe depression could benefit from antidepressants, it is disconcerting that significant proportion of patients with less severe disorders also received anti-depressant prescription despite the availability of non-pharmacological treatment options. In some of these less severe cases providing antidepressants could be counterproductive, hampering patients from finding non-

pharmacological solutions, thereby weakening their empowerment in a situation where regaining control is essential for recovery (296). Further, when patients are prescribed antidepressants in the absence of proven indications, they are still subject to potential side effects, adverse events, along with the unnecessary cost (287). The results of our study highlight reasons to be cautious about the proposed screening and treatment for common mental disorders in primary care. To address these concerns there is an urgent need to develop strategies in primary care practices to target the use of antidepressants to those patients who clearly benefit and limit unnecessary prescriptions.

Figure 4.1. Trial profile

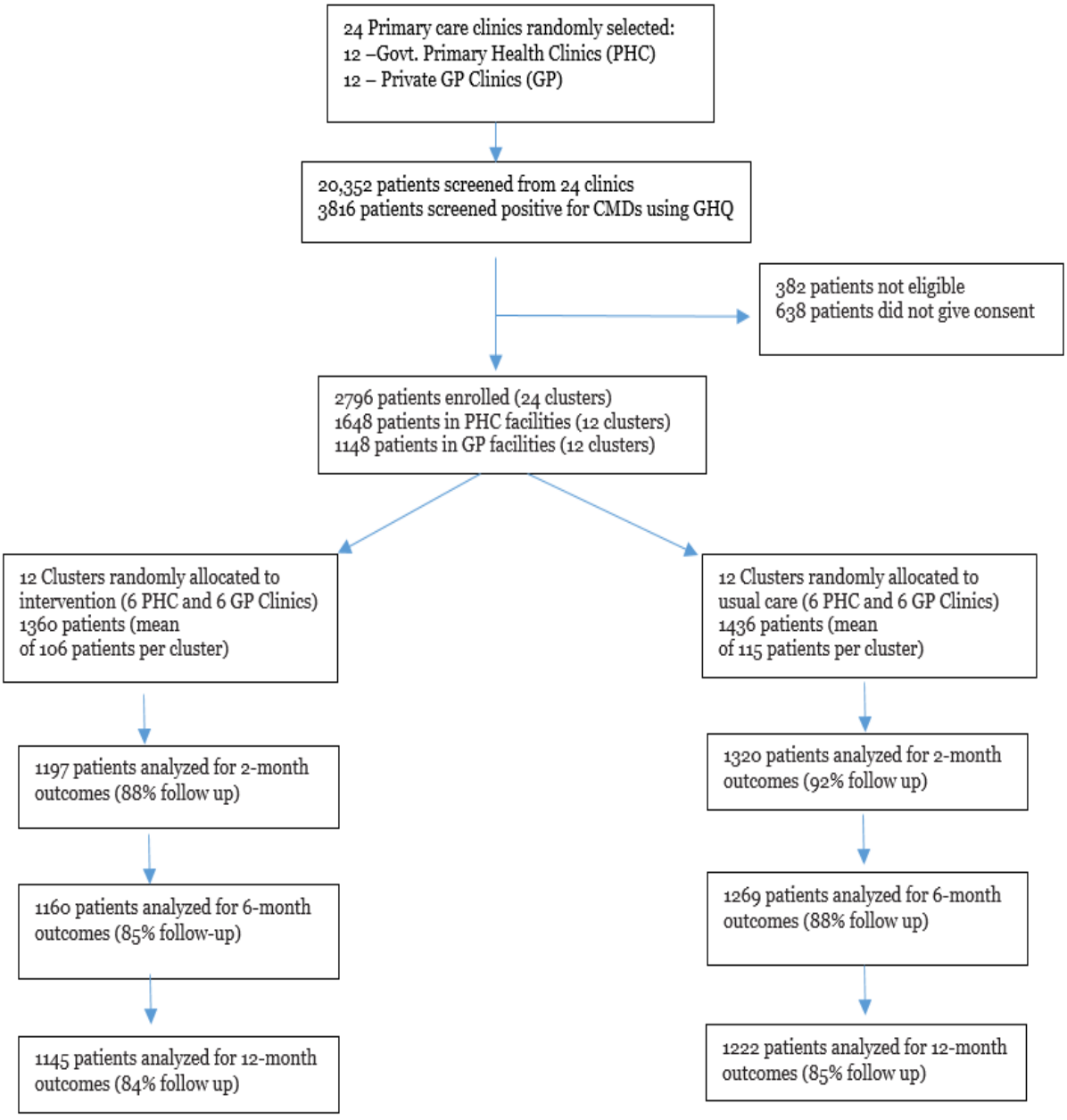

Table 4.1. Symptoms represented in the 14 sections of the CIS-R interview (213)

Defining Symptoms	Symptom description
Somatic symptoms	Aches, pains or any sort of discomfort that was brought on or made worse because you were feeling low, anxious or stressed.
Concentration/ forgetfulness	Problems with concentrating on what you were doing or forgetting things.
Sleep Problems	Problems with trying to get to sleep or with getting back to sleep, or sleeping more than usual.
Irritability	Feeling irritable or short tempered with those around you (over things that seem trivial looking back on them).
Worry about physical health	Worrying about your own physical health (all respondents) or worrying that you might have a serious physical illness (only respondents who didn't report a long-standing illness, disability or infirmity).
Depression	Feeling sad, miserable or depressed, or not being able to enjoy or take an interest in things as much as usual.
Depressive ideas	Feeling guilty, feeling hopeless, feeling not as good as others and thoughts of suicide (only respondents who scored 1 or more in the previous Depression section.)
Worry	Worrying about anything other than your own physical health.
Anxiety	Feeling anxious or nervous, or finding your muscles tense or that you couldn't relax.
Phobias	Feeling anxious, nervous or tense about any specific things or situations when there was no real danger, or avoiding any situation or thing because it would have made you feel nervous or anxious, even though there was no real danger.
Panic	Anxiety or tension getting so bad that you got in a panic (for example, feeling that you might collapse or lose control unless you did something about it).
Compulsions	Finding that you kept on doing things again and again when you knew you had already done them (for example, checking things like taps or washing yourself when you had already done so).
Obsessions	Having thoughts or ideas over and over again that you found unpleasant and that you would have preferred not to think about, that still kept on coming into your mind.

Table 4.2. Possible ICD-10 diagnosis derived from CIS-R algorithm [13]

PANIC: (D) panic disorder (f41.0)
GAD: (D) generalised anxiety disorder (f41.1)
MADD: (D) mixed anxiety/depressive disorder (f41.2)
OCD: (D) obsessive compulsive disorder (f42)
PHOB: (D) any phobia - combined category
DEP: (D) depressive episode - combined category
NEUROTIC: (D) Any neurotic disorder - CIS-R
F3200: (D) mildep w/o somsym - ICD-10 diagnosis f32.00
F3201: (D) mildep with somsym - ICD-10 diagnosis f32.01
F3210: (D) moddep w/o somsym - ICD-10 diagnosis f32.10
F3211: (D) moddep with somsym - ICD-10 diagnosis f32.11
F4000: (D) agora w/o panic - ICD-10 diagnosis f40.00
F4001: (D) agora with panic - ICD-10 diagnosis f40.01
SEVDEP: (D) severe depression - ICD-10 diagnosis f32.2
MILDDEP: (D) mild depression
MODDEP: (D) moderate depression
SOCPHOB: (D) social phobia - ICD-10 diagnosis f40.1
SPECPHOB: (D) specific (isol) phobia - ICD-10
AGORA: (D) any agoraphobia

Table 4.3 list of recoded predictors

Mean age	Age in completed years
Gender	Male Female
Marital status	Single or married Widowed or separated
Education	Above primary (elementary) school Primary school or below
Ethnicity	Goan Immigrant
Financial situation	Comfortable or Just about getting by Finding it difficult to make ends meet (extreme difficulty)
Long standing physical illness/disability	No Yes

Table 4.4 Characteristics of the study participants

	All participants (n=2796)	**Women** n=2305 (82%)	**Men** n=491 (18%)
	N (%)	N (%)	N (%)
Age *(n=2796)*			
18-29	294 (10.5)	239 (10.4)	55 (11.2)
30-39	571 (20.4)	466 (20.2)	105 (21.4)
40-49	733 (26.2)	628 (27.3)	105 (21.4)
50-59	534 (19.1)	438 (19)	96 (19.6)
60 & above	664 (23.8)	534 (23.2)	130 (26.5)
Marital Status *(n=2511)*			
Never married	159 (6.3)	100 (4.8)	59 (14.1)
Married	1618 (64.4)	1278 (61.1)	340 (81.3)
Widowed/separated	734 (29.2)	725 (34.2)	19 (4.6)
Ethnic group *(n=2510)*			
Goan	2401 (95.7)	2013 (96.2)	388 (92.8)
Migrant	109 (4.3)	79 (3.8)	30 (7.2)
Education *(n=2508)*			
Above primary school	929 (37.0)	710 (34.0)	219 (52.5)
Primary school or below	1579 (63.0)	1381 (66.0)	198 (47.5)
Financial situation *(n=2506)*			
Comfortable or Just about getting by	1361 (54.3)	1105 (52.9)	256 (61.4)
Finding it difficult	1145 (45.7)	984 (47.1)	161 (38.6)
Long standing physical illness/ disability *(n=2425)*			
No	1280 (52.8)	1066 (52.6)	214 (53.8)
Yes	1145 (47.2)	961 (47.4)	184 (46.2)

Table 4.5 Baseline diagnosis

Diagnosis	**Total** % (N)	**Women** % (N)	**Men** % (N)
Mixed anxiety depressive disorder	36.9 (1032)	37.0 (852)	36.7 (180)
Moderate to Severe depression	21.1 (589)	21.5 (496)	18.9 (93)
Mild depression	6.3 (134)	6.3 (145)	6.5 (32)
Generalized Anxiety disorder	5.9 (164)	6.5 (149)	3.1 (15)
Phobias	5.2 (146)	5.4 (124)	4.5 (22)
Panic disorder	4.8 (134)	4.4 (102)	6.5 (32)
No disorder	20.0 (554)	19.0 (437)	23.9 (117)

Table 4.6. Patient characteristics associated with antidepressant prescription

	Prescribed antidepressants			
	Yes % (N)	**No % (N)**	**Total % (N)**	**Adjusted OR***
Gender				
male	41.8 (205)	58.3 (286)	100 (491)	1
female	48.4 (1115)	51.6 (1190)	100 (2305)	1.29 (1.04-1.60)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Age				
18-29 years	37.4 (110)	62.6 (184)	100 (294)	1
30-39 years	42.6 (243)	57.4 (328)	100 (571)	1.38 (1.01-1.89)
40-49 years	48.0 (352)	52.0 (381)	100 (733)	1.69 (1.25-2.30)
50-59 years	48.3 (258)	51.7 (276)	100 (534)	1.56 (1.13-2.15)
60 years and over	53.8 (357)	46.2 (307)	100 (664)	1.80 (1.32-2.47)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Marital Status				
Single	42.1 (67)	57.9 (92)	100 (159)	1
married	45.6 (737)	54.5 (881)	100 (1618)	1.06 (0.73-1.54)
separated/widowed	53.0 (389)	47.0 (345)	100 (734)	1.05 (0.68-1.62)
Total	47.5 (1193)	52.5 (1318)	100 (2511)	
Ethnicity				
Goan	47.5 (1151)	52.1 (1250)	100 (2401)	1
Migrant	37.6 (41)	62.4 (68)	100 (109)	0.74 (0.48-1.13)
Total	47.5 (1192)	52.5 (1318)	100 (2510)	
Economic situation				
living comfortably	45.3 (115)	54.7 (139)	100 (254)	1
just about getting by	47.8 (529)	52.2 (578)	100 (1107)	1.16 (0.85-1.58)
finding it difficult to make	47.9 (548)	52.1 (597)	100 (1145)	1.14 (0.83-1.57)
Total	47.6 (1192)	52.4 (1314)	100 (2506)	
Education				
Above Primary school	45.2 (420)	54.8 (509)	100 (929)	1
Primary school or Below	48.9 (772)	51.1 (807)	100 (1579)	1.10 (0.89-1.35)
Total	47.5 (1192)	52.5 (1316)	100 (2508)	
Long standing physical				
No	44.8 (573)	55.2 (707)	100 (1280)	1
Yes	50.5 (578)	49.5 (567)	100 (1145)	1.00 (0.83-1.21)
Total	47.5 (1151)	52.5 (1274)	100 (2425)	

