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Abstract

Objectives: To estimate the level of clinical detection and treatment initiation for depression and alcohol use disorder (AUD) in low- and middle-income country (LMIC) settings

Design: Five cross-sectional studies

Setting: Adult outpatient services in 36 primary health care facilities in Sodo District, Ethiopia (9 facilities); Sehore District, India (3); Chitwan District, Nepal (8); Dr Kenneth Kaunda District, South Africa (3); and Kamuli District, Uganda (13).

Participants: Between 760 and 1893 adults were screened in each district. Across 5 districts, between 4.2 and 20.1% screened positive for depression and between 1.2 and 16.4% screened positive for AUD. 96% of screen-positive participants provided details about their clinical consultations that day.

Primary outcomes: Detection of depression, treatment initiation for depression, detection of AUD, treatment initiation for AUD

Results: Among depression screen-positive participants, clinical detection of depression ranged from 0% in India to 11.7% in Nepal. Small proportions of screen-positive participants received treatment (0% in Ethiopia, India and South Africa to 4.2% in Uganda). Among AUD screen-positive participants, clinical detection of AUD ranged from 0% in Ethiopia and India to 7.8% in Nepal. Treatment was 0% in all countries aside Nepal, where it was 2.2%.

Conclusions: The findings of this study suggest large detection and treatment gaps for adult primary care patients, which are likely contributors to the population-level mental health treatment gap in LMIC. Primary care facilities remain unfulfilled intervention points for reducing the population-level burden of disease in LMIC.

Strengths and limitations of the study

- This was a multi-country survey of diverse clinical settings, with large sample sizes, structured interviews, and used of validated screening tools to identify cases.
- The methods used here are demonstrably flexible and are replicable in other low-income settings, particularly for monitoring and evaluation purposes.
- We used highly sensitive and non-specific coding criteria for our primary outcomes (i.e. detection and treatment initiation), and so outcome misclassification is possible.

Keywords: depression, alcohol use disorder, primary care, detection, treatment, low- and middle-income countries

BACKGROUND

Mental, Neurological and Substance use disorders (MNS) contribute significantly to the Global Burden of Disease (GBD) and account for one in every 10 lost years of health globally.[1] In 2010, the absolute Disability-Adjusted Life-Years (DALYs) due to MNS disorders was 258 million DALYs which is 10.4% of the total disease burden. MNS disorders were also the leading cause of years lived with disability globally.[1] In addition to this, MNS disorders act as a significant risk factor for premature death [2] and also accounts for substantial adverse social and economic consequences.[1,3] Depression accounts for 40.5% of DALYs caused by mental and substance use disorders while Alcohol Use Disorders (AUD) account for 9.6%.[4]

In low- and middle-income countries (LMICs) the population-level treatment gap is estimated to be between 76.3% and 91.9% for depression and between 94.9% and 97.2% for AUD.[5] There is an emerging evidence base demonstrating that depression and AUD can be treated by primary care providers in LMIC [6]; the World Health Organization's mhGAP guidelines support integration of mental health services into primary care as a means of narrowing the treatment gap.[7] People affected by depression and AUD often present in primary health care facilities [8,9] though not specifically for these disorders. These disorders co-occur with both acute and chronic medical problems; an untreated mental health disorder worsens the prognosis for the co-morbid condition.[10,11] The population-level treatment gap can be reduced by enhancing the capacity of primary care staff to detect, diagnose and treat these disorders.[12] Clinical detection of depression is estimated to be 47% from a meta-analysis of 41 studies conducted in primary care settings [13] and 42% for AUD from a meta-analysis of 12 studies. [14] However, these meta-analyses were not able to identify studies conducted in LMIC settings, where the majority of people with depression and AUD in the world live, and where a paucity of mental health in the pre-service training of general health care providers as well as competing demands in under-resourced healthcare systems likely compromise the ability of clinicians to detect mental disorders. Little is therefore known regarding the detection levels of depression and AUD in primary care settings in LMICs.

The aims of this report were to describe the methods and baseline findings of a multi-round study to measure the level of clinical detection and treatment initiation for depression and for AUD among adult attendees of primary health care facilities in five low- and middle-income country districts.

METHODS

Context, setting and participants

PRIME is a six-year multi-country research program consortium which, in collaboration with national and district Ministries of Health, has developed Mental Health Care Plans to support delivery of services for mental disorders in the public sector in Ethiopia (Sodo District), India (Sehore District, Madhya Pradesh State), Nepal (Chitwan District), South Africa (Dr Kenneth Kaunda District, North West Province), and Uganda (Kamuli District).[15,16] Two key research questions of the PRIME evaluation – detailed in a separate report [17] - were to assess the change in detection and change in initiation of treatment among adults presenting in primary health facilities, as a consequence of implementing the district mental healthcare plans. These questions were investigated by conducting cross-sectional facility-based patient surveys before and after the mental healthcare plan implementation. The two populations of interest for the study were the adult patients who screened positive 1) for depression and 2) for AUD.

Details about the study settings and clinics are in Table 1.

Table 1. Geographic and health facility characteristics of PRIME implementation areas, 2013-2014.

Country	Ethiopia	India	Nepal	South Africa	Uganda
Implementation area	Sodo District	Sehore and Shyampur sub-districts of Sehore District, Madhya Pradesh	Chitwan District*	Orkney catchment area of Matlosana sub-district of Dr Kenneth Kaunda District, Northwest Province	Kamuli District
Population	161,952	212,192	108,368	90,000	518,200
Area, km^2	867	1,039	342	31	4,278
# and type of health facility	8 public and 1 private health clinics	3 Community Health Centres	9 Health Posts and 1 Primary Health Care Centre**	1 Community Health Centre (CHC) and 3 Primary Health Care (PHC) clinics***	12 Health Centres (Level III and IV) 1 primary care department in the district hospital
Primary provider types	Health Officer	Medical Officer	Medical officers, Health Assistants, Auxiliary Health Workers	Nurse, PHC doctor	Medical Officer
Primary care services provided in the facilities	Primary care, Emergency; delivery care, mother and baby care, family planning and immunization	Primary, acute, Reproductive and child health	Outpatient; immunization; family planning; safe motherhood and new born care; anti- and post-natal care; delivery of babies.	Chronic care	Outpatient; emergency; immunization; maternal and child health; family planning, health education and Primary care in general including mental health

* Implementation area consists of 10 of the 38 Village Development Committees/Municipalities of Chitwan District
** 222 study participants from 2 of the 10 health facilities are excluded from analysis
*** 1 of the 3 PHC clinics was an implementation pilot site and was excluded from study data collection.

The choice of included clinics was determined by the availability of staff who were planned to have authority to detect/ diagnose, prescribe and/or refer for depression and AUD, as per the mental healthcare plan. Thus, clinics such as health posts (Level I and II) in Uganda were excluded. In South Africa, one of the PHC clinics was excluded from the study due to mental health care plan training prior to the baselines survey round. In South Africa, nurses in the primary care clinics could refer suspected cases to a physician (for both disorders) and provide brief counselling (for non-dependent alcohol use disorder) and so these clinics were included. Only patients attending for chronic care services (e.g. HIV, tuberculosis, diabetes, hypertension, etc) were eligible for this study, reflecting eligibility for treatment in accordance with the South African mental health care plan. In Nepal, clinicians working in two clinics received mental health training prior to the baseline survey round; these clinics are included for clinical-level descriptive reporting but participants from these clinics are excluded for analysis here. All clinics were government run, aside one in Ethiopia.