*Odds ratio adjusted for gender and age

Table 4.7. Clinical features associated with antidepressant prescription

	Prescribed antidepressants			
	Yes	**No**	Total	**Adjusted OR***
GHQ Case designation				
mild	28.7 (437)	71.3 (1087)	100 (1524)	1
mod/severe	69.4 (883)	30.6 (389)	100 (1272)	6.54 (5.42-7.9)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
CIS-R Score				
<12	30.7 (177)	69.3 (400)	100 (577)	1
≥12	51.5 (1143)	48.5 (1076)	100 (2219)	2.63 (2.10-3.28)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Any ICD 10 Diagnosis				
No	31.1 (172)	69.0 (382)	100 (554)	1
Yes	51.2 (1148)	48.8 (1094)	100 (2242)	2.55 (2.03-3.18)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Diagnosis				
No disorder	31.1 (172)	69.0 (382)	100 (554)	1
Mod-Severe	59.8 (352)	40.2 (237)	100 (589)	3.97 (3.01-5.25)
Panic	49.3 (66)	50.8 (68)	100 (134)	2.44 (1.59-3.76)
Mild Depression	46.3 (82)	53.7 (95)	100 (177)	2.43 (1.65-3.56)
Phobias	52.7 (77)	47.3 (69)	100 (146)	3.20 (2.09-4.89)
Generalized anxiety	50.0 (82)	50.0 (82)	100 (164)	2.38 (1.61-3.52)
Mixed anxiety depressive	47.4 (489)	52.6 (543)	100 (1032)	1.99 (1.56-2.55)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	

*Odds ratio adjusted for gender and age

Table 4.8 Symptoms associated with antidepressant prescription

	Prescribed antidepressants			
Symptoms	Yes	No	Total	Adjusted OR*
Somatic symptoms				
Less than 2 symptoms	43.1 (521)	56.9 (688)	100 (1209)	1
2 or more Symptoms	50.4 (799)	49.7 (788)	100 (1587)	1.61 (1.35-1.92)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Fatigue				
Less than 2 symptoms	36.7 (182)	63.3 (314)	100 (496)	1
2 or more Symptoms	49.8 (1138)	50.5 (1162)	100 (2300)	1.76 (1.40-2.20)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Concentration				
Less than 2 symptoms	38.6 (427)	61.4 (680)	100 (1107)	1
2 or more Symptoms	52.9 (893)	47.1 (796)	100 (1689)	1.86 (1.56-2.22)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Sleep problems				
Less than 2 symptoms	36.5 (322)	63.5 (561)	100 (883)	1
2 or more Symptoms	52.2 (998)	47.8 (915)	100 (1913)	1.97 (1.64-2.37)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Irritability				
Less than 2 symptoms	44.7 (883)	55.3 (1093)	100 (1976)	1
2 or more Symptoms	53.3 (437)	46.7 (383)	100 (820)	1.6 (1.32-1.93)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Worry about physical health problems				
Less than 2 symptoms	43.6 (583)	56.4 (753)	100 (1336)	1
2 or more Symptoms	50.5 (737)	49.54 (723)	100 (1460)	1.34 (1.13-1.59)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Depression				
Less than 2 symptoms	39.4 (517)	60.7 (797)	100 (1314)	1
2 or more Symptoms	54.2 (803)	45.8 (679)	100 (1482)	2.00 (1.67-2.35)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Depressive Ideas				
Less than 2 symptoms	35.3 (321)	64.7 (588)	100 (909)	1
2 or more Symptoms	52.9 (999)	47.1 (888)	100 (1887)	2.03 (1.69-2.44)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Worry				
Less than 2 symptoms	41.6 (424)	58.4 (595)	1019 (1009)	1
2 or more Symptoms	50.4 (896)	49.6 (881)	1777 (100)	1.46 (1.21-1.75)
Total	47.2 (1320)	52.8 (1476)	2796 (100)	
Anxiety				
Less than 2 symptoms	45.3 (995)	54.7 (1200)	100 (2195)	1
2 or more Symptoms	54.1 (325)	45.9 (276)	100 (601)	1.37 (1.10-1.68)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Phobias				
Less than 2 symptoms	45.22 (1022)	54.8 (1238)	100 (2260)	1
2 or more Symptoms	55.6 (298)	44.4 (238)	100 (536)	1.71 (1.38-2.12)
Total	47.2 (1320	52.8 (1476)	100 (2796))	

*Odds ratio adjusted for gender and age

Table 4.8 contd. Symptoms associated with antidepressant prescription

	Prescribed antidepressants			
Symptoms	Yes	No	Total	Adjusted OR
Panic				
Less than 2 symptoms	44.7 (933)	55.3 (1154)	100 (2087)	1
2 or more Symptoms	54.6 (387)	45.4 (322)	100 (709)	1.5 (1.22-1.83)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	

*****Odds ratio adjusted for gender and age

Table 4.9. Multivariate model* –likelihood of antidepressant prescription by presenting symptoms

	Odds ratio	[95% Confidence interval]
Somatic symptoms	1.14	(0.94-1.39)
Fatigue	1.11	(0.86-1.42)
Concentration	1.36	(1.13-1.65)
Sleep problems	1.59	(1.31-1.93)
Irritability	1.18	(0.97-1.45)
Worry-physical health	0.96	(0.80-1.16)
Depression	1.36	(1.12-1.65)
Depressive ideas	1.38	(1.12-1.71)
Worry	1.07	(0.88-1.30)
Anxiety	1.29	(1.01-1.64)
Phobias	0.96	(0.76-1.22)
Panic	1.05	(0.84-1.32)
Age	1.01	(1.01-1.02)
Sex	1.20	(0.96-1.51)

*Odds ratio adjusted for gender, age and presenting symptoms

Table 4.10. Differences in antidepressant prescription by types of clinics and diagnosis

Diagnosis	Usual Care	Collaborative stepped care[1]	Adjusted OR[2]
No disorder	38.4 (112)	22.9 (60)	2.20 (1.01-4.79)
Mild depression	49.1 (54)	42.0 (28)	1.47 (0.56-3.85)
Mod-Severe	55.8 (198)	65.8 (154)	0.62 (0.35-1.10)
Mixed anxiety depressive	53.5 (252)	42.3 (237)	1.28 (0.55-3.02)
Other diagnosis	48.6 (101)	52.5 (124)	0.78 (0.34-1.83)

1. Reference group
2. Odds ratio adjusted for gender and age

Table 4.11. Clinic related factors associated with antidepressant prescription

	Prescribed Antidepressants			Adj. OR*
	Yes	No	Total	
Clinic type			I	
Free public primary care	42.9 (707)	57.1 (941)	100 (1648)	1
Private GP Clinic	53.4 (613)	46.6 (535)	100 (1148)	1.63 (0.77-3.42)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	
Treatment model				
Collaborative stepped care	44.3 (603)	55.7 (757)	100 (1360)	1
Usual care	49.9 (717)	50.1 (719)	100 (1436)	1.15 (0.46-1.29)
Total	47.2 (1320)	52.8 (1476)	100 (2796)	

*Odds ratio adjusted for gender and age

Chapter 5: Conclusion

The idea for this dissertation stems from my interest in psychological distress among primary care patients. During my training and practice as a primary care physician in India, I often came across patients with psychological distress, especially women and older adults. They repeatedly present with pain symptoms, tiredness, insomnia and nonspecific somatic complaints. Most primary care physicians agree that some of these patients could be suffering from common mental disorders such as depression or anxiety disorder.

However, patients seldom received any mental health interventions in our clinics due to a number of reasons. First, as is typical in primary care clinics in a low or middle income country, the physician has to attend to about 100 to 200 out-patients a day. In such settings there is no time to explore presenting complaints to discern if it is a mental disorder or non-pathological distress. Generally, there are no other trained staff available to explore mental health issues or provide psychosocial support. Mental health specialists and trained counsellors are only available at tertiary level clinics that are not easily accessible. Second, primary care physicians have limited training in mental health care and are concerned about possible adverse effects of psychotropic medications. In addition, without regular follow up it is difficult to monitor antidepressants and other psychotropic medications. Third, due to stigma associated with mental disorders, physicians tend to avoid difficult conversations on mental health or referrals to a mental health specialist, unless patients present with conspicuous or moderate to severe symptoms of mental disorders. Further, for most patients, psychological distress is triggered by stressors such as socioeconomic distress, domestic violence or spousal alcohol abuse that are considered beyond the scope of the narrow bio-medically oriented services provided at the primary care clinic.

In this context, when global mental health initiatives announced a call to action to address the unmet treatment need for mental disorders and integrate mental health care into primary care, we

were cautiously optimistic. Since 2007 a number of large trials in primary care involving collaborative stepped care and task sharing demonstrated that with the help of lay health workers mental health treatments can be delivered to people identified with common mental disorders in primary care (297). However, several aspects of these studies made many primary care physicians like me concerned. For instance, the proportion of patients identified as needing treatment by screening was implausibly high, even for those of us sensitive about common mental disorders in primary care. Further, the collaborative stepped care and task sharing model envisaged in global mental health trials are resource intensive, and out of reach for most public primary health centers, not to mention private GP clinics (solo practices) on which the majority of patients in countries like India rely on. Finally, there is skepticism regarding the sustainable effects of treatments, considering the fact that for most patients, the cycle of psychosocial disadvantage and economic distress that triggered the crisis remained unresolved.

While the movement for global mental health focused on trials evaluating strategies to integrate and scale up mental health care through primary care, we felt that several fundamental questions regarding screening and its benefits were ignored. For instance, what is the implication of a positive screening? Are all screened positive patients in need of mental health interventions or are many of them just experiencing temporary non-pathological distress? How would the primary care system realistically respond to screened positive patients, especially in the absence of a comprehensive mental health program that is out of reach for most clinics? Are there alternative models to address psychological distress that are more suited to the realities of routine primary care? The overarching goal of this dissertation was to explore some of these issues related to primary care based screening of common mental disorders in low and middle income countries.

My review of the literature spanning four decades could not find any studies that directly examined the effectiveness of screening by comparing the outcomes between a screened and non-

screened group of primary care patients in a low or middle income country. Nevertheless, I identified several studies that shed light on the challenges of screening for mental disorders in primary care in these countries. In chapter two, I discussed these issues under three broad themes. First, concerns about the fidelity with which screening is implemented, particularly poor cross cultural adaptation of screening instruments, flawed validation of scales, use of non-validated screening and diagnostic instruments, and misinterpretation of a positive screen as a diagnosis of mental disorder. Scales that were originally developed as screening instruments are routinely used both as diagnostic instruments (without considering exclusion criteria) and monitoring clinical improvement (298). Second, identification of patients in need of mental health treatment by screening is problematic. For the majority of patients identified by screening, psychological distress has a short self-remitting course that may not merit any biomedical intervention. At the same time, there is also a significant proportion of patients who experience persistent distress, and they are more likely to have serious physical illness or ongoing adverse life experiences. Unfortunately, screening and physician notification seldom results in further diagnosis, appropriate treatment or improved access to mental health interventions. Finally, the evidence on the benefit of treatment for common mental disorders in primary care is mixed, and it is difficult to discern the components of interventions that are effective. Benefits of interventions are most evident in short term (2-3 months) follow-up, while it is less so in long term follow-up. Overall there is some evidence to suggest that interventions that also addresses psychosocial issues surrounding psychological distress could be beneficial.

I further examined these issues, specifically, the clinical course of common mental disorders identified by screening in primary care based on data from one of the largest primary care based trials, the MANAS study, from India. The study not only confirmed the transient nature of psychological distress among a significant proportion of screened positive patients, but also found the futility of using current psychiatric diagnostic categories among screened positive patients in primary care. This finding

supports the concern of many psychiatric researchers from low and middle income countries that the current classification (e.g. DSM-IV/5 and ICD-10/11) and their scaled down versions for primary care are not useful in primary care (239). We found poor diagnostic stability for ICD-10 based diagnoses, and the most stable and prevalent diagnosis was mixed anxiety and depressive disorder, which is no longer included in the latest versions of DSM or ICD. About one-fifth of the screened positive patients experienced persistent distress during one year follow up especially women, those with lower education, those with long standing physical illnesses and disability, and those who faced severe economic hardships. While biomedical interventions may help in temporary relief of symptoms for such patients, without serious efforts to improve socioeconomic constrains and structural inequality that these patients face those interventions could remain inconsequential.

In the final paper I took a step further and examined the management of screened positive patients, especially prescription of antidepressants. The study represents a scenario that would become common if screening for mental disorders becomes a routine practice in primary care clinics and private GP clinics in low and middle income countries. I found that antidepressants are widely prescribed following screening. While patients with severe depression were the most likely to receive a prescription, it is deeply troubling that close to half of the patients with milder disorders and about one-third of patients without any diagnosis also received an antidepressant prescription. A clinical interview following screening is necessary to minimize over diagnosis or under diagnosis of mental disorder (299). In a busy primary care clinic this is difficult and we found that introducing screening could lead to irrational prescription of antidepressants, most likely due to the busy primary care physician accepting the simple screening as a diagnosis. These results highlight a real risk of misdiagnosis of mental disorders and over-prescription of antidepressants in primary care, an unfortunate situation that with which many high-income countries are already struggling.

In essence, this dissertation goes against the prevailing convictions that support routine screening in primary care in low and middle income countries. Many scholars recommend screening based on recent trials from low and middle income countries that showed benefits of collaborative stepped care model and task sharing in treating mental disorders in primary care. As a matter of fact, what those trials found was a modest benefit of screening followed by intervention when sufficient resources are in place and extensive efforts are made to ensure adequate treatment and follow-up. However, in reality, in the absence of such resources and efforts, screening could inappropriately expend scarce resources and result in unintentional consequences. More patients will be misdiagnosed if they are simply identified by screening instruments without proper clinical evaluation and, in the absence of interventions that are socio-culturally acceptable and easily accessible they end up receiving inappropriate antidepressant prescriptions.

Nonetheless, this dissertation does not downplay the importance of mental disorders in primary care. The analyses indicate that a significant percentage of primary care patients experience persistent and possibly pathological distress linked to depressive and anxiety disorders. Given that the evidence does not support routine screening in primary care as a strategy, what would be a better way to identify these patients who might benefit from interventions?

We found that about 40-60% of screened positive patients have psychological distress that is temporary and self-limiting, hence one possible approach is a follow up screening within a short period for all those who screened positive during the first visit, and offering treatment to only those who remained screened positive at the second screening. This might help to avoid treating those patients with psychological distress that is temporary and self-limiting, which is often non-pathological. Ideally the second screening should be done at the home of the patient by a health worker but could also be done at the clinics. As shown in a study from primary care clinics in Chile, more than half of the screened positive women screened negative during a follow-up screening at the clinic within two weeks (41).

Although, this strategy may not help to discern those screened positive individuals with chronic, yet non-pathological distress caused by ongoing socioeconomic problems from those with depressive or anxiety disorders. Researchers have also suggested using higher threshold for intervening as in a recent trial for depression in India that screened and enrolled patients with moderate to severe depression only (11). However, future studies are required to examine the feasibility of repeated screening, the recommended duration between screenings and the usefulness of a higher diagnostic threshold.

Further, there is a greater role for primary care physicians, alternative care providers (spiritual guides, indigenous medical practitioners etc.), and the local community in addressing the unmet need for mental health care. The *movement for global mental health* is often depicted as an active partnership involving institutions and researchers, practitioners, patient groups, and grass root movements in high income countries and in low and middle income countries. However, in reality the voice of local practitioners, patients and communities from low and middle income countries are nearly absent in these partnerships. Thus, there seems to be a disconnect between the ideas and belief systems of the community, the frontline practitioners and the global mental health movement. This is most evident in the approaches to addressing psychological distress in the community and primary care, especially related to discerning pathological and non-pathological psychological distress. More than a 100 years ago Karl Jaspers the icon of modern psychiatry stated very clearly that:

> *"What health and illness mean in general are matters which concern the physician least of all. He deals scientifically with life processes and with particular illnesses. What is 'ill' in general depends less on the judgement of the physician than on the judgement of the patient and on the dominant views in any given cultural circle" (300).*

This poses an important question, that is, what is a mental illness in a given cultural circle? When patients manifest obvious abnormalities and dysfunctions as in severe mental disorders, it is easy

to define a mental illness. However, when it comes to common mental disorders such as anxiety and depressive disorders, there are differences in defining mental disorders and the treatment needs. What academic researchers consider as a disorder and the unmet need for treatment may not align with the beliefs and perceptions of local practitioners, patients and the community. Although addressing the unmet need for mental health care in primary care is the driving force behind screening for mental disorders in primary care, the community's perception of mental disorders, and the felt need of individuals and the community regarding mental health care in these diverse cultural settings are often ignored. It is obvious that to implement a successful screening program we need the cooperation of people and they have to agree with the diagnosis and with the intervention. However, patients' beliefs about the causes of psychological distress, the need for treatment, and outcome expectations are seldom systematically studied before initiating routine screening programs. Consequently, when it comes to psychological distress identified by screening in primary care, there is often limited acceptance of screening programs by frontline care providers and patients, and poor compliance to treatments. This is a serious flaw in our attempt to integrate mental health into primary care and address the treatment gap. We need to focus on qualitatively studies to understand these issues and empower local practitioners and communities to define their mental health care needs.

One of the main reasons for a false positive screening may be the screening context. As discussed in chapter 3, opportunistic screening in primary care occurs at an inopportune moment for patients as they face stress related to physical illness, looming health care expenses and an often unpleasant and overcrowded primary care clinic. Misdiagnosis of situational distress as a mental disorder is a strong possibility in this context, especially when using screening without clinical judgment. Moving case finding from the clinic to the community and focusing on high risk groups is a strategy that is now being implemented under the "Mental Health for All" program in the State of Kerala in India. This program has implemented two types of case findings. In the first model, community health workers also

known as ‘ASHA’ (Accredited Social Health Activist), visit homes in their community to identify people with mental disorders using a family screening questionnaire. Screened positive patients are encouraged to attend a program conducted at regular intervals at the family health center (recently renamed primary care clinic) in the community by the district mental health team. In this program screened positive patients are diagnosed following detailed clinical evaluation by a specialist and a treatment plan is developed in consultation with the primary care physician together with the community health worker. The community health worker acts as a case manager for diagnosed patients and encourages medication adherence and regular follow up. In addition, the local council members are involved in the program to provide access to social welfare schemes. This program was recently implemented in 279 communities and 12,540 new cases of mental disorders have been identified (301). Unlike research projects and primary care based intervention trials that we discussed earlier, this program was largely developed by local experts with active participation of community stakeholders. They were attentive to avoid unnecessary diagnoses and prescription, and the program was geared towards identifying more severe mental disorders. A recent report from the program shows that unlike routine screening in primary care that identifies large numbers of people with conditions such as dysthymia and subsyndromal depression, the new program has larger proportions of people with severe mental disorders (29% with schizophrenia and psychotic disorders, 16% bipolar disorders, 11% depressive disorders, 6% anxiety disorders)(301). In the second model, screening is aimed at identifying depression in high risk groups by a Junior Public Health Nurse (JPHN). High risk cases are identified for screening by a community health worker, who also resides in the community. High risk cases include patients under palliative care and their care givers, those with substance abuse and their family members, history of deliberate self-harm, family members of those who committed suicide and those with chronic non communicable diseases. Screened positive patients are diagnosed by the primary care physician trained by the district mental health program and treated in consultation with a specialist associated with the

district mental health program. However, both these programs have not been formally evaluated for their effectiveness or portability to other low and middle income country settings.

To sum up, although psychological distress is common in primary care patients, the number of patients that need mental health treatment may not be many. Current evidence does not favor routine screening in primary care as an effective strategy to identify those in need of treatment; instead screening could lead to over diagnosis and inappropriate antidepressant prescriptions. To address psychological distress and unmet need for treatment in low and middle income countries, there is an urgent need to focus on locally driven and culturally relevant approaches to case finding and intervention.

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Appendix

Appendix A: Search terms used for literature review

Pubmed Search:

(((((((((("developing countries"[MeSH Terms:noexp] OR "africa"[MeSH Terms:noexp] OR "africa, northern"[MeSH Terms:noexp] OR "africa south of the sahara"[MeSH Terms:noexp] OR "africa, central"[MeSH Terms:noexp] OR "africa, eastern"[MeSH Terms:noexp] OR "africa, southern"[MeSH Terms:noexp] OR "africa, western"[MeSH Terms:noexp] OR "asia"[MeSH Terms:noexp] OR "asia, central"[MeSH Terms:noexp] OR "asia, southeastern"[MeSH Terms:noexp] OR "asia, western"[MeSH Terms:noexp] OR "caribbean region"[MeSH Terms:noexp] OR "west indies"[MeSH Terms:noexp] OR "south america"[MeSH Terms:noexp] OR "latin america"[MeSH Terms:noexp] OR "central america"[MeSH Terms:noexp] OR "afghanistan"[MeSH Terms:noexp] OR "albania"[MeSH Terms:noexp] OR "algeria"[MeSH Terms:noexp] OR "american samoa"[MeSH Terms:noexp] OR "angola"[MeSH Terms:noexp] OR "Antigua and Barbuda"[Mesh:noexp] OR "argentina"[MeSH Terms:noexp] OR "armenia"[MeSH Terms:noexp] OR "azerbaijan"[MeSH Terms:noexp] OR "bahrain"[MeSH Terms:noexp] OR "bangladesh"[MeSH Terms:noexp] OR "barbados"[MeSH Terms:noexp] OR "benin"[MeSH Terms:noexp] OR "republic of belarus"[MeSH Terms:noexp] OR "belize"[MeSH Terms:noexp] OR "bhutan"[MeSH Terms:noexp] OR "bolivia"[MeSH Terms:noexp] OR "bosnia and herzegovina"[MeSH Terms:noexp] OR "botswana"[MeSH Terms:noexp] OR "brazil"[MeSH Terms:noexp] OR "bulgaria"[MeSH Terms:noexp] OR "burkina faso"[MeSH Terms:noexp] OR "burundi"[MeSH Terms:noexp] OR "cambodia"[MeSH Terms:noexp] OR "cameroon"[MeSH Terms:noexp] OR "cabo verde"[MeSH Terms:noexp] OR "central african republic"[MeSH Terms:noexp] OR "chad"[MeSH Terms:noexp] OR "chile"[MeSH Terms:noexp] OR "china"[MeSH Terms:noexp] OR "colombia"[MeSH Terms:noexp] OR "comoros"[MeSH Terms:noexp] OR "congo"[MeSH Terms:noexp] OR "costa rica"[MeSH Terms:noexp] OR "cote d'ivoire"[MeSH Terms:noexp] OR "croatia"[MeSH Terms:noexp] OR "cuba"[MeSH Terms:noexp] OR "cyprus"[MeSH Terms:noexp] OR "czechoslovakia"[MeSH Terms:noexp] OR "czech republic"[MeSH Terms:noexp] OR "slovakia"[MeSH Terms:noexp] OR "djibouti"[MeSH Terms:noexp] OR "Democratic Republic of the Congo"[Mesh:noexp] OR "dominica"[MeSH Terms:noexp] OR "dominican republic"[MeSH Terms:noexp] OR "timor-leste"[MeSH Terms:noexp] OR "ecuador"[MeSH Terms:noexp] OR "egypt"[MeSH Terms:noexp] OR "el salvador"[MeSH Terms:noexp] OR "eritrea"[MeSH Terms:noexp] OR "estonia"[MeSH Terms:noexp] OR "ethiopia"[MeSH Terms:noexp] OR "fiji"[MeSH Terms:noexp] OR "gabon"[MeSH Terms:noexp] OR "gambia"[MeSH Terms:noexp] OR "Georgia (Republic)"[Mesh:noexp] OR "ghana"[MeSH Terms:noexp] OR "greece"[MeSH Terms:noexp] OR "grenada"[MeSH Terms:noexp] OR "guatemala"[MeSH Terms:noexp] OR "guinea"[MeSH Terms:noexp] OR "guinea-bissau"[MeSH Terms:noexp] OR "guam"[MeSH Terms:noexp] OR "guyana"[MeSH Terms:noexp] OR "haiti"[MeSH Terms:noexp] OR "honduras"[MeSH Terms:noexp]