Sample size

For each country and disorder the sample size was set to have 80% power and a two-sided alpha of 0.05 for the two primary aims: 1) to detect a change in detection and 2) to detect a change in initiation of evidence-based treatment for depression and for AUD between the baseline and follow-up round. The baseline round was set prior to implementation of the mental health care plan and follow-up round was scheduled to start at least 18 months later, which assumed the plan had been fully embedded for several months. Country teams in Nepal and Uganda planned to conduct an interim survey round immediately after embedding, to assess the short-term effect of implementation on detection and treatment. Findings from interim and follow-up surveys will be detailed in future reports. Depending on country, the baseline level of detection was assumed to be 0-5%, and at follow-up targeted to reach 20-30%. The required sample size was adjusted to account for the possibility of false positives generated by screening tools, using site-specific figures for the positive predictive value. Within each country, whichever disorder required the higher sample size dictated the sample size. This sample size was increased by a factor of 2-3x to facilitate equity analyses, e.g. comparisons of outcomes by sex or by socioeconomic status. The target sample sizes for each country in each study round were 1000 in Ethiopia, 760 in India, 1400 in Nepal, 1200 in South Africa and 1800 in Uganda. Within each country the total target sample size was then allocated by clinic in proportion to measures of clinic outpatient volume, such that busier clinics were allocated a larger recruitment target than less busy clinics.

Details of the sampling and data collection procedures in Table 2.

Table 2. Sample selection and data collection procedures for facility surveys, 2013-2014.

Country site	Ethiopia	India	Nepal	South Africa	Uganda
Survey dates	June-July 2013	Aug-Oct 2013	Sept 2013-Feb 2014	Feb-April 2014	July-Nov 2013
Study language	Amharic	Hindi	Nepali	English, seTswana	English, Luganda
Recruitment / sampling method	Consecutive sampling of adults at registration	Systematic sampling of every 5th adult at registration	Random selection of 1 adult from those who arrived since last interview started	Opportunistic sampling of adult volunteers in chronic care clinic waiting area	Consecutive sampling of adults at registration
Consent documented with	Signature or thumbprint	Signature or thumbprint	Signature or verbal affirmation	Signature or signed 'X' with independent witness signature	Signature or verbal affirmation.
# approached	1014	760	1553	9780	1922
# eligible	1014	760	1553	1322	1922
# consented (% consent rate)	1014 (100)	760 (100)	1474 (94.9)	1322 (100)	1893 (98.5)
Questionnaire data collection mode	Paper-and-pencil, double data entry with EpiInfo 3.1	Android mobile device	Android mobile device	Android mobile device	Android mobile device
Depression screen positive is PHQ-9 >=	10	10	10	10	10
AUD screen positive is AUDIT>=	8	8	9	16	8
Clinical consultation form	Purpose-built form	Extracted from clinical records maintained at the facility	Purpose-built form	Extracted from clinic records	Consultation notes extracted from patient's notebook as part of the exit questionnaire

Sampling and recruitment

Inclusion criteria for participation were as follows: above age of majority in the country (i.e. 16 years or 18 years); fluency in a local study language; time and ability to complete the full interview; and willingness to provide informed consent. Exclusion criteria were as follows: incapacity to provide informed consent (e.g. presence of severe intellectual disability, currently experiencing an acute medical issue). The research team for each country trained its interviewers to assess eligibility.

Logistic and cultural constraints dictated the sampling procedure within each country, meaning that random selection for a representative sample was not always possible. In Ethiopia and Uganda, to minimize disruption, consecutive sampling of all eligible patients upon registration minimized the amount of time research staff spent in the clinics. In South Africa, research staff provided a group orientation to the study to all patients in the waiting room, and then asked interested patients to self-nominate for recruitment. In India, research assistants approached every fifth patient registering at reception and assessed them for eligibility. Among eligible patients approached, over 94% consented to participate in all countries.

Data collection procedures

The facility interview was comprised of a screening questionnaire, an exit questionnaire and/or a clinical consultation form. Interviewers administered the two-part screening questionnaire, with part 1 used to identify probable cases. For probable cases and optionally for probable non-cases, interviewers completed part 2 of the screening questionnaire. For these same participants, the interviewer completed the exit questionnaire with the participant and/or requested a consultation form from that participant's clinician. In Uganda patients maintained their own medical files in a notebook which is handed over to clinicians during consultations, and so the clinical consultation form data were synonymous with exit questionnaire data. The data collection flow chart for each country is shown as Supplemental Figures 1a-1e.

The sections within the screening interview questionnaire are described in Table 3.

Table 3. Screening interview sections for PRIME facility detection study, 2013-2014.

Section	# items	Source
		Part 1
Basic demographic characteristics	5	Purpose-built for PRIME
Alcohol use disorder screening	10	Alcohol Use Disorder Identification Test (AUDIT) [18]
Alcohol: recent treatment history and intentions	23	Purpose-built for PRIME
Alcohol: internalized stigma	20	Adapted from the Composite International Diagnostic Interview Services module [19] and the Barriers to Access to Care Evaluation Scale [20]
Depression screening	9	Patient's Health Questionnaire (PHQ-9) [21]
Depression symptoms in the past 12 months	1	Purpose-built for PRIME
Depression: recent treatment history and intentions	23	Purpose-built for PRIME
Depression: internalized stigma	20	Adapted from the Composite International Diagnostic Interview Services module [19] and the Barriers to Access to Care Evaluation Scale [20]
Suicidality	7	Adapted from the Composite International Diagnostic Interview (CIDI) suicidality module [19]
		Part 2
Disability	12	World Health Organization Disability Assessment Schedule (WHODAS) 2.0 [22]
Detailed sociodemographic characteristics	18	Purpose-built for PRIME

Data collection measures

Part 1 of the screening questionnaire consisted of sections on sociodemographic characteristics, screening for depression, depression symptoms in the past 12 months (aside in Ethiopia), and screening for AUD. A probable case of depression was a participant who was PHQ-9 positive or had recent depression symptoms, and a probable case of AUD was a participant who was AUDIT positive. Probable cases completed disorder-specific sections about recent (12 month) history of treatment seeking for their most recent episode of symptoms, and about internalized stigma. Part 2 consisted sections about sociodemographic characteristics and disability status. The exit questionnaire and clinical consultation form were thematically similar, and consisted of a mix of open- and closed-ended questions about that day's clinical consultation, and specifically about diagnoses, advice, referrals and prescriptions. Each country developed their own exit questionnaire and clinical consultation form to enable data collection by interviewers with the participant and by the clinician directly, respectively, in recognition of the context specific nature of patient-clinician interactions and the local idioms of distress. In addition to the questionnaire items described here, which were largely consistent across PRIME country sites, research teams included country-specific questions and sections, which will be described in future reports. See PRIME website (www.prime.uct.ac.za) for the purpose-built sections of the PRIME questionnaires.

Mental health measures

The denominators for the primary outcome measures consist of those participants who screen positive for depression or for AUD, using the PHQ-9 and AUDIT, respectively. The PHQ-9 is a widely used screening tool that has been validated for use in all five countries.[23–27]. In this study, Cronbach's alpha for the PHQ-9 ranged between 0.74 in India and 0.80 in Nepal. A score of 10 or more on the PHQ-9 screen was considered a positive screen. The AUDIT tool has been validated in India, Nepal and South Africa [28–30] and in countries neighbouring Uganda.[31,32] In this study, Cronbach's alpha for AUDIT ranged from 0.66 in Uganda to 0.88 in Nepal. An AUDIT score of ≥20 was considered to indicate alcohol dependence, while scores of 16-19 and 8-15 were classified as harmful and hazardous drinking, respectively. A score of 8 or more in Ethiopia, India and Uganda, 9 or more in Nepal and 16 or more in South Africa, was considered a positive screen. The higher cut off

score in South Africa was set to account for services being targeted to those with harmful and dependent alcohol use.

Outcome assessment

The numerators for the primary outcome measures were derived from participant exit questionnaire data when available (India, Nepal, South Africa, Uganda), and alternatively from the clinician consultation form data (Ethiopia). Given the sparse level of detail patients were expected to recall and/or clinicians were expected to record, cross-country variation in the terminology around detection and treatment, as well as expected low levels of detection and treatment at baseline, highly sensitive and non-specific coding criteria – detailed in Table 4 - were adopted and used for the outcomes' numerators. These criteria were informed by WHO's mhGAP guidelines.[7]

Table 4: Criteria used to assess detection and treatment of depression and alcohol use disorders in the PRIME facility detection study, 2013-2014.