OR "hungary"[MeSH Terms:noexp] OR "india"[MeSH Terms:noexp] OR "indonesia"[MeSH Terms:noexp] OR "iran"[MeSH Terms:noexp] OR "iraq"[MeSH Terms:noexp] OR "jamaica"[MeSH Terms:noexp] OR "jordan"[MeSH Terms:noexp] OR "kazakhstan"[MeSH Terms:noexp] OR "kenya"[MeSH Terms:noexp] OR "korea"[MeSH Terms:noexp] OR "kosovo"[MeSH Terms:noexp] OR "kyrgyzstan"[MeSH Terms:noexp] OR "laos"[MeSH Terms:noexp] OR "latvia"[MeSH Terms:noexp] OR "lebanon"[MeSH Terms:noexp] OR "lesotho"[MeSH Terms:noexp] OR "liberia"[MeSH Terms:noexp] OR "libya"[MeSH Terms:noexp] OR "lithuania"[MeSH Terms:noexp] OR "macedonia (republic)"[MeSH Terms:noexp] OR "madagascar"[MeSH Terms:noexp] OR "malaysia"[MeSH Terms:noexp] OR "malawi"[MeSH Terms:noexp] OR "mali"[MeSH Terms:noexp] OR "malta"[MeSH Terms:noexp] OR "mauritania"[MeSH Terms:noexp] OR "mauritius"[MeSH Terms:noexp] OR "mexico"[MeSH Terms:noexp] OR "micronesia"[MeSH Terms:noexp] OR "middle east"[MeSH Terms:noexp] OR "moldova"[MeSH Terms:noexp] OR "mongolia"[MeSH Terms:noexp] OR "montenegro"[MeSH Terms:noexp] OR "morocco"[MeSH Terms:noexp] OR "mozambique"[MeSH Terms:noexp] OR "myanmar"[MeSH Terms:noexp] OR "namibia"[MeSH Terms:noexp] OR "nepal"[MeSH Terms:noexp] OR "netherlands antilles"[MeSH Terms:noexp] OR "new caledonia"[MeSH Terms:noexp] OR "nicaragua"[MeSH Terms:noexp] OR "niger"[MeSH Terms:noexp] OR "nigeria"[MeSH Terms:noexp] OR "oman"[MeSH Terms:noexp] OR "pakistan"[MeSH Terms:noexp] OR "palau"[MeSH Terms:noexp] OR "panama"[MeSH Terms:noexp] OR "papua new guinea"[MeSH Terms:noexp] OR "paraguay"[MeSH Terms:noexp] OR "peru"[MeSH Terms:noexp] OR "philippines"[MeSH Terms:noexp] OR "poland"[MeSH Terms:noexp] OR "portugal"[MeSH Terms:noexp] OR "puerto rico"[MeSH Terms:noexp] OR "romania"[MeSH Terms:noexp] OR "russia"[MeSH Terms:noexp] OR "Russia (Pre-1917)"[Mesh:noexp] OR "rwanda"[MeSH Terms:noexp] OR "Saint Kitts and Nevis"[Mesh:noexp] OR "saint lucia"[MeSH Terms:noexp] OR "Saint Vincent and the Grenadines"[Mesh:noexp] OR "samoa"[MeSH Terms:noexp] OR "saudi arabia"[MeSH Terms:noexp] OR "senegal"[MeSH Terms:noexp] OR "serbia"[MeSH Terms:noexp] OR "montenegro"[MeSH Terms:noexp] OR "seychelles"[MeSH Terms:noexp] OR "sierra leone"[MeSH Terms:noexp] OR "slovenia"[MeSH Terms:noexp] OR "sri lanka"[MeSH Terms:noexp] OR "somalia"[MeSH Terms:noexp] OR "south africa"[MeSH Terms:noexp] OR "sudan"[MeSH Terms:noexp] OR "suriname"[MeSH Terms:noexp] OR "swaziland"[MeSH Terms:noexp] OR "syria"[MeSH Terms:noexp] OR "tajikistan"[MeSH Terms:noexp] OR "tanzania"[MeSH Terms:noexp] OR "thailand"[MeSH Terms:noexp] OR "togo"[MeSH Terms:noexp] OR "tonga"[MeSH Terms:noexp] OR "Trinidad and Tobago"[Mesh:noexp] OR "tunisia"[MeSH Terms:noexp] OR "turkey"[MeSH Terms:noexp] OR "turkmenistan"[MeSH Terms:noexp] OR "uganda"[MeSH Terms:noexp] OR "ukraine"[MeSH Terms:noexp] OR "uruguay"[MeSH Terms:noexp] OR "ussr"[MeSH Terms:noexp] OR "uzbekistan"[MeSH Terms:noexp] OR "vanuatu"[MeSH Terms:noexp] OR "venezuela"[MeSH Terms:noexp] OR "vietnam"[MeSH Terms:noexp] OR "yemen"[MeSH Terms:noexp] OR "yugoslavia"[MeSH Terms:noexp] OR "zambia"[MeSH Terms:noexp] OR "zimbabwe"[MeSH Terms:noexp]) OR (Macedonia[tw] OR Madagascar[tw] OR Malagasy Republic[tw] OR Malaysia[tw] OR Malaya[tw] OR Malay[tw] OR Sabah[tw] OR Sarawak[tw] OR Malawi[tw] OR Nyasaland[tw] OR Mali[tw] OR Malta[tw] OR Marshall Islands[tw] OR

Mauritania[tw] OR Mauritius[tw] OR Agalega Islands[tw] OR Mexico[tw] OR Micronesia[tw] OR Middle East[tw] OR Moldova[tw] OR Moldovia[tw] OR Moldovian[tw] OR Mongolia[tw] OR Montenegro[tw] OR Morocco[tw] OR Ifni[tw] OR Mozambique[tw] OR Myanmar[tw] OR Myanma[tw] OR Burma[tw] OR Namibia[tw] OR Nepal[tw] OR Netherlands Antilles[tw] OR New Caledonia[tw] OR Nicaragua[tw] OR Niger[tw] OR Nigeria[tw] OR Northern Mariana Islands[tw] OR Oman[tw] OR Muscat[tw] OR Pakistan[tw] OR Palau[tw] OR Palestine[tw] OR Panama[tw] OR Paraguay[tw] OR Peru[tw] OR Philippines[tw] OR Philipines[tw] OR Phillipines[tw] OR Phillippines[tw] OR Poland[tw] OR Portugal[tw] OR Puerto Rico[tw] OR Romania[tw] OR Rumania[tw] OR Roumania[tw] OR Russia[tw] OR Russian[tw] OR Rwanda[tw] OR Ruanda[tw] OR Saint Kitts[tw] OR St Kitts[tw] OR Nevis[tw] OR Saint Lucia[tw] OR St Lucia[tw] OR Saint Vincent[tw] OR St Vincent[tw] OR Grenadines[tw] OR Samoa[tw] OR Samoan Islands[tw] OR (Navigator[TIAB] AND Island[tw]) OR (Navigator[TIAB] AND Islands[tw]) OR Sao Tome[tw] OR Saudi Arabia[tw] OR Senegal[tw] OR Serbia[tw] OR Montenegro[tw] OR Seychelles[tw] OR Sierra Leone[tw] OR Slovenia[tw] OR Sri Lanka[tw] OR Ceylon[tw] OR Solomon Islands[tw] OR Somalia[tw] OR Sudan[tw] OR Suriname[tw] OR Surinam[tw] OR Swaziland[tw] OR Syria[tw] OR Tajikistan[tw] OR Tadzhikistan[tw] OR Tadjikistan[tw] OR Tadzhik[tw] OR Tanzania[tw] OR Thailand[tw] OR Togo[tw] OR Togolese Republic[tw] OR Tonga[tw] OR Trinidad[tw] OR Tobago[tw] OR Tunisia[tw] OR Turkey[tw] OR Turkmenistan[tw] OR Turkmen[tw] OR Uganda[tw] OR Ukraine[tw] OR Uruguay[tw] OR USSR[tw] OR Soviet Union[tw] OR Union of Soviet Socialist Republics[tw] OR Uzbekistan[tw] OR Uzbek[TIAB] OR Vanuatu[tw] OR New Hebrides[tw] OR Venezuela[tw] OR Vietnam[tw] OR Viet Nam[tw] OR West Bank[tw] OR Yemen[tw] OR Yugoslavia[tw] OR Zambia[tw] OR Zimbabwe[tw] OR Rhodesia[tw]) OR (Africa[tw] OR Asia[tw] OR Caribbean[tw] OR West Indies[tw] OR South America[tw] OR Latin America[tw] OR Central America[tw] OR Afghanistan[tw] OR Albania[tw] OR Algeria[tw] OR Angola[tw] OR Antigua[tw] OR Barbuda[tw] OR Argentina[tw] OR Armenia[tw] OR Armenian[tw] OR Aruba[tw] OR Azerbaijan[tw] OR Bahrain[tw] OR Bangladesh[tw] OR Barbados[tw] OR Benin[tw] OR Byelarus[tw] OR Byelorussian[tw] OR Belarus[tw] OR Belorussian[tw] OR Belorussia[tw] OR Belize[tw] OR Bhutan[tw] OR Bolivia[tw] OR Bosnia[tw] OR Herzegovina[tw] OR Hercegovina[tw] OR Botswana[tw] OR Brasil[tw] OR Brazil[tw] OR Bulgaria[tw] OR Burkina Faso[tw] OR Burkina Fasso[tw] OR Upper Volta[tw] OR Burundi[tw] OR Urundi[tw] OR Cambodia[tw] OR Khmer Republic[tw] OR Kampuchea[tw] OR Cameroon[tw] OR Cameroons[tw] OR Cameron[tw] OR Cape Verde[tw] OR Central African Republic[tw] OR Chad[tw] OR Chile[tw] OR China[tw] OR Colombia[tw] OR Comoros[tw] OR Comoro Islands[tw] OR Comores[tw] OR Mayotte[tw] OR Congo[tw] OR Zaire[tw] OR Costa Rica[tw] OR Cote d'Ivoire[tw] OR Ivory Coast[tw] OR Croatia[tw] OR Cuba[tw] OR Cyprus[tw] OR Czechoslovakia[tw] OR Czech Republic[tw] OR Slovakia[tw] OR Slovak Republic[tw] OR Djibouti[tw] OR French Somaliland[tw] OR Dominica[tw] OR Dominican Republic[tw] OR East Timor[tw] OR (East[TIAB] AND Timur[tw]) OR Timor Leste[tw] OR Ecuador[tw] OR Egypt[tw] OR United Arab Republic[tw] OR El Salvador[tw] OR Eritrea[tw] OR Estonia[tw] OR Ethiopia[tw] OR Fiji[tw] OR Gabon[tw] OR Gabonese Republic[tw] OR Gambia[tw] OR Gaza[tw] OR Georgia Republic[tw] OR Georgian Republic[tw] OR Ghana[tw] OR Gold Coast[tw] OR Greece[tw] OR Grenada[tw] OR Guatemala[tw]