Detection of depression	**Treatment of depression**
Included: • Diagnosis of "depression" • Diagnosis of "stress", "distress", "behavioural problem", "mental disorder", or "psychiatric problem" • Diagnosis assumed if unambiguous depression treatment given *Excluded:* • Diagnosis of "anxiety", "insomnia", "tension headache", "stress headache", "schizophrenia", "epilepsy", "bipolar", "central nervous system problem"	*Included:* • Prescription of SSRI (e.g. fluoxetine) • Referral to a mental health specialist • Advice on stress reduction or management - only with depression diagnosis • Prescription of tricyclic antidepressant (e.g. amitriptyline) only with depression diagnosis • Referral to counselling or talking treatment – only with depression diagnosis *Excluded:* • Diazepam prescription • Non-specific referrals (e.g. "hospital")
Detection of alcohol use disorder	**Treatment of alcohol use disorder**
Included: • Diagnosis of "AUD", "alcohol problem" or "drinking problem" • Diagnosis assumed if unambiguous AUD treatment given *Excluded:* • Drug abuse or other substance use problems	*Included:* • Referral to a mental health or addictions specialist • Prescription of diazepam or Vitamin B – only with AUD diagnosis • Counselling or talking treatment – only with AUD diagnosis *Excluded:* • Non-specific referrals (e.g. "hospital")

Abbreviations: AUD, alcohol use disorder; SSRI, selective serotonin reuptake inhibitor

Outcome assessors (TR, SS and SDR) independently double-coded the outcomes for detection (Yes/No) and treatment (Yes/No) with 99% initial scoring agreement. Disagreements were resolved through further discussion.

Analysis

First, the sociodemographic characteristics and mental health screening scores of participants were summarised by presenting the median and interquartile range for continuous measures and counts and percentages for categorical measures. Second, for depression screen-positive participants, the numbers and proportions who had outcome data, were detected for depression, and who had initiation of minimally adequate evidence-based treatment were reported. The same figures were reported for AUD screen-positive participants and AUD. Finally, depression and AUD detection figures are reported for participants who were depression and AUD screen-negative and who did not have depression symptoms over the past 12 months. These latter figures are indicators – though not definitive evidence - for either mis- or over-diagnosis. All analyses were conducted in Stata 14.1 (StataCorp, College Station, TX, USA), and stratified by country. (See supplemental file 'stata do file code.docx')

Ethics

All participants gave written or verbal informed consent prior to being interviewed (Table 2). The informed consent form made clear there would be no negative effects for non-participation. In South Africa, participants were provided a 30 Rand (~2.80 USD) supermarket voucher as a token of appreciation. In all countries, participants who endorsed questionnaire items about suicidality were referred to a provider in the clinic.

The institutional review boards of the World Health Organization (Geneva, Switzerland), University of Cape Town (South Africa), College of Health Sciences of Addis Ababa University (Ethiopia), Indian Council of Medical Research (New Delhi, India), Sangath (Goa, India), Nepal Health Research Council (Kathmandu, Nepal), Makerere University (Kampala, Uganda), and the National Council of Science and Technology (Kampala, Uganda) reviewed and approved the protocols and informed consent procedures for this study.

Patient involvement

The PRIME interventions and evaluations were informed through Theory of Change workshops held in each country [33]. These workshops included national- and district-level representatives, health service providers, and, in some countries, mental health service users.

RESULTS

The demographic and mental health screening characteristics of participants are detailed in Table 5.

Table 5: Demographic and mental health characteristics for facility detection survey participants, 2013-14

Country site [sample size]	**Ethiopia** [n=1014] Median (IQR) or n (%)	**India** [n=760] Median (IQR) or n (%)	**Nepal*** [n=1252] Median (IQR) or n (%)	**South Africa** [n=1322] Median (IQR) or n (%)	**Uganda** [n=1893] Median (IQR) or n (%)
Age, years	30 (23-45)	37 (27-51)	36 (27-50)	46 (37-56)	28 (22-37)
Female	551 (54.3)	386 (50.8)	813 (64.9)	992 (75.0)	1500 (79.2)
Education					
Less than primary	692 (68.3)	381 (50.1)	444 (35.5)	308 (23.3)	174 (9.2)
Primary	230 (22.7)	186 (24.5)	253 (20.2)	829 (62.7)	1113 (58.8)
Secondary or more	91 (9.0)	193 (25.4)	555 (44.3)	185 (14.0)	606 (32.0)
PHQ-9 score	4 (1-7)	6 (4-9)	4 (2-7)	3 (1-6)	2 (1-4)
PHQ-9 positive**	117 (11.5)	153 (20.1)	186 (14.9)	107 (8.1)	80 (4.2)
Depression symptoms in past 12 months		110 (14.5)	174 (13.9)	157 (11.9)	159 (8.4)
AUDIT score	2 (0-5)	0 (0-0)	0 (0-1)	0 (0-4)	0 (0-0)
Alcohol abstinent	275 (27.1)	659 (86.7)	849 (67.8)	724 (54.8)	1475 (77.9)
AUDIT positive**	166 (16.4)	35 (4.6)	92 (7.3)	43 (3.2)	23 (1.2)
Dependent alcohol use	37 (3.6)	3 (0.4)	32 (2.6)	21 (1.6)	2 (0.1)

* Excluding 222 patients from 2 clinics

** Using country-specific cut off scores (Table 2)

Ages ranged from a median of 28 years in Uganda to 46 years in South Africa. The majority of participants in all countries were female, from 51% in India to 79% in Uganda. The proportion of participants who screened positive for depression ranged between 20% in India to 4.2% in Uganda, for depression symptoms in the past 12 months ranged between 8% in Uganda to 14% in India, and for AUDIT between 1% in Uganda and 16% in Ethiopia. These probable cases were asked to complete the Exit interview and/or their clinicians asked to complete a consultation form. Outcome data were available for 96% of these participants (from clinical consultation forms or exit questionnaires), though exit questionnaire completion was lower for depression screen-positive participants in Uganda (48/80, 60%), and AUD screen-positive participants in South Africa (38/43, 90%) and Uganda (18/23, 78%), respectively. Non-completion was primarily due to participants having to leave the clinic immediately or the interviewer being unable to locate the participant after their consultation.

The proportions of screen-positive participants who were detected and who started treatment are presented Table 6.

Table 6. Detection and treatment among screen-positive adults in PRIME implementation clinics, 2013-2014.

Country site	Ethiopia	India	Nepal	South Africa	Uganda
Depression					
Outcome data collected / screen positive	117/117	153/153	179/186	103/107	48/80
Detected, n (%, 95% CI)	12/117 (10.3, 5.9-17.2)	0/153 (0.0)	21/179 (11.7, 7.8-17.3)	6/103 (5.8, 2.6-12.4)	2/48 (4.2, 1.0-15.4)
Treatment initiated, n (%, 95% CI)	0/117 (0.0)	0/153 (0.0)	1/179 (0.5, 0.0-3.9)	0/103 (0.0)	2/48 (4.2, 1.0-15.4)
Alcohol Use Disorder (AUD)					
Outcome data collected / screen positive	166/166	35/35	90/92	38/43	18/23
Detected, n (%, 95% CI)	0/166 (0.0)	0/35 (0.0)	7/90 (7.8, 3.7-15.6)	0/38 (0.0)	1/18 (5.6, 0.7-32.2)
Treatment initiated, n (%, 95% CI)	0/116 (0.0)	0/35 (0.0)	2/90 (2.2, 0.5-8.6)	0/38 (0.0)	0/18 (0.0)

Among depression screen-positive participants, detection of depression ranged from 0% in India to 11.7% in Nepal. Small proportions of screen-positive participants received treatment (0% in Ethiopia, India and South Africa to 4.2% in Uganda). Among AUD screen-positive participants, detection of AUD ranged from 0% in Ethiopia and India to 7.8% in Nepal. Treatment was 0% in all countries aside Nepal, where it was 2.2%.

For probable non-cases, detection of depression ranged from 0/557 (0.0%) in India to 3/74 (4.0%) in Nepal, and detection of AUD ranged from 0/557 (0.0%) in India to 2/74 (2.7%) in Nepal. Treatment was almost entirely absent. (See Table 7)

Table 7. Detection and treatment among probable non-cases in PRIME implementation clinics, 2013-2014.