OR Guinea[tw] OR Guam[tw] OR Guiana[tw] OR Guyana[tw] OR Haiti[tw] OR Honduras[tw] OR Hungary[tw] OR India[tw] OR Maldives[tw] OR Indonesia[tw] OR Iran[tw] OR Iraq[tw] OR Isle of Man[tw] OR Jamaica[tw] OR Jordan[tw] OR Kazakhstan[tw] OR Kazakh[tw] OR Kenya[tw] OR Kiribati[tw] OR Korea[tw] OR Kosovo[tw] OR Kyrgyzstan[tw] OR Kirghizia[tw] OR Kyrgyz Republic[tw] OR Kirghiz[tw] OR Kirgizstan[tw] OR "Lao PDR"[tw] OR Laos[tw] OR Latvia[tw] OR Lebanon[tw] OR Lesotho[tw] OR Basutoland[tw] OR Liberia[tw] OR Libya[tw] OR Lithuania[tw])) OR ("developing country"[tw] OR "developing countries"[tw] OR "developing nation"[tw] OR "developing nations"[tw] OR "developing population"[tw] OR "developing populations"[tw] OR "developing world"[tw] OR "less developed country"[tw] OR "less developed countries"[tw] OR "less developed nation"[tw] OR "less developed nations"[tw] OR "less developed world"[tw] OR "lesser developed countries"[tw] OR "lesser developed nations"[tw] OR "under developed country"[tw] OR "under developed countries"[tw] OR "under developed nations"[tw] OR "under developed world"[tw] OR "underdeveloped country"[tw] OR "underdeveloped countries"[tw] OR "underdeveloped nations"[tw] OR "underdeveloped population"[tw] OR "underdeveloped world"[tw] OR "middle income country"[tw] OR "middle income countries"[tw] OR "middle income nation"[tw] OR "middle income nations"[tw] OR "middle income population"[tw] OR "middle income populations"[tw] OR "low income country"[tw] OR "low income countries"[tw] OR "low income nation"[tw] OR "low income nations"[tw] OR "low income population"[tw] OR "low income populations"[tw] OR "lower income country"[tw] OR "lower income countries"[tw] OR "lower income nations"[tw] OR "lower income population"[tw] OR "lower income populations"[tw] OR "underserved countries"[tw] OR "underserved nations"[tw] OR "underserved population"[tw] OR "underserved populations"[tw] OR "under served population"[tw] OR "under served populations"[tw] OR "deprived countries"[tw] OR "deprived population"[tw] OR "deprived populations"[tw] OR "poor country"[tw] OR "poor countries"[tw] OR "poor nation"[tw] OR "poor nations"[tw] OR "poor population"[tw] OR "poor populations"[tw] OR "poor world"[tw] OR "poorer countries"[tw] OR "poorer nations"[tw] OR "poorer population"[tw] OR "poorer populations"[tw] OR "developing economy"[tw] OR "developing economies"[tw] OR "less developed economy"[tw] OR "less developed economies"[tw] OR "underdeveloped economies"[tw] OR "middle income economies"[tw] OR "low income economy"[tw] OR "low income economies"[tw] OR "low gdp"[tw] OR "low gnp"[tw] OR "low gross domestic"[tw] OR "low gross national"[tw] OR "lower gdp"[tw] OR "lower gross domestic"[tw] OR lmic[tw] OR lmics[tw] OR "third world"[tw] OR "lami country"[tw] OR "lami countries"[tw] OR "transitional country"[tw] OR "transitional countries"[tw])) OR "world health organization"[MeSH]) AND **("1975/01/01"[PDat] : "2017/12/31"[PDat]))) AND** ("mental disorders"[MeSH Terms] OR "behavioral symptoms"[MeSH Terms] OR "Affective symptoms"[MeSH] OR "adjustment disorders"[MeSH Terms] OR "anxiety disorders"[MeSH Terms] OR "Stress, Psychological"[MeSH] OR "stress disorders, traumatic, acute"[MeSH] OR "obsessive-compulsive disorder"[MeSH Terms] OR "panic disorder"[MeSH Terms] OR "phobic disorders"[MeSH Terms] OR "mood disorders"[MeSH Terms] OR "somatoform disorders"[MeSH Terms] OR "Depressive Disorder"[TIAB] AND "Major depression"[TIAB] OR

psychopathology[TIAB] OR "Adjustment disorder"[TIAB] OR "Anxiety disorder"[TIAB] OR post-traumatic[TIAB] OR "Panic disorder"[TIAB] OR Phobic[TIAB] OR phobia[TIAB] OR "Mood disorder"[TIAB] OR "Affective disorder"[TIAB] OR depression[TIAB] OR depressive[TIAB] OR "psychological distress"[TIAB] OR "Obsessive-Compulsive Disorder"[TIAB] OR Psychiatric[TIAB] OR ("somatoform"[TIAB] AND "disorders"[TIAB]) OR "somatoform disorders"[TIAB])) **AND** ("Psychiatric Status Rating Scales"[MeSH] OR "Depression/diagnosis"[Majr] OR "Mental Disorders/diagnosis"[Mesh] OR "Mental Disorders/epidemiology"[MAJR] OR "Surveys and Questionnaires"[MeSH] OR "Patient Health Questionnaire"[MeSH] OR "Brief Psychiatric Rating Scale"[MeSH] OR "early diagnosis"[MeSH] OR "psychometrics"[MeSH] OR "mass screening"[MeSH] OR "mass screening"[TIAB] OR "screened"[TIAB] OR screening[TIAB] OR "case finding"[TIAB] OR "questionnaire"[TIAB] OR "questionnaires"[TIAB] OR "scales"[TIAB] OR scale[TIAB] OR interview[TIAB] OR "screener"[TIAB] OR schedule[TIAB])) **AND** ("Primary Health Care"[MeSH] OR "Physicians, Primary Care"[MeSH] OR "Family Practice"[MeSH] OR "General Practice"[MeSH] OR "Private Practice"[MeSH] OR "Ambulatory Care"[MeSH] OR "Ambulatory Care Facilities"[MeSH] OR "Outpatient Clinics, Hospital"[MeSH] OR "General Practitioners"[MeSH] OR "Physicians, Family"[MeSH] OR "Family Practice"[MeSH] OR "primary care"[TIAB] OR "primary-care"[TIAB] OR "primary health clinic"[TIAB] OR "primary health clinics"[TIAB] OR "primary health care"[TIAB] OR "primary healthcare"[TIAB] OR "general health clinic"[TIAB] OR "general health clinics"[TIAB] OR "GP Clinic"[TIAB] OR "GP Clinics"[TIAB] OR "general Practitioner"[TIAB] OR "general Practitioners"[TIAB] OR "outpatient clinic"[TIAB] OR "outpatient clinics"[TIAB] OR "private clinics"[TIAB] OR "private clinic"[TIAB] OR "primary health centers"[TIAB] OR "primary health center"[TIAB] OR "primary health unit"[TIAB] OR "primary health units"[TIAB] OR "primary health facility"[TIAB] OR "primary health facilities"[TIAB] OR "primary health service"[TIAB] OR "primary health services"[TIAB] OR "primary health professionals"[TIAB] OR "primary health centre"[TIAB] OR "primary health centres"[TIAB] OR "primary health clinic"[TIAB])) **NOT** (Diabetes[Title] OR Diabetic[Title] OR Cancer[Title] OR cardiac[Title] OR cardiology[Title] OR cardiologist[Title] OR heart[Title] OR coronary[Title] OR stroke[Title] OR renal[Title] OR asthma[Title] OR Tuberculosis[Title] OR TB[Title] OR malaria[Title] OR AIDS[Title] OR HIV[Title] OR gynecology[Title] OR pulmonary[Title] OR dermatology[Title] OR skin[Title] OR Dementia[Title] OR posttraumatic[Title] OR traumatic[Title] OR immunodeficiency[Title] OR brain[Title] OR Parkinson's[Title] OR hypertension[Title] OR ADHD[Title] OR epilepsy[Title] OR gastro[Title] OR PTSD[Title] OR arthritis[Title] OR psoriasis[Title] OR erectile[Title] OR cardiovascular[Title] OR injury[Title] OR seizure[Title] OR suicide[Title] OR infection[Title] OR cognitive[Title] OR cerebral[Title] OR venous[Title] OR neurology[Title] OR dental[Title] OR sexual[Title] OR Drug[Title] OR drugs[Title] OR alcohol[Title] OR alcoholic[Title] OR addiction[Title] OR Poisoning[Title] OR poisonings[Title] OR alcoholism[Title] OR alcoholics[Title] OR cannabis[Title] OR tobacco[Title] OR smoking[Title] OR opium[Title] OR

benzodiazepine[Title] OR buprenorphine[Title] OR clozapine[Title] OR opiate[Title] OR opioid[Title] OR addict[Title] OR addiction[Title] OR pregnant[Title] OR pregnancy[Title] OR postpartum[Title] OR post-partum[Title] OR partum[Title] OR antenatal[Title] OR perinatal[Title] OR Postnatal[Title] OR Obstetric[Title] OR birth[Title] OR abortion[Title] OR feeding[Title] OR infant[Title] OR vaccination[Title] OR breast[Title] OR Student[Title] OR students[Title] OR children[Title] OR teenage[Title] OR teen[Title] OR teenagers[Title] OR pediatric[Title] OR paediatric[Title] OR Childhood[Title] OR Adolescent[Title] OR Adolescence[Title] OR Adolescents'[Title] OR Adolescents[Title] OR injury[Title] OR veteran[Title] OR veterans[Title] OR girl[Title] OR boy[Title] OR immigrant[Title] OR immigrants[Title] OR migration[Title] OR migrant[Title] OR migrants[Title] OR infant[Title] OR child[Title] OR graduate[Title] OR military[Title] OR refugee[Title] OR caregiver[Title] OR caregivers[Title] OR asylum[Title] OR gastrointestinal[Title] OR prenatal[Title] OR blood[Title] OR fibromyalgia[Title] OR postmenopausal[Title] OR perimenopausal[Title] OR Menopausal[Title])

Appendix B: Key features of studies reviewed

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Fekadu, Abebaw, et al. "Recognition of depression by primary care clinicians in rural Ethiopia." BMC family practice 18.1 (2017): 56	Ethiopia	Screening	Cross-sectional	PHQ-9	Primary care physician
Simon, Gregory, et al. "Somatic symptoms of distress: an international primary care study." Psychosomatic medicine58.5 (1996): 481-488.	Nigeria, China, India, Brazil, Chile , Turkey	Screening	Cross-sectional	GHQ-12	CIDI-PC
Weiller, E., et al. "The relevance of recurrent bried depression in primary care." European archives of psychiatry and clinical neuroscience 244.4 (1994): 182-189.	Nigeria, China, India, Brazil, Chile , Turkey	Screening	Cross-sectional	GHQ-12	CIDI
Salve, Harshal, et al. "Prevalence of psychiatric morbidity at Mobile Health Clinic in an urban community in North India." General hospital psychiatry 34.2 (2012)	India	Screening	Cross-sectional	PHQ-9	MINI
Thom, R. G. M., R. M. Zwi, and S. G. Reinach. "The prevalence ofpsychiatric disorders at a primary care clinic in Soweto, Johannesburg." South African Medical Journal 83.9 (1993): 653-655.	South Africa	Screening	Cross-sectional	SRQ-20	PSE
Zailinawati, Abu-Hassan, Danielle Mazza, and Cheong Lieng Teng. "Prevalence of insomnia and its impact on daily function amongst Malaysian primary care patients." Asia Pacific family medicine 11.1 (2012): 9.	Malaysia	Diagnosis	Cross-sectional	PHQ-9	None
Udedi, Michael. "The prevalence of depression among patients and its detection by primary health care workers at Matawale Health Centre (Zomba)." Malawi Medical Journal26.2 (2014): 34-37.	Malawi	Screening	Cross-sectional	SRQ-20	SCID

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Sidik, Sherina Mohd, Bruce Arroll, and Felicity Goodyear-Smith. "Prevalence of anxiety among women attending a primary care clinic in Malaysia." Br J Gen Pract 61.587 (2011): e326-e332.	Malaysia	Diagnosis	Cross-sectional	GAD-7	None
Qin, Xiaoxia, et al. "Prevalence and rates of recognition of depressive disorders in internal medicine outpatient departments of 23 general hospitals in Shenyang, China." Journal of affective disorders 110.1 (2008): 46-54.	China	Screening	Cross-sectional	GHQ-12	SCID
Qin, Xiaoxia, et al. "Prevalence and rates of recognition of anxiety disorders in internal medicine outpatient departments of 23 general hospitals in Shenyang, China." General hospital psychiatry 32.2 (2010): 192-200.	China	Screening	Cross-sectional	GHQ-12	SCID
Simon, Gregory E., et al. "Prevalence and predictors of depression treatment in an international primary care study." American Journal of Psychiatry 161.9 (2004): 1626-1634.	Russia, Brazil	Screening	Longitudinal	CES-D	CIDI, Anxiety Section Hopkins Symptom Check list (SCL-)
Strauss, P. R., et al. "Identification of depression in a rural general practice." South African Medical Journal 85.8 (1995): 755-759.	South Africa	Screening	Cross-sectional	New Screener	CIDI
Schaefert, Rainer, et al. "Psychological and behavioral variables associated with the somatic symptom severity of general hospital outpatients in China." General hospital psychiatry 35.3 (2013): 297-303.	China	Screening	Cross-sectional	PHQ-15	MINI
Simon, Gregory E., et al. "Understanding cross-national differences in depression prevalence." Psychological medicine32.4 (2002): 585-594.	Nigeria, China, India, Brazil, Chile , Turkey	Screening	Cross-sectional	GHQ-12	CIDI