Country site (# depression and AUD screen-negative and no depression symptoms in 12 months)	**Ethiopia** (n=752)	**India** (n=557)	**Nepal** (n=74)	**South Africa** (n=113)	**Uganda** (n=332)
Depression					
Detected, n (%)	16/752 (2.1)	0/557 (0.0)	3/74 (4.1)	4/113 (3.5)	2/332 (0.6)
Treatment initiated, n (%)	0/752 (0.0)	0/557 (0.0)	0/74 (0.0)	3/113 (2.6)	1/332 (0.3)
Alcohol use disorder					
Detected, n (%)	0/752 (0.0)	0/557 (0.0)	2/74 (2.7)	2/113 (1.8)	1/332 (0.3)
Treatment initiated, n (%)	0/752 (0.0)	0/557 (0.0)	0/74 (0.0)	0/113 (0.0)	1/332 (0.3)

DISCUSSION

This study establishes the magnitude of the detection gap for adults attending primary care in diverse LMIC settings. There were low levels of detection of depression from screen-positive participants in Ethiopia, Nepal, South Africa and Uganda and no detection in India. There was no detection of AUD among screen-positive participants outside Nepal and Uganda. Conversely, there was almost no evidence of mis- or over-diagnosis of depression or AUD among participants who screened negative.

The detection figures observed here are substantially lower than the average figures found by Mitchell et al. for detection of depression (47%) and for AUD (42%) by primary care providers in high income countries.[13,14] As studies of clinical detection in LMIC settings were not available for these meta-analyses, this study fills a key gap in our understanding of the detection gap globally. These findings provide insight into how the population-level treatment gap in LMIC is at least partially attributable to a facility-level detection gap.

While detection levels were low, the facility-level treatment gap approached 100% in most settings. The treatment outcome definitions used here were broad and included provision of advice or referrals to specialist care, both of which clinicians were able to dispense prior to implementation of the PRIME mental health care plans. The first barrier for providing treatment at the health facility is detection, and, as reported above, across all settings detection levels were extremely low. The findings of this study indicate consistent missed opportunities for providing evidence-based care across these diverse LMIC settings. Improving clinical detection and treatment of depression and AUD by primary care providers remains an area where intervention development is required; the PRIME consortium will evaluate its own interventions – the plans for which have described in detail [34–38] - in follow-ups to this report.

The PRIME Facility Detection study uses widely-validated screening tools to identify probable cases. While diagnostic interviews are the gold standard for identifying cases, screening tools are usable by trained interviewers rather than clinicians, and so the methods used here are more easily replicable for monitoring and evaluation activities in other LMIC settings. Our outcome data were collected directly from the participants and clinicians rather than from a health management information system, which is also a replicable monitoring method for LMIC settings.

There are several limitations to our study. First, screening tools (PHQ-9 and AUDIT) were used to identify probable cases of depression and AUD; an unknown number of screen-positive cases are actually false positive cases. As such it is not appropriate to interpret the proportions of participants who screen positive as prevalence figures. Further, a 100% detection figure is not a desirable goal, as it indicates diagnosis among false positive cases. Screening misclassification is likely to be similar in the follow-up round, and so the denominators for detection and treatment are equally biased across rounds and allows a valid comparison across time to be made. Second, non-random sampling was used to select some patients for interviews. As we plan to use the same sampling plan within each country, again, the selection bias is likely similar between rounds and valid comparisons of change are possible. In contrast the loss to follow-up for screen-positive participants in Nepal, South Africa and Uganda, could result in biased findings, as the characteristics of lost participants is unknown.

A third limitation concerns the outcome definitions for detection and treatment. Given the limitations of using patient- and clinician-reported data, with issues around recall and specificity, we opted to use extremely sensitive yet non-specific thresholds of evidence for coding detection or treatment as having occurred. The detection and treatment figures reported here should therefore be regarded as the upper bound of possibility: some of those coded as having been detected with depression may have other mental health disorders, and some of those coded as having treatment may not have what is considered to be minimally-adequate evidence-based care. Again, the bias due to these misclassifications will be equal in the follow up round. Use of cross-country coding criteria facilitates comparisons across diverse settings, and in future reports each country can use these criteria and/or develop their own more locally-appropriate and specific criteria. This process has been completed in Sodo District, Ethiopia, where detection outcomes have been reported separately for using specific criteria for depression and non-specific criteria for common mental disorder.[39]

We plan to repeat this survey in each of the implementation sites. By comparing the baseline versus follow-up figures within each country, we will be able to determine whether the level of detection and level of initiation of evidence-based treatment for depression and for AUD has increased as a result of implementing mental health care plans. We will also be able to assess whether the improved detection and improved treatment provision is equitable by age, sex and other socio-economic factors. With the help of Theory of Change framework and process evaluation data collected over the implementation phase,[17] we will try to explain

the reasons for improvement/non-improvement of detection and initiation of treatment for depression and for AUD, along identifying with the factors relating to detection.

Further research can identify the patient-, clinician- and system-level characteristics associated with detection, as a means of further refining interventions. Some of these characteristics are already potential targets for intervention, and have been identified in previous studies: On the patient level, those who have higher level of perceived need[40] and lower levels of internalized stigma[13,14] are more likely to receive a diagnosis. On the clinician level, detection improves with longer consultation time,[41,42] adequate training, a stronger therapeutic alliance,[13] and with contractual incentives.[43] And on the health-system level, detection is likely to improve with the availability of medications and health providers at PHC level who have the authority to prescribe psychotropic medication, as well as referral pathways to counsellors. Also important are buy-in and support from leadership who give priority to mental health[1], governance and supervisory structures to develop and execute standardized protocols,[44] and a functional health management information system[45] to monitor and feed back on clinical activity. A combination of these patient-, clinician- and system- level characteristics may explain some of the substantially lower detection figures for depression and AUD found here from our LMIC settings compared to those found in meta-analyses by Mitchell et al. in HIC settings.

Conclusion

The findings of this study suggest large detection and treatment gaps for adult primary care patients, which are likely contributors to the population-level mental health treatment gap in LMIC. Primary care centres remain unfulfilled intervention points for reducing the population-level burden of disease in LMIC.

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Competing interests

None declared

Authors contributions

Conceptualization SDR, MJ, IP, FK, CL, AF, RS

Design SDR, TR, GM, NPL, AB, IP, FK, CL, AF, RS

Data acquisition TR, GM, VM, SS, NPL, OS, JS

Data analysis SDR

Data interpretation SDR, CL, RS

Drafting SDR, TR, CL, RS

Critical revision GM, VM, SS, NPL, OS, JS, MJ, AB, IP, FK, CL, AF, RS

Final approval SDR, TR, GM, VM, SS, NPL, OS, JS, MJ, AB, IP, FK, CL, AF, RS

Accountability SDR, TR, GM, VM, SS, NPL, OS, JS, MJ, AB, IP, FK, CL, AF, RS

Data sharing statement: Statistical code (Stata) is available as supplementary material. While we cannot make the dataset publicly available, we will consider all request to provide a minimal dataset to interested researchers via the PRIME consortium Expression of interest form here: **http://www.prime.uct.ac.za/contact-us**.

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participants.

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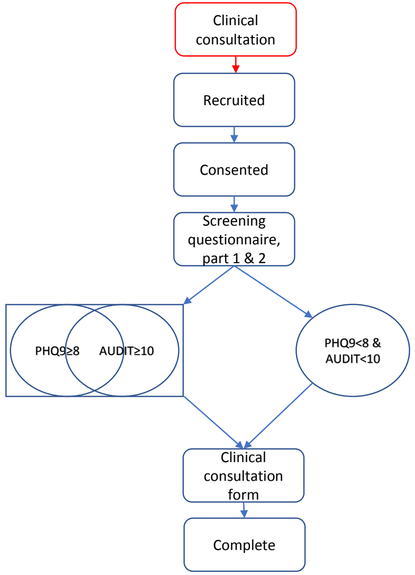
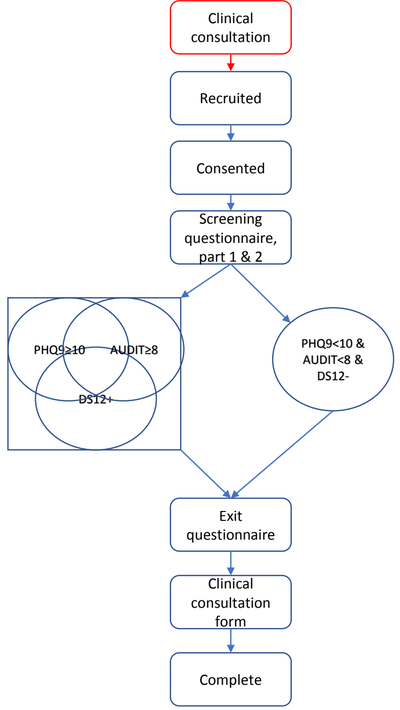
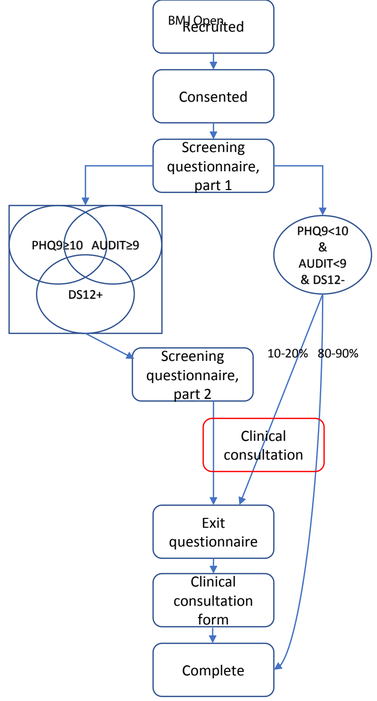
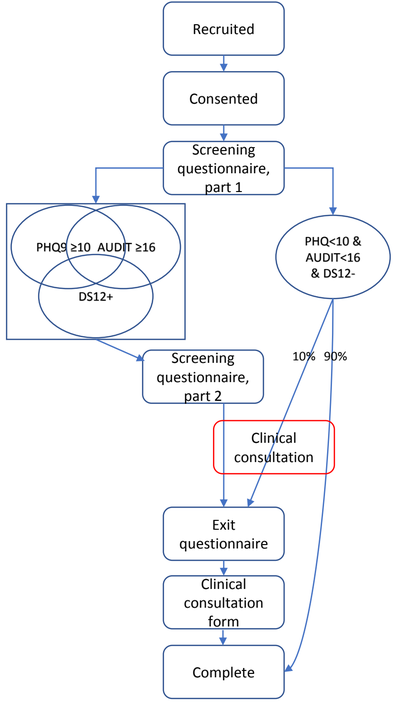
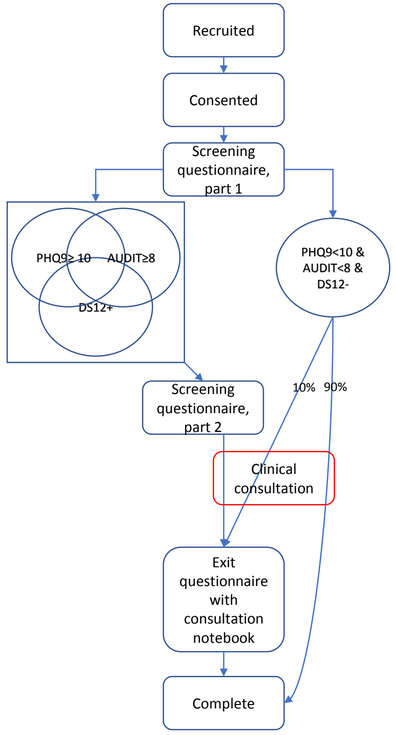

Clinical consultation
Recruited
Consented
Screening questionnaire, part 1 & 2
PHQ9≥8
AUDIT≥10
PHQ9<8 & AUDIT<10
Clinical consultation form
Complete


Clinical consultation
Recruited
Consented
Screening questionnaire, part 1 & 2
PHQ9≥10
AUDIT≥8
DS12+
PHQ9<10 & AUDIT<8 & DS12-
Exit questionnaire
Clinical consultation form
Complete


Recruited
Consented
Screening questionnaire, part 1
PHQ9≥10
AUDIT≥9
DS12+
PHQ9<10 & AUDIT<9 & DS12-
Screening questionnaire, part 2
10-20%
80-90%
Clinical consultation
Exit questionnaire
Clinical consultation form
Complete


Recruited
Consented
Screening questionnaire, part 1
PHQ9 ≥10
AUDIT ≥16
DS12+
PHQ<10 & AUDIT<16 & DS12-
Screening questionnaire, part 2
10%
90%
Clinical consultation
Exit questionnaire
Clinical consultation form
Complete


Recruited
Consented
Screening questionnaire, part 1
PHQ9≥ 10
AUDIT≥8
DS12+
PHQ9<10 & AUDIT<8 & DS12-
Screening questionnaire, part 2
10%
90%
Clinical consultation
Exit questionnaire with consultation notebook
Complete

```
*****************************
*** Baseline FDS & Methods ***
*****************************
use "C:\PRIME\FDS\UCT\FDS.dta" if round==1, clear
	keep country cname idate _screenexit _dxtx ///
		age sex educ_3c emp ///
		phq? totalphq phqpos dephis aud? aud10 totalaud audpos aud_5c ///
		detect_* treat_* medname*

	drop if mi(sex)
	table country, c(N idate min idate max idate)

	bysort country: alpha phq?, item
	mvencode aud1-aud10, mv(.=0) over
	bysort country: alpha aud1-aud10, item

***************
*** TABLE 1 ***
***************
	* Number of FDS clinics per country
	bysort country: distinct cname
	* Drop Nepal clinics which got training before baseline
	drop if cname==36 | cname==37

***************
*** TABLE 2 ***
***************
	* Age
	tabstat age, by(country) col(stat) stat(n p50 p25 p75) f(%9.3g)
	* % Female
	tab sex country, col
	* Education
	tab educ_3c country, col
	* Employment - propose using unemployed/non-income/income
	* tab emp country, col nolabel
```

```
****************
*** TABLE 6 ***
****************
        * DEPRESSION
        * Median PHQ9 score
        tabstat totalphq, by(country) col(stat) stat(n p50 p25 p75) f(%9.3g)
        * PHQ9+ screening cut off score
        table country phqpos, c(min totalphq max totalphq)
        * PHQ9+ proportion
        table country, c(n phqpos sum phqpos mean phqpos) f(%9.3g)
        tab country dephis, row
        * PHQ9+ proportion and 95% CI
        * prop phqpos, over(country)
        * Retained for exit interview
        tab country _screenexit if phqpos, m
        * Dx Tx for PHQ9+
        foreach var of varlist detect_dd treat_dd {
                tab country `var'  if phqpos==1 & _screenexit!=1, row
                prop `var' if phqpos==1 & _screenexit!=1, over(country)
                }
        * ALCOHOL
        * Mean AUDIT
        tabstat totalaud, by(country) col(stat) stat(n p50 p25 p75) f(%9.3g)
        * AUDIT cut off score
        table country audpos, c(min totalaud max totalaud)
        * AUDIT+ proportion
        table country, c(n audpos sum audpos mean audpos) f(%9.3g)
        * Abstinent and dependent proportions
        tab aud_5c country, col
        * AUDIT+ proportion and 95% CI
        * prop audpos, over(country)
        * Retained for exit interview
        tab country _screenexit if audpos, m
        * Dx Tx for AUDIT+
        table country if audpos==1 & _screenexit!=1, c(freq sum detect_aud mean detect_aud sum treat_aud mean treat_aud) f(%9.3g)
        prop detect_aud treat_aud if audpos==1 & _screenexit!=1, over(country)
```

```
****************
*** TABLE 7 ***
****************
        * Screen negatives
        mrtab phqpos dephis audpos, by(country) incl
        foreach var of varlist detect_dd treat_dd detect_aud treat_aud {
                tab country `var' if phqpos!=1 & audpos!=1 & dephis!=1, row
                }
```

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	11
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	15
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	11
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	16
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	16
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	16
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	19
		(b) Give reasons for non-participation at each stage	18
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	17
		(b) Indicate number of participants with missing data for each variable of interest	18
Outcome data	15*	Report numbers of outcome events or summary measures	19
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	19
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	22
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	23
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	22
Generalisability	21	Discuss the generalisability (external validity) of the study results	22
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	24

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Detection and treatment initiation for depression and alcohol use disorders: facility-based cross-sectional studies in five low- and middle-income country districts

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Abstract

Objectives: To estimate the proportion of adult primary care outpatients who are clinically detected and initiate treatment for depression and alcohol use disorder (AUD) in low- and middle-income country (LMIC) settings.