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Sorsdahl, Katherine, et al. "The time is now: missed opportunities to address patient needs in community clinics in Cape Town, South Africa." Tropical Medicine & International Health 15.10 (2010): 1218-1226.	South Africa	Diagnosis	Cross-sectional	PHQ-4	None
Weobong, Benedict, et al. "Sustained effectiveness and cost-effectiveness of the Healthy Activity Programme, a brief psychological treatment for depression delivered by lay counsellors in primary care: 12-month follow-up of a randomised controlled trial." PLoS medicine 14.9 (2017): e1002385.	India	Diagnosis	RCT	PHQ-9	None
Todd, C., et al. "The onset of common mental disorders in primary care attenders in Harare, Zimbabwe." Psychological medicine 29.1 (1999): 97-104.	Zimbabwe	Diagnosis	Longitudinal	SSQ	None
Penayo, Ulises, Gunnar Kullgren, and Trinidad Caldera. "Mental disorders among primary health care patients in Nicaragua." Acta Psychiatrica Scandinavica 82.1 (1990): 82-85.	Trinidad	Screening	Cross-sectional	SRQ-20	Clinical (HSR-Health stall rating scale)
Reeler, C. H., and Williams AP. "Psychopathology in primary care patients: a four year study in rural and urban settings in Zimbabwe." Central African Journal of Medicine 39.1 (1993): 1-7.	Zimbabwe	Diagnosis	Multiple CS	SRQ-20	None
Ormel, J., et al. "Onset of disability in depressed and non-depressed primary care patients." Psychological medicine29.4 (1999): 847-853.	Nigeria, China, India, Brazil, Chile , Turkey	Screening	Longitudinal	GHQ-12	CIDI
Varma, S. L., and M. Z. Azhar. "Psychiatric symptomatology in a primary health setting in Malaysia." Medical Journal of Malaysia 50 (1995): 11-11.	Malaysia	Diagnosis	Cross-sectional	MHIS	None
Sen, Biswajit. "Psychiatric phenomena in primary health care their extent and nature." Indian Journal of Psychiatry 29.1 (1987): 33.	India	Screening	Cross-sectional	SRQ-20	CIS

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Zaidan, Ziad. "Psychiatric Morbidity in Primary Healthcare Setting in Irbid, Jordan: Prevallence, Recognition and Management Arab Jurnal of Psychiatry 2006	Jordan	Screening	Cross-sectional	GHQ-28	Physician also diagnosed but GHQ considered as gold standard
Shamasundar, C., et al. "Psychiatric morbidity in a general practice in an Indian city." Br Med J (Clin Res Ed) 292.6537 (1986): 1713-1715.	India	Screening	Cross-sectional	GHQ-12	sample of GHQ+ diagnosed with IPSS (Indian scale)
Portugal, Flávia Batista, et al. "Psychiatric morbidity and quality of life of primary care attenders in two cities in Brazil." Jornal Brasileiro de Psiquiatria 63.1 (2014): 23-32.	Brazil	Diagnosis	Cross-sectional	GHQ-12	None
ZamZam, Ruzanna, et al. "Psychiatric morbidity among adult patients in a semi-urban primary care setting in Malaysia." International journal of mental health systems 3.1 (2009): 13.	Malaysia	Diagnosis	Cross-sectional	PHQ	None
Patel, Vikram, et al. "The Healthy Activity Program (HAP), a lay counsellor-delivered brief psychological treatment for severe depression, in primary care in India: a randomised controlled trial." The Lancet 389.10065 (2017): 176-185.	India	Diagnosis	RCT	PHQ-9	None
Patel, Vikram, et al. "Lay health worker led intervention for depressive and anxiety disorders in India: impact on clinical and disability outcomes over 12 months." The British Journal of Psychiatry 199.6 (2011): 459-466.	India	Screening	Cluster RCT	GHQ-12	CIS-R
Patel, Vikram, et al. "Outcome of common mental disorders in Harare, Zimbabwe." The British Journal of Psychiatry 172.1 (1998): 53-57.	Zimbabwe	Diagnosis	Longitudinal	SSQ	None

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Patel, Vikram, et al. "The Shona Symptom Questionnaire: the development of an indigenous measure of common mental disorders in Harare." Acta Psychiatrica Scandinavica 95.6 (1997): 469-475.	Zimbabwe	Screening	Cross-sectional	SSQ	CISR and EMIC criteria
Patel, Vikram, J. Pereira, and A. H. Mann. "Somatic and psychological models of common mental disorder in primary care in India." Psychological medicine 28.1 (1998): 135-143.	India	Screening	Cross-sectional	GHQ-12	CIS-R
Ohaeri, Jude Uzoma, and Olabisi Adebayo Odejide. "Somatization symptoms among patients using primary health care facilities in a rural community in Nigeria." The American journal of psychiatry 151.5 (1994): 728.	Nigeria	Diagnosis	Cross-sectional	GHQ-28	None
Udedi, Michael, et al. "Health service utilization by patients with common mental disorder identified by the Self-reporting Questionnaire in a primary care setting in Zomba, Malawi: a descriptive study." International Journal of Social Psychiatry60.5 (2014): 454-461.	Malawi	Diagnosis	Cross-sectional	SRQ-20	None
Ormel, Johan, et al. "Common mental disorders and disability across cultures: results from the WHO Collaborative Study on Psychological Problems in General Health Care." Jama272.22 (1994): 1741-1748.	Brazil	Screening	Cross-sectional	GHQ-12	CIDI
Patel, Vikram, et al. "Common mental disorders in primary care in Harare, Zimbabwe: associations and risk factors." The British Journal of Psychiatry 171.1 (1997): 60-64.	Zimbabwe	Diagnosis	Case Control	SSQ	None
Villamil-Salcedo, Valerio, Blanca E. Vargas-Terrez, and Adriana Díaz-Anzaldúa. "Collaborative Care model in mental health. Scope and experiences after three years of activity in Mexico City." Primary health care research & development18.3 (2017): 227-234.	Mexico	Screening	Cross-sectional	K-10	Physician

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Srinivasan, Tirupati N., and Thanjavur R. Suresh. "Clinical Relationship Between Nonspecific And Specific Symptoms In Non-Psychotic Morbidity." Indian journal of psychiatry 31.3 (1989): 241.	India	Screening	Cross-sectional	New Screener	Physician
ERBAYDAR, NÜKET PAKSOY, and NESRİN ÇİLİNGİROĞLU. "Chronic pain and depression: a descriptive survey among adult primary health care centre patients." Turkish Journal of Medical Sciences 40.5 (2010): 707-714.	Turkey	Diagnosis	Cross-sectional	BDI	None
Sood, Rita, Manju Mehta, and V. Kumar. "Neuroticism in a family practice population in India." International journal of social psychiatry 42.1 (1996): 58-67.	India	Diagnosis	Cross-sectional	PGI-HQ	None
Ying, Derek Gard-Ching, et al. "Frequency of generalized anxiety disorder in Chinese primary care." Postgraduate medicine 122.4 (2010): 32-38.	China	Diagnosis	Cross-sectional	GAD-7	None
Petersen, I., et al. "The feasibility of adapted group-based interpersonal therapy (IPT) for the treatment of depression by community health workers within the context of task shifting in South Africa." Community mental health journal 48.3 (2012): 336-341.	South Africa	Diagnosis	RCT	SRQ-20	None
Oduwole, O. O., and A. O. Ogunyemi. "Validity of the GHQ-30 in a Nigerian medical outpatient clinic." The Canadian Journal of Psychiatry 34.1 (1989): 20-23.	Nigeria	Screening	Cross-sectional	GHQ-30	Semistructures Psych Interview
Niemi, Maria, et al. "Community-based intervention for depression management at the primary care level in Ha Nam Province, Vietnam: a cluster-randomised controlled trial." Tropical Medicine & International Health 21.5 (2016): 654-661.	Vietnam	Screening	Cluster RCT	PHQ-9	MINI

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Nguyen, Nguyen-Lan D., D. Daniel Hunt, and Craig S. Scott. "Screening for depression in a primary care setting in Vietnam." The Journal of nervous and mental disease 193.2 (2005): 144-147.	Vietnam	Diagnosis	Cross-sectional	VDS	None
Mohd-Sidik, Sherina, et al. "Screening for depression with a brief questionnaire in a primary care setting: validation of the two questions with help question (Malay version)." The International Journal of Psychiatry in Medicine 41.2 (2011): 143-154.	Malaysia	Screening	Cross-sectional	New Screener	CIDI
Maziak, Wasim, et al. "Socio-demographic correlates of psychiatric morbidity among low-income women in Aleppo, Syria." Social science & medicine 54.9 (2002): 1419-1427.	Syria	Diagnosis	Cross-sectional	SRQ-20	None
Mari, Jair de Jesus. "Psychiatric morbidity in three primary medical care clinics in the city of Sao Paulo." Social Psychiatry and Psychiatric Epidemiology 22.3 (1987): 129-138.	Brazil	Screening	Cross-sectional	SRQ-20	CIS
Maniam, T. "Psychiatric morbidity in an urban general practice." The Medical journal of Malaysia 49.3 (1994): 242-246.	Malaysia	Diagnosis	Cross-sectional	GHQ-30	None
Wright, C., M. K. Nepal, and W. D. A. Bruce-Jones. "Mental health patients in primary health care services in Nepal." Asia Pacific Journal of Public Health 3.3 (1989): 224-230.	Nepal	Diagnosis	Cross-sectional	SRQ-20	None
Lima, Ana Flávia Barros da Silva, and Marcelo Pio de Almeida Fleck. "Quality of life, diagnosis, and treatment of patients with major depression: a prospective cohort study in primary care." Revista Brasileira de Psiquiatria 33.3 (2011): 245-251.	Brazil	Screening	Longitudinal	CES-D	CIDI

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Li, Haiyan, et al. "Major depressive disorder and suicide risk among adult outpatients at several general hospitals in a Chinese Han population." PloS one 12.10 (2017): e0186143.	China	Screening	Cross-sectional	PHQ-9	MINI
Lasebikan, V. O., A. Ejidokun, and O. A. Coker. "Prevalence of mental disorders and profile of disablement among primary health care service users in Lagos Island." Epidemiology Research International 2012 (2012).	Nigeria	Screening	Cross-sectional	GHQ-12	ICD-10 PHC Checklist
Khoo, E. M., et al. "Somatisation disorder and its associated factors in multiethnic primary care clinic attenders." International journal of behavioral medicine 19.2 (2012): 165-173.	Malaysia	Diagnosis	Cross-sectional	SSC	None
Kauye, F., R. Jenkins, and A. Rahman. "Training primary health care workers in mental health and its impact on diagnoses of common mental disorders in primary care of a developing country, Malawi: a cluster-randomized controlled trial." Psychological medicine 44.3 (2014): 657-666.	Malawi	Screening	Multiple CS	SRQ-20	SCID
Jenkins, Rachel, et al. "Short structured general mental health in service training programme in Kenya improves patient health and social outcomes but not detection of mental health problems-a pragmatic cluster randomised controlled trial." International journal of mental health systems 7.1 (2013): 25.	Kenya	Diagnosis	Cluster RCT	GHQ-12	None
Jegede, R. O., et al. "Psychiatric morbidity in a Nigerian general out-patient clinic." West African journal of medicine9.3 (1990): 177-186.	Nigeria	Screening	Cross-sectional	CES-D	Clinical diagnosis