Design: Five cross-sectional studies

Setting: Adult outpatient services in 36 primary health care facilities in Sodo District, Ethiopia (9 facilities); Sehore District, India (3); Chitwan District, Nepal (8); Dr Kenneth Kaunda District, South Africa (3); and Kamuli District, Uganda (13).

Participants: Between 760 and 1893 adults were screened in each district. Across 5 districts, between 4.2 and 20.1% screened positive for depression and between 1.2 and 16.4% screened positive for AUD. 96% of screen-positive participants provided details about their clinical consultations that day.

Primary outcomes: Detection of depression, treatment initiation for depression, detection of AUD, treatment initiation for AUD

Results: Among depression screen-positive participants, clinical detection of depression ranged from 0% in India to 11.7% in Nepal. Small proportions of screen-positive participants received treatment (0% in Ethiopia, India and South Africa to 4.2% in Uganda). Among AUD screen-positive participants, clinical detection of AUD ranged from 0% in Ethiopia and India to 7.8% in Nepal. Treatment was 0% in all countries aside Nepal, where it was 2.2%.

Conclusions: The findings of this study suggest large detection and treatment gaps for adult primary care patients, which are likely contributors to the population-level mental health treatment gap in LMIC. Primary care facilities remain unfulfilled intervention points for reducing the population-level burden of disease in LMIC.

Strengths and limitations of the study

- This was a multi-country survey of diverse clinical settings, with large sample sizes, structured interviews, and used of validated screening tools to identify cases.
- The methods used here are demonstrably flexible and are replicable in other low-income settings, particularly for monitoring and evaluation purposes.

- We used highly sensitive and non-specific coding criteria for our primary outcomes (i.e. detection and treatment initiation), and so outcome misclassification is possible.

Keywords: depression, alcohol use disorder, primary care, detection, treatment, low- and middle-income countries

BACKGROUND

Mental, Neurological and Substance use disorders (MNS) contribute significantly to the Global Burden of Disease (GBD) and account for one in every 10 lost years of health globally.[1] In 2010, the absolute Disability-Adjusted Life-Years (DALYs) due to MNS disorders was 258 million DALYs which is 10.4% of the total disease burden. MNS disorders were also the leading cause of years lived with disability globally.[1] In addition to this, MNS disorders act as a significant risk factor for premature death [2] and also accounts for substantial adverse social and economic consequences.[1,3] Depression accounts for 40.5% of DALYs caused by mental and substance use disorders while Alcohol Use Disorders (AUD) account for 9.6%.[4]

In low- and middle-income countries (LMICs) the population-level treatment gap is estimated to be between 76.3% and 91.9% for depression and between 94.9% and 97.2% for AUD.[5] There is an emerging evidence base demonstrating that depression and AUD can be treated by primary care providers in LMIC [6]; the World Health Organization's mhGAP guidelines support integration of mental health services into primary care as a means of narrowing the treatment gap.[7] People affected by depression and AUD often present in primary health care facilities [8,9] though not specifically for these disorders. These disorders co-occur with both acute and chronic medical problems; an untreated mental health disorder worsens the prognosis for the co-morbid condition.[10,11] The population-level treatment gap can be reduced by enhancing the capacity of primary care staff to detect, diagnose and treat these disorders.[12] Clinical detection of depression is estimated to be 47% from a meta-analysis of 41 studies conducted in primary care settings [13] and 42% for AUD from a meta-analysis of 12 studies. [14] However, these meta-analyses were not able to identify studies conducted in LMIC settings, where the majority of people with depression and AUD in the world live, and where a paucity of mental health in the pre-service training of general health care providers as well as competing demands in under-resourced healthcare systems likely compromise the ability of clinicians to detect mental disorders. Little is therefore known regarding the detection levels of depression and AUD in primary care settings in LMICs.

The aims of this report were to estimate the proportion of adult primary care outpatients who are clinically detected and initiate treatment for depression and alcohol use disorder (AUD) in low- and middle-income country (LMIC) settings.

METHODS

Context, setting and participants

PRIME is a six-year multi-country research program consortium which, in collaboration with national and district Ministries of Health, has developed Mental Health Care Plans to support delivery of services for mental disorders in the public sector in Ethiopia (Sodo District), India (Sehore District, Madhya Pradesh State), Nepal (Chitwan District), South Africa (Dr Kenneth Kaunda District, North West Province), and Uganda (Kamuli District).[15,16] Two key research questions of the PRIME evaluation – detailed in a separate report [17] - were to assess the change in detection and change in initiation of treatment among adults presenting in primary health facilities, as a consequence of implementing the district mental healthcare plans. These questions were investigated by conducting cross-sectional facility-based patient surveys before and after the mental healthcare plan implementation. The two populations of interest for the study were the adult patients who screened positive 1) for depression and 2) for AUD.

Details about the study settings and clinics are in Table 1.

Table 1. Geographic and health facility characteristics of PRIME implementation areas, 2013-2014.

Country	Ethiopia	India	Nepal	South Africa	Uganda
Implementation area	Sodo District	Sehore and Shyampur sub-districts of Sehore District, Madhya Pradesh	Chitwan District*	Orkney catchment area of Matlosana sub-district of Dr Kenneth Kaunda District, Northwest Province	Kamuli District
Population	161,952	212,192	108,368	90,000	518,200
Area, km^2	867	1,039	342	31	4,278
# and type of health facility	8 public and 1 private health clinics	3 Community Health Centres	9 Health Posts and 1 Primary Health Care Centre**	1 Community Health Centre (CHC) and 3 Primary Health Care (PHC) clinics***	12 Health Centres (Level III and IV) 1 primary care department in the district hospital
Primary provider types	Health Officer	Medical Officer	Medical officers, Health Assistants, Auxiliary Health Workers	Nurse, PHC doctor	Medical Officer
Primary care services provided in the facilities	Primary care, Emergency; delivery care, mother and baby care, family planning and immunization	Primary, acute, Reproductive and child health	Outpatient; immunization; family planning; safe motherhood and new born care; anti- and post-natal care; delivery of babies.	Chronic care	Outpatient; emergency; immunization; maternal and child health; family planning, health education and Primary care in general including mental health

* Implementation area consists of 10 of the 38 Village Development Committees/Municipalities of Chitwan District
** 222 study participants from 2 of the 10 health facilities are excluded from analysis
*** 1 of the 3 PHC clinics was an implementation pilot site and was excluded from study data collection.

The choice of included clinics was determined by the availability of staff who were planned to have authority to detect/ diagnose, prescribe and/or refer for depression and AUD, which, per the respective country's mental healthcare plan included clinics with health officers, medical officers, health assistants and auxiliary health workers, nurses and doctors. In South Africa, one of the PHC clinics was excluded from the study due to mental health care plan training prior to the baselines survey round. In South Africa, nurses in the primary care clinics could refer suspected cases to a physician (for both disorders) and provide brief counselling (for non-dependent alcohol use disorder) and so these clinics were included. Only patients attending for chronic care services (e.g. HIV, tuberculosis, diabetes, hypertension, etc) were eligible for this study, reflecting eligibility for treatment in accordance with the South African mental health care plan. In Nepal, clinicians working in two clinics received mental health training prior to the baseline survey round; these clinics are included for clinical-level descriptive reporting but participants from these clinics are excluded for analysis here. All clinics were government run, aside one in Ethiopia.

Sample size

For each country and disorder the sample size was set to have 80% power and a two-sided alpha of 0.05 for the two primary aims: 1) to detect a change in detection and 2) to detect a change in initiation of evidence-based treatment for depression and for AUD between the baseline and follow-up round. The baseline round was set prior to implementation of the mental health care plan and follow-up round was scheduled to start at least 18 months later, which assumed the plan had been fully embedded for several months. Country teams in Nepal and Uganda planned to conduct an interim survey round immediately after embedding, to assess the short-term effect of implementation on detection and treatment. Findings from interim and follow-up surveys will be detailed in future reports. Depending on country, the baseline level of detection was assumed to be 0-5%, and at follow-up targeted to reach 20-30%. The required sample size was adjusted to account for the possibility of false positives generated by screening tools, using site-specific figures for the positive predictive value. Within each country, whichever disorder required the higher sample size dictated the sample size. This sample size was increased by a factor of 2-3x to facilitate equity analyses, e.g. comparisons of outcomes by sex or by socioeconomic status. The target sample sizes for each country in each study round were 1000 in Ethiopia, 760 in India, 1400 in Nepal, 1200 in South Africa and 1800 in Uganda. Within each country the total target sample size was then

allocated by clinic in proportion to measures of clinic outpatient volume, such that busier clinics were allocated a larger recruitment target than less busy clinics.

Details of the sampling and data collection procedures in Table 2.

Table 2. Sample selection and data collection procedures for facility surveys, 2013-2014.

Country site	Ethiopia	India	Nepal	South Africa	Uganda
Survey dates	June-July 2013	Aug-Oct 2013	Sept 2013-Feb 2014	Feb-April 2014	July-Nov 2013
Study language	Amharic	Hindi	Nepali	English, seTswana	English, Luganda
Recruitment / sampling method	Consecutive sampling of adults at registration	Systematic sampling of every 5th adult at registration	Random selection of 1 adult from those who arrived since last interview started	Opportunistic sampling of adult volunteers in chronic care clinic waiting area	Consecutive sampling of adults at registration
Consent documented with	Signature or thumbprint	Signature or thumbprint	Signature or verbal affirmation	Signature or signed 'X' with independent witness signature	Signature or verbal affirmation.
# approached	1014	760	1553	9780	1922
# eligible	1014	760	1553	1322	1922
# consented (% consent rate)	1014 (100)	760 (100)	1474 (94.9)	1322 (100)	1893 (98.5)
Questionnaire data collection mode	Paper-and-pencil, double data entry with EpiData 3	Android mobile device	Android mobile device	Android mobile device	Android mobile device
Depression screen positive is PHQ-9 >=	10	10	10	10	10
AUD screen positive is AUDIT>=	8	8	9	16	8
Clinical consultation form	Purpose-built form	Extracted from clinical records maintained at the facility	Purpose-built form	Extracted from clinic records	Consultation notes extracted from patient's notebook as part of the exit questionnaire

Sampling and recruitment

Inclusion criteria for participation were as follows: above age of majority in the country (i.e. 16 years or 18 years); fluency in a local study language; time and ability to complete the full interview; and willingness to provide informed consent. Exclusion criteria were as follows: incapacity to provide informed consent (e.g. presence of severe intellectual disability, currently experiencing an acute medical issue). The research team for each country trained its interviewers to assess eligibility.

Logistic and cultural constraints dictated the sampling procedure within each country, meaning that random selection for a representative sample was not always possible. In Ethiopia and Uganda, to minimize disruption, consecutive sampling of all eligible patients upon registration minimized the amount of time research staff spent in the clinics. In South Africa, research staff provided a group orientation to the study to all patients in the waiting room, and then asked interested patients to self-nominate for recruitment. In India, research assistants approached every fifth patient registering at reception and assessed them for eligibility. Among eligible patients approached, over 94% consented to participate in all countries.

Data collection procedures

The facility interview was comprised of a screening questionnaire, an exit questionnaire and/or a clinical consultation form. Interviewers administered the two-part screening questionnaire, with part 1 used to identify probable cases. For probable cases and optionally for probable non-cases, interviewers completed part 2 of the screening questionnaire. For these same participants, the interviewer completed the exit questionnaire with the participant and/or requested a consultation form from that participant's clinician. In Uganda patients maintained their own medical files in a notebook which is handed over to clinicians during consultations, and so the clinical consultation form data were synonymous with exit questionnaire data. The data collection flow chart for each country is shown as Supplemental Figures 1a-1e.

The sections within the screening interview questionnaire are described in Table 3.

Table 3. Screening interview sections for PRIME facility detection study, 2013-2014.

Section	# items	Source
		Part 1
Basic demographic characteristics	5	Purpose-built for PRIME
Alcohol use disorder screening	10	Alcohol Use Disorder Identification Test (AUDIT) [18]
Alcohol: recent treatment history and intentions	23	Purpose-built for PRIME
Alcohol: internalized stigma	20	Adapted from the Composite International Diagnostic Interview Services module [19] and the Barriers to Access to Care Evaluation Scale [20]
Depression screening	9	Patient's Health Questionnaire (PHQ-9) [21]
Depression symptoms in the past 12 months	1	Purpose-built for PRIME
Depression: recent treatment history and intentions	23	Purpose-built for PRIME
Depression: internalized stigma	20	Adapted from the Composite International Diagnostic Interview Services module [19] and the Barriers to Access to Care Evaluation Scale [20]
Suicidality	7	Adapted from the Composite International Diagnostic Interview (CIDI) suicidality module [19]
		Part 2
Disability	12	World Health Organization Disability Assessment Schedule (WHODAS) 2.0 [22]
Detailed sociodemographic characteristics	18	Purpose-built for PRIME

Data collection measures

Part 1 of the screening questionnaire consisted of sections on sociodemographic characteristics, screening for depression, depression symptoms in the past 12 months (aside in Ethiopia), and screening for AUD. A probable case of depression was a participant who was PHQ-9 positive or had recent depression symptoms, and a probable case of AUD was a participant who was AUDIT positive. Probable cases completed disorder-specific sections about recent (12 month) history of treatment seeking for their most recent episode of symptoms, and about internalized stigma. Part 2 consisted sections about sociodemographic characteristics and disability status. The exit questionnaire and clinical consultation form were thematically similar, and consisted of a mix of open- and closed-ended questions about that day's clinical consultation, and specifically about diagnoses, advice, referrals and prescriptions. Each country developed their own exit questionnaire and clinical consultation form to enable data collection by interviewers with the participant and by the clinician directly, respectively, in recognition of the context specific nature of patient-clinician interactions and the local idioms of distress. In addition to the questionnaire items described here, which were largely consistent across PRIME country sites, research teams included country-specific questions and sections, which will be described in future reports. See PRIME website (www.prime.uct.ac.za) for the purpose-built sections of the PRIME questionnaires.

Mental health measures

The denominators for the primary outcome measures consist of those participants who screen positive for depression or for AUD, using the PHQ-9 and AUDIT, respectively. The PHQ-9 is a widely used screening tool that has been validated for use in all five countries.[23–27]. In this study, Cronbach's alpha for the PHQ-9 ranged between 0.74 in India and 0.80 in Nepal. A score of 10 or more on the PHQ-9 screen was considered a positive screen. The AUDIT tool has been validated in India, Nepal and South Africa [28–30] and in countries neighbouring Uganda.[31,32] In this study, Cronbach's alpha for AUDIT ranged from 0.66 in Uganda to 0.88 in Nepal. An AUDIT score of ≥20 was considered to indicate alcohol dependence, while scores of 16-19 and 8-15 were classified as harmful and hazardous drinking, respectively. A score of 8 or more in Ethiopia, India and Uganda, 9 or more in Nepal and 16 or more in South Africa, was considered a positive screen. The higher cut off

score in South Africa was set to account for services being targeted to those with harmful and dependent alcohol use.