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Ihezue, U. H., and N. Kumaraswamy. "Prevalence of depressive symptoms among patients attending a general outpatient clinic." Acta Psychiatrica Scandinavica 73.4 (1986): 395-398.	Nigeria	Diagnosis	Cross-sectional	SDS (Zung)	None
Hussein, A. H., and A. A. Sa'adoon. "Prevalence of anxiety and depressive disorders among primary health care attendees in Al-Nasiriyah, Iraq." Journal of Muslim Mental Health 1.2 (2006): 171-176.	Iraq	Diagnosis	Cross-sectional	PHQ	None
Husain, Nusrat, et al. "Psychological distress among patients attending a general medical outpatient clinic in Pakistan." General hospital psychiatry 26.4 (2004): 277-281.	Pakistan	Diagnosis	Cross-sectional	SRQ-20	None
Havenaar, Juhan M., et al. "Common mental health problems in historically disadvantaged urban and rural communities in South Africa: prevalence and risk factors." Social Psychiatry and Psychiatric Epidemiology 43.3 (2008): 209-215.	South Africa	Diagnosis	Cross-sectional	SRQ-20	None
Gureje, Oye, and B. Obikoya. "Somatization in primary care: pattern and correlates in a clinic in Nigeria." Acta psychiatrica scandinavica 86.3 (1992): 223-227.	Nigeria	Screening	Cross-sectional	GHQ-12	CIDI
Gureje, Oye. "Psychological disorders and symptoms in primary care." Social psychiatry and psychiatric epidemiology37.5 (2002): 220-224.	Nigeria	Screening	Longitudinal	GHQ-12	CIDI
Herrman, Helen, et al. "Longitudinal investigation of depression outcomes in primary care in six countries: the LIDO study. Functional status, health service use and treatment of people with depressive symptoms." Psychological medicine 32.5 (2002): 889-902	Russia, Brazil	Diagnosis	Cross-sectional	CES-D	None

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Grunauer, Michelle, et al. "Tablet-based screening of depressive symptoms in quito, Ecuador: efficiency in primary care." International journal of family medicine 2014 (2014).	Ecuadoe	Diagnosis	Cross-sectional	GHQ-12	CGI- S (overall clin impression - no diagnosis)
GONCALVES, DANIEL A., et al. "Brazilian multicenter study of common mental disorders in primary care: rates and related social and sociodemographic factors." (2014).	Brazil	Diagnosis	Cross-sectional	GHQ-12	None
El-Rufaie, O. E. F. A., A. A. Albar, and B. K. Al-Dabal. "Identifying anxiety and depressive disorders among primary care patients: a pilot study." Acta psychiatrica scandinavica77.3 (1988): 280-282.	Saudi Arabia	Diagnosis	Cross-sectional	HADS	None
Sen, Biswajit, and Paul Williams. "The extent and nature of depressive phenomena in primary health care: a study in Calcutta, India." The British Journal of Psychiatry 151.4 (1987): 486-493.	India	Screening	Cross-sectional	SDQ-9	CIS
Patel, V., and A. Mann. "Etic and emic criteria for non-psychotic mental disorder: a study of the CISR and care provider assessment in Harare." Social psychiatry and psychiatric epidemiology 32.2 (1997): 84-89.	Zimbabwe	Screening	Cross-sectional	SSQ	CIS-R
Mirza, Ilyas, et al. "Eliciting explanatory models of common mental disorders using the Short Explanatory Model Interview (SEMI) Urdu adaptation--a pilot study." JPMA. The Journal of the Pakistan Medical Association 56.10 (2006): 461-463.	Pakistan	Diagnosis	Cross-sectional	GHQ-12	None
Patel, Vikram, et al. "Effectiveness of an intervention led by lay health counsellors for depressive and anxiety disorders in primary care in Goa, India (MANAS): a cluster randomised controlled trial." The Lancet 376.9758 (2010): 2086-2095.	India	Screening	Cluster RCT	GHQ-12	CIS-R

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Harding, Timothy W., et al. "Mental disorders in primary health care: a study of their frequency and diagnosis in four developing countries." Psychological medicine 10.2 (1980): 231-241.	Colombia, India, Sudan< Philippines	Screening	Cross-sectional	SRQ-20	PSE
Hanlon, Charlotte, et al. "Validity of brief screening questionnaires to detect depression in primary care in Ethiopia." Journal of affective disorders 186 (2015): 32-3	Ethiopia	Screening	Cross-sectional	SRQ-20	MINI by Psych Nurse
Gureje, Oye, et al. "Somatization in cross-culural perspective: A World Health Organization study in Primary Care." The American Journal of Psychiatry 154.7 (1997): 989.	Nigeria	Screening	Cross-sectional	GHQ-12	CIDI-PC
Gomes, Viviane Ferrari, Tatiana Longo Borges Miguel, and Adriana Inocenti Miasso. "Common mental disorders: socio-demographic and pharmacotherapy profile." Revista latino-americana de enfermagem 21.6 (2013): 1203-1211.	Brazil	Diagnosis	Cross-sectional	SRQ-20	None
Goldberg, David P., et al. "Screening for anxiety, depression, and anxious depression in primary care: A field study for ICD-11 PHC." Journal of affective disorders 213 (2017): 199-206.	Brazil, China, Mexico, Pakistan	Screening	Cross-sectional	New Screener	CIS-R
Fortes, Sandra, Luiz Augusto Brites Villano, and Claudia S. Lopes. "Nosological profile and prevalence of common mental disorders of patients seen at the Family Health Program (FHP) units in Petropolis, Rio de Janeiro." Revista Brasileira de Psiquiatria 30.1 (2008): 32-37.	Brazil	Screening	Cross-sectional	GHQ-12	CIDI
Diminić-Lisica, Ines, et al. "Comorbid chronic diseases in depressed and non-depressed patients in family practice." Psychiatria Danubina 22.2 (2010): 236-240.	Croatia	Diagnosis	Cross-sectional	BDI	None

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Dhadphale, Manohar, Graham Cooper, and Lesley Cartwright-Taylor. "Prevalence and presentation of depressive illness in a primary health care setting in Kenya." The American journal of psychiatry 146.5 (1989): 659.	Kenya	Screening	Cross-sectional	SRQ-20	Standard Psych Interview
Fleck, Marcelo Pio De Almeida, et al. "Major depression and its correlates in primary care settings in six countries: 9-month follow-up study." The British Journal of Psychiatry 186.1 (2005): 41-47.	Russia, Brazil	Screening	Longitudinal	CES-D	CIDI
Daradkeh, T. K., et al. "Psychiatric morbidity and its sociodemographic correlates among women in Irbid, Jordan." (2006).	Jordan	Screening	Cross-sectional	SRQ-20	PHQ
Chibanda, Dixon, et al. "Effect of a primary care–based psychological intervention on symptoms of common mental disorders in Zimbabwe: a randomized clinical trial." Jama316.24 (2016): 2618-2626.	Zimbabwe	Diagnosis	RCT	SSQ	None (PHQ used as proxy)
Chowdhary, Neerja, et al. "The Healthy Activity Program lay counsellor delivered treatment for severe depression in India: systematic development and randomised evaluation." The British Journal of Psychiatry (2015): bjp-bp.	India	Diagnosis	RCT	PHQ-9	None
Castelo, Milena S., et al. "Screening for bipolar disorder in the primary care: a Brazilian survey." Journal of affective disorders143.1 (2012): 118-124.	Brazil	Diagnosis	Cross-sectional	MDQ	None
Carvalho, André F., et al. "Screening for bipolar depression in family medicine practices: Prevalence and clinical correlates." Journal of affective disorders 162 (2014): 120-127.	Brazil	Diagnosis	Cross-sectional	CES-D	None
Diop, B., et al. "Diagnosis and symptoms of mental disorder in a rural area of Senegal." African journal of medicine and medical sciences 11.3 (1982): 95-103.	Senegal	Diagnosis	Cross-sectional	SRQ-24	None

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Martyns-Yellowe, I. S. "The development of a culture specific screening questionnaire NSRQ-20 for use in psychiatric epidemiology: a preliminary report." Culture, medicine and psychiatry 19.1 (1995): 113-123.	Nigeria	Diagnosis	Cross-sectional	NSRQ-20	None
Haroz, E. E., et al. "Development and cross-cultural testing of the International Depression Symptom Scale (IDSS): a measurement instrument designed to represent global presentations of depression." Global Mental Health 4 (2017).	Myanmar	Screening	Cross-sectional	IDSS	SCID
Gonçalves, Daniel A., et al. "Determinants of common mental disorders detection by general practitioners in the primary health care in Brazil." The International Journal of Psychiatry in Medicine 41.1 (2011): 3-13.	Brazil	Screening	Cross-sectional	GHQ-12	Physician (not as 2nd stage- just comparis0n)
Muhwezi, Wilson Winstons, Hans Ågren, and Seggane Musisi. "Detection of major depression in Ugandan primary health care settings using simple questions from a subjective well-being (SWB) subscale." Social Psychiatry and Psychiatric Epidemiology 42.1 (2007): 61-69.	Uganda	Screening	Cross-sectional	SWB	MINI
Kohrt, Brandon A., et al. "Detection of depression in low resource settings: validation of the Patient Health Questionnaire (PHQ-9) and cultural concepts of distress in Nepal." BMC psychiatry 16.1 (2016): 58.	Nepal	Screening	Cross-sectional	PHQ-9	CIDI
Vöhringer, Paul A., et al. "Detecting mood disorder in resource-limited primary care settings: comparison of a self-administered screening tool to general practitioner assessment." Journal of medical screening 20.3 (2013): 118-124.	Chile	Screening	Cross-sectional	PHQ-9	SCID

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Patel, V., et al. "Detecting common mental disorders in primary care in India: a comparison of five screening questionnaires." Psychological medicine 38.2 (2008): 221-228.	India	Screening	Cross-sectional	GHQ-12	CIS-R
Borges, Tatiana Longo, et al. "Common mental disorders in primary health care units: Associated factors and impact on quality of life." Journal of the American Psychiatric Nurses Association 22.5 (2016): 378-386.	Brazil	Diagnosis	Cross-sectional	SRQ-20	None
Bhatia, M. S., et al. "Psychiatric morbidity in patients attending medical outpatient department." Journal of the Indian Medical Association 86.2 (1988): 36.	India	Screening	Cross-sectional	PGI-HQ	Psychiatrist
Barkow, Katrin, et al. "Risk factors for new depressive episodes in primary health care: an international prospective 12-month follow-up study." Psychological medicine 32.4 (2002): 595-607.	Nigeria, China, India, Brazil, Chile , Turkey	Screening	Longitudinal	GHQ-12	CIDI
Barkow, Katrin, et al. "Identification of somatic and anxiety symptoms which contribute to the detection of depression in primary health care." European Psychiatry 19.5 (2004): 250-257.	Nigeria, China, India, Brazil, Chile , Turkey	Screening	Cross-sectional	GHQ-12	CIDI-PC
Becker, Susan M. "Detection of somatization and depression in primary care in Saudi Arabia." Social psychiatry and psychiatric epidemiology 39.12 (2004): 962-966.	Saudi Arabia	Diagnosis	Cross-sectional	PHQ	None
Alqahtani, Mohammed M., and Peter Salmon. "Prevalence of somatization and minor psychiatric morbidity in primary healthcare in Saudi Arabia: a preliminary study in Asir region." Journal of family & community medicine 15.1 (2008): 27.	Saudi Arabia	Diagnosis	Cross-sectional	GHQ-12	None

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Jegede, R. "Depressive symptomatology in patients attending a hospital-based general out-patient clinic." African journal of medicine and medical sciences 7.4 (1978): 207-210.	Nigeria	Diagnosis	Cross-sectional	SDS (Zung)	None
Anandakumar, D., et al. "Depressive disorder in patients attending the outpatient department of a tertiary care hospital in Colombo." Ceylon Medical Journal 61.3 (2016).	Sri Lanka	Diagnosis	Cross-sectional	CES-D	None
Monroe, Cara E., et al. "Correlates of symptoms of depression and anxiety among clinic outpatients in Western Jamaica." The West Indian medical journal 62.6 (2013): 533.	Jamaica	Diagnosis	Cross-sectional	BDI	None
Obadeji, Adetunji, et al. "Assessment of Depression in a Primary Care Setting in Nigeria using the PHQ-9." Journal of family medicine and primary care 4.1 (2015): 30.	Nigeria	Diagnosis	Cross-sectional	PHQ-9	None
Tripathi, Adarsh, et al. "An exploratory multi-centric depression screening study in primary care setting from India." International Medical Journal 23.2 (2016): 122-124.	India	Diagnosis	Cross-sectional	PHQ-9	None
Mohit, Ahmad, et al. "A Study of Depression Screening in Primary Care Setting of Iran." International Medical Journal23.2 (2016).	Iran	Diagnosis	Cross-sectional	PHQ-9	None
Zhang, Layan, et al. "A Study of Depression Screening in Primary Care Setting of China." International Medical Journal23.2 (2016).	China	Diagnosis	Cross-sectional	PHQ-9	None
Jeyabalan, S., et al. "A risk score to diagnose depression in general practice." Australian family physician 36.11 (2007): 969.	India	Screening	Cross-sectional	New Screener	CIS-R
Hamid, Hamada, et al. "A primary care study of the correlates of depressive symptoms among Jordanian women." Transcultural psychiatry 41.4 (2004): 487-496.	Jordan	Diagnosis	Cross-sectional	BDI	None

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Oladeji, Bibilola D., et al. "A pilot randomized controlled trial of a stepped care intervention package for depression in primary care in Nigeria." BMC psychiatry 15.1 (2015): 96.	Nigeria	Diagnosis	RCT	PHQ-9	None
De Jong, Joop TVM. "A comprehensive public mental health programme in Guinea-Bissau: a useful model for African, Asian and Latin-American countries." Psychological Medicine26.1 (1996): 97-108.	Guinea-Bissau	Screening	Cross-sectional	SRQ-20	PSE, DAF by Psychiatrist
Mari, Jair De Jesus, and Paul Williams. "A comparison of the validity of two psychiatric screening questionnaires (GHQ-12 and SRQ-20) in Brazil, using Relative Operating Characteristic (ROC) analysis." Psychological medicine 15.3 (1985): 651-659.	Brazil	Screening	Cross-sectional	GHQ-12	CIS
Asibong, U. E., et al. "Patient characteristics that may predict the likelihood of the presence of mental health problems in patients attending the general outpatient clinic of a tertiary hospital in South-South Nigeria." Mental health in family medicine 7.3 (2010): 169.	Nigeria	Screening	Cross-sectional	GHQ-12	GP (considered as under report)
Araya, Ricardo, et al. "Treating depression in primary care in low-income women in Santiago, Chile: a randomised controlled trial." The Lancet 361.9362 (2003): 995-1000.	Chile	Screening	RCT	GHQ-12	MINI
Alic, Alma, et al. "Screening for depression patients in family medicine." Medical Archives 68.1 (2014): 37.	Bosnia and Herzegovina1	Diagnosis	Cross-sectional	BDI	None
Al-Khathami, Abdallah D., and Danny O. Ogbeide. "Prevalence of mental illness among Saudi adult primary-care patients in Central Saudi Arabia." Saudi medical journal 23.6 (2002): 721-724.	Saudi Arabia	Diagnosis	Cross-sectional	RAD	None

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Al-Jaddou, H., and A. Malkawi. "Prevalence, recognition and management of mental disorders in primary health care in Northern Jordan." Acta psychiatrica scandinavica 96.1 (1997): 31-35.	Jordan	Screening	Cross-sectional	GHQ-28	GP (considered as under report)
Al Haddad, M. K., et al. "Psychiatric morbidity in primary care." (1999).	Bahrain	Diagnosis	Cross-sectional	GHQ-28	None
Bălănescu, Paul, et al. "Depression Screening in Primary Care and Correlations with Comorbidities in Romania." International Medical Journal 23.2 (2016).	Romania	Diagnosis	Cross-sectional	PHQ-9	None
Maharaj, Rohan G. "Depression and the nature of Trinidadian family practice: a cross-sectional study." BMC family practice 8.1 (2007): 25.	Trinidad	Diagnosis	Cross-sectional	SDS (Zung)	None
Shittu, Rasaki O., et al. "Depression and sleep problems in a Nigerian family practice setting." Int J Dream Res 7 (2014): 113-120	Nigeria	Diagnosis	Cross-sectional	PHQ-9	None
Husain, Nusrat, et al. "Antidepressant and group psychosocial treatment for depression: a rater blind exploratory RCT from a low income country." Behavioural and cognitive psychotherapy42.6 (2014): 693-705.	Pakistan	Screening	RCT	SRQ-20	CIS-R
Sen, Biswajit. "An analysis of the nature of depressive phenomena in primary health care utilising multivariate statistical techniques." Acta Psychiatrica Scandinavica 76.1 (1987): 28-32.	India	Screening	Cross-sectional	SRQ-20	CIS
Abiodun, O. A. "A study of mental morbidity among primary care patients in Nigeria." Comprehensive psychiatry 34.1 (1993): 10-13.	Nigeria	Screening	Cross-sectional	GHQ-12	PSE
de Jong, Joop TVM, Guus AJ de Klein, and Sineke GHMM ten Horn. "A baseline study on mental disorders in Guiné-Bissau." The British Journal of Psychiatry 148.1 (1986): 27-32.	Guinea-Bissau	Screening	Cross-sectional	SRQ-20	PSE, DAF by Psychiatrist

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Nakku, J. E. M., et al. "Validity and diagnostic accuracy of the Luganda version of the 9-Item and 2-Item Patient Health Questionnaire for detecting major depressive disorder in rural Uganda." Global Mental Health 3 (2016).	Uganda	Screening	Cross-sectional	PHQ-9	MINI
Araya, R., R. Wynn, and G. Lewis. "Comparison of two self administered psychiatric questionnaires (GHQ-12 and SRQ-20) in primary care in Chile." Social Psychiatry and Psychiatric Epidemiology 27.4 (1992): 168-173.	Chile	Screening	Cross-sectional	GHQ-12	CIS-R
Ndetei, David M., et al. "The prevalence of mental disorders in adults in different level general medical facilities in Kenya: a cross-sectional study." Annals of General Psychiatry 8.1 (2009): 1.	Kenya	Screening	Cross-sectional	BDI	MMSE
Rezaki MS et al. Results from the Ankara Centre. In:Ustun TB, Sartorius N (eds), Mental illness in general health care: An international study. Chicbester:John Wiley, 1995.	Turkey	Screening	Cross-sectional	GHQ-12	CIDI-PC
V.G. MAVREAS, et al. Results from the Athens Centre. In:Ustun TB, Sartorius N (eds), Mental illness in general health care: An international study. Chicbester:John Wiley, 1995.	Greece	Screening	Cross-sectional	GHQ-12	CIDI-PC
Gureje, et al. Results from the Ibadan Centre. In:Ustun TB, Sartorius N (eds), Mental illness in general health care: An international study. Chicbester:John Wiley, 1995.	Nigeria	Screening	Cross-sectional	GHQ-12	CIDI-PC
Patel, Vikram, et al. "Efficacy and cost-effectiveness of drug and psychological treatments for common mental disorders in general health care in Goa, India: a randomised, controlled trial." The Lancet 361.9351 (2003): 33-39.	India	Screening	RCT	GHQ-5	CIS-R

Title	Country	Screening Instrument used for:	Study Design	Primary screener	Clin Diag OR Diagnostic Instrument.
Villano et al. Results from the Rio de Janerio Centre. In:Ustun TB, Sartorius N (eds), Mental illness in general health care: An international study. Chicbester:John Wiley, 1995.B220	Brazil	Screening	Cross-sectional	GHQ-12	CIDI-PC
Urzua et al. Results from the Santiago de Chile Centre. In:Ustun TB, Sartorius N (eds), Mental illness in general health care: An international study. Chicbester:John Wiley, 1995.B220	Chile	Screening	Cross-sectional	GHQ-12	CIDI-PC
Yan, HQ et al. Results from the Shanghai Centre. In:Ustun TB, Sartorius N (eds), Mental illness in general health care: An international study. Chicbester:John Wiley, 1995.B220	China	Screening	Cross-sectional	GHQ-12	CIDI-PC
Pereira, Jerson, and Vikram Patel. "Which antidepressants are best tolerated in primary care? A pilot randomized trial from Goa." Indian Journal of Psychiatry 41.4 (1999): 358.	India	Screening	RCT	GHQ-5	CIS-R
Channabasavanna SM, Sriram TG, Kumar K. Results from the Bangalore Centre. In:Ustun TB, Sartorius N (eds), Mental illness in general health care: An international study. Chicbester:John Wiley, 1995.	India	Screening	Cross-sectional	GHQ-12	CIDI-PC
Dhadphale, Lesley, Ellison Manohar, and H. Russel. "Frequency of mental disorders among outpatients at a rural district hospital in Kenya." Central African journal of medicine28.4 (1982): 85-89.	Kenya	Screening	Cross-sectional	SRQ-20	Standard Psych Interview
DHADPHALE, MANOHAR, and RUSSELL H. ELLISON. "The frequency of mental disorders in the outpatients of two Nyanza hospitals." JOURNAL OF MEDICINE 29.2 (1983).	Kenya	Screening	Cross-sectional	SRQ-20	Standard Psych Interview

Appendix C: Cluster analyses and bootstrapping method

Analysis of individual level data from cluster randomized trials

Secondary analyses of individual level data from cluster randomized trials pose some analytical challenges. Analyzing clustered data requires models that take into account the correlation between observations in a cluster. Clustered data analyzed with a model that assumes independence of observations will result in an inflated Type-I error rate [1].

Statistical techniques commonly used to analyze clustered data can be broadly divided into design-based methods and model-based methods [3]. Design based methods such as the generalized estimating equations (GEE) and the cluster robust error estimate apply statistical corrections to standard error estimates (and parameter estimates in GEE) to account for clustered observations [4]. Model-based method such as the multilevel models (MLM) account for clustering by directly specifying the between cluster variations and including it in the likelihood. A major limitation of all these methods is that the validity of their estimates is assured only if the number of clusters is reasonably large. Simulation studies demonstrate that GEEs underestimate the standard error when the number of clustering units is below 40 [5, 6]. For multilevel models a commonly cited minimum recommendation is 30 clusters with 30 units within each cluster [7]. Fortunately, several new analytic techniques have emerged that improve the parameter and variance estimates with a smaller number of clusters [2].

Bootstrapping

A bootstrap approach can help to estimate standard errors that appropriately account for intra-cluster correlation in the clustered data setting [8]. Bootstrapping takes repeated random samples with replacement from the original sample. From each of these samples the statistic of interest is calculated, and the distribution of the statistic across newly generated samples is used to infer the distribution of the original sample statistic [9]. It has been demonstrated that if there is a small number of cluster, bootstrapping methods reduce bias and improve inference for variance components as well as fixed

effects [10]. In 2008 Cameron el al. investigated the relative performance of a number of bootstrap methods and found that a variant of bootstrap method, the wild cluster bootstrap method, is most effective in addressing the downward bias in standard errors in situations with few clusters [8]. In their Monte Carlo simulations, the risk of incorrectly rejecting a null hypothesis was close to 5%, even with as few as six clusters, and without significant loss of power after accounting for sample size [8].

Since wild bootstraps is seen as a technique that resamples residuals in a way that captures any heteroscedasticity in the underlying errors it has been largely limited to linear models where residuals are straightforward to obtain. A new variant of wild bootstrap, the score bootstrap developed by Kline and Santos adapts the wild bootstrap parameter estimation "to the class of *extremum estimators"*, which includes maximum likelihood (ML) [11, 12]. The score bootstrap estimates the regression model once and assigns scores for all observations, and then implements wild-cluster bootstrap, perturbing the scores by bootstrap weights at each step [13]. Perturbed scores for each bootstrap replication is used to build a test statistic, and the distribution of test statistics is used for inference [13]. The score bootstrap performs well in non-linear models such as logit and probit even with very few clustering units as demonstrated in Monte Carlo simulations and other studies [11, 14]. We used cluster wild bootstrap implemented using the user-written *'cgmwildboot*' command for linear regression models (available from https://sites.google.com/site/judsoncaskey/data) in Stata 14.2. For logistic regression models we used score bootstraps for regression analyses implemented through the boottest package in Stata 14.2.

References

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Appendix D: Screening Questionnaire (GHQ 12)

We would like to know if you have had any medical complaints and how your health has been in general over the past two weeks

Instructions :

Shaded Questions if answered as No code 1 and If yes code 0 Unshaded questions if answered as Yes code 1 and if No code 0

	Start time: **Have you recently:**	
GHQ 1	been able to concentrate on whatever you're doing?	
GHQ 2	lost much sleep over worry?	
GHQ 3	felt that you are playing a useful part in things?	
GHQ 4	felt capable of making decisions about things?	
GHQ 5	felt constantly under strain?	
GHQ 6	felt you could overcome your difficulties?	
GHQ 7	been able to enjoy your normal day-to-day activities?	
GHQ 8	been able to face up to your problems?	
GHQ 9	been feeling unhappy and depressed?	
GHQ 10	been losing confidence in yourself ?	
GHQ 11	been thinking of yourself as a worthless person?	
GHQ 12	been feeling reasonably happy, all things considered ?	
Total Score		
End time:		