Outcome assessment

The numerators for the primary outcome measures were derived from participant exit questionnaire data when available (India, Nepal, South Africa, Uganda), and alternatively from the clinician consultation form data (Ethiopia). Given the sparse level of detail patients were expected to recall and/or clinicians were expected to record, cross-country variation in the terminology around detection and treatment, as well as expected low levels of detection and treatment at baseline, highly sensitive and non-specific coding criteria – detailed in Table 4 - were adopted and used for the outcomes' numerators. These criteria were informed by WHO's mhGAP guidelines.[7]

Table 4: Criteria used to assess detection and treatment of depression and alcohol use disorders in the PRIME facility detection study, 2013-2014.

Detection of depression	**Treatment of depression**
Included: • Diagnosis of "depression" • Diagnosis of "stress", "distress", "behavioural problem", "mental disorder", or "psychiatric problem" • Diagnosis assumed if unambiguous depression treatment given *Excluded:* • Diagnosis of "anxiety", "insomnia", "tension headache", "stress headache", "schizophrenia", "epilepsy", "bipolar", "central nervous system problem"	*Included:* • Prescription of SSRI (e.g. fluoxetine) • Referral to a mental health specialist • Advice on stress reduction or management - only with depression diagnosis • Prescription of tricyclic antidepressant (e.g. amitriptyline) only with depression diagnosis • Referral to counselling or talking treatment – only with depression diagnosis *Excluded:* • Diazepam prescription • Non-specific referrals (e.g. "hospital")
Detection of alcohol use disorder	**Treatment of alcohol use disorder**
Included: • Diagnosis of "AUD", "alcohol problem" or "drinking problem" • Diagnosis assumed if unambiguous AUD treatment given *Excluded:* • Drug abuse or other substance use problems	*Included:* • Referral to a mental health or addictions specialist • Prescription of diazepam or Vitamin B – only with AUD diagnosis • Counselling or talking treatment – only with AUD diagnosis *Excluded:* • Non-specific referrals (e.g. "hospital")

Abbreviations: AUD, alcohol use disorder; SSRI, selective serotonin reuptake inhibitor

Outcome assessors (TR, SS and SDR) independently double-coded the outcomes for detection (Yes/No) and treatment (Yes/No) with 99% initial scoring agreement. Disagreements were resolved through further discussion.

Analysis

First, the sociodemographic characteristics and mental health screening scores of participants were summarised by presenting the median and interquartile range for continuous measures and counts and percentages for categorical measures. Second, for depression screen-positive participants, the numbers and proportions who had outcome data, were detected for depression, and who had initiation of minimally adequate evidence-based treatment were reported. The same figures were reported for AUD screen-positive participants and AUD. Finally, depression and AUD detection figures are reported for participants who were depression and AUD screen-negative and who did not have depression symptoms over the past 12 months. These latter figures are indicators – though not definitive evidence - for either mis- or over-diagnosis. All analyses were conducted in Stata 14.1 (StataCorp, College Station, TX, USA), and stratified by country. (See supplemental file 'stata do file code.docx')

Ethics

All participants gave written or verbal informed consent prior to being interviewed (Table 2). The informed consent form made clear there would be no negative effects for non-participation. In South Africa, participants were provided a 30 Rand (~2.80 USD) supermarket voucher as a token of appreciation. In all countries, participants who endorsed questionnaire items about suicidality were referred to a provider in the clinic.

The institutional review boards of the World Health Organization (Geneva, Switzerland), University of Cape Town (South Africa), College of Health Sciences of Addis Ababa University (Ethiopia), Indian Council of Medical Research (New Delhi, India), Sangath (Goa, India), Nepal Health Research Council (Kathmandu, Nepal), Makerere University (Kampala, Uganda), and the National Council of Science and Technology (Kampala, Uganda) reviewed and approved the protocols and informed consent procedures for this study.

Patient involvement

The PRIME interventions and evaluations were informed through Theory of Change workshops held in each country [33]. These workshops included national- and district-level representatives, health service providers, and, in some countries, mental health service users.

RESULTS

The demographic and mental health screening characteristics of participants are detailed in Table 5.

Table 5: Demographic and mental health characteristics for facility detection survey participants, 2013-14

Country site [sample size]	**Ethiopia** [n=1014] Median (IQR) or n (%)	**India** [n=760] Median (IQR) or n (%)	**Nepal*** [n=1252] Median (IQR) or n (%)	**South Africa** [n=1322] Median (IQR) or n (%)	**Uganda** [n=1893] Median (IQR) or n (%)
Age, years	30 (23-45)	37 (27-51)	36 (27-50)	46 (37-56)	28 (22-37)
Female	551 (54.3)	386 (50.8)	813 (64.9)	992 (75.0)	1500 (79.2)
Education					
Less than primary	692 (68.3)	381 (50.1)	444 (35.5)	308 (23.3)	174 (9.2)
Primary	230 (22.7)	186 (24.5)	253 (20.2)	829 (62.7)	1113 (58.8)
Secondary or more	91 (9.0)	193 (25.4)	555 (44.3)	185 (14.0)	606 (32.0)
PHQ-9 score	4 (1-7)	6 (4-9)	4 (2-7)	3 (1-6)	2 (1-4)
PHQ-9 positive**	117 (11.5)	153 (20.1)	186 (14.9)	107 (8.1)	80 (4.2)
Depression symptoms in past 12 months		110 (14.5)	174 (13.9)	157 (11.9)	159 (8.4)
AUDIT score	2 (0-5)	0 (0-0)	0 (0-1)	0 (0-4)	0 (0-0)
Alcohol abstinent	275 (27.1)	659 (86.7)	849 (67.8)	724 (54.8)	1475 (77.9)
AUDIT positive**	166 (16.4)	35 (4.6)	92 (7.3)	43 (3.2)	23 (1.2)
Dependent alcohol use	37 (3.6)	3 (0.4)	32 (2.6)	21 (1.6)	2 (0.1)

* Excluding 222 patients from 2 clinics

Ages ranged from a median of 28 years in Uganda to 46 years in South Africa. The majority of participants in all countries were female, from 51% in India to 79% in Uganda. The proportion of participants who screened positive for depression ranged between 20% in India to 4.2% in Uganda, for depression symptoms in the past 12 months ranged between 8% in Uganda to 14% in India, and for AUDIT between 1% in Uganda and 16% in Ethiopia. These probable cases were asked to complete the Exit interview and/or their clinicians asked to complete a consultation form. Outcome data were available for 96% of these participants (from clinical consultation forms or exit questionnaires), though exit questionnaire completion was lower for depression screen-positive participants in Uganda (48/80, 60%), and AUD screen-positive participants in South Africa (38/43, 90%) and Uganda (18/23, 78%), respectively. Non-completion was primarily due to participants having to leave the clinic immediately or the interviewer being unable to locate the participant after their consultation.

The proportions of screen-positive participants who were detected and who started treatment are presented Table 6.

Table 6. Detection and treatment among screen-positive adults in PRIME implementation clinics, 2013-2014.

Country site	Ethiopia	India	Nepal	South Africa	Uganda
Depression					
Outcome data collected / screen positive	117/117	153/153	179/186	103/107	48/80
Detected, n (%, 95% CI)	12/117 (10.3, 5.9-17.2)	0/153 (0.0)	21/179 (11.7, 7.8-17.3)	6/103 (5.8, 2.6-12.4)	2/48 (4.2, 1.0-15.4)
Treatment initiated, n (%, 95% CI)	0/117 (0.0)	0/153 (0.0)	1/179 (0.5, 0.0-3.9)	0/103 (0.0)	2/48 (4.2, 1.0-15.4)
Alcohol Use Disorder					
Outcome data collected / screen positive	166/166	35/35	90/92	38/43	18/23
Detected, n (%, 95% CI)	0/166 (0.0)	0/35 (0.0)	7/90 (7.8, 3.7-15.6)	0/38 (0.0)	1/18 (5.6, 0.7-32.2)
Treatment initiated, n (%, 95% CI)	0/116 (0.0)	0/35 (0.0)	2/90 (2.2, 0.5-8.6)	0/38 (0.0)	0/18 (0.0)

Among depression screen-positive participants, detection of depression ranged from 0% in India to 11.7% in Nepal. Small proportions of screen-positive participants received treatment (0% in Ethiopia, India and South Africa to 4.2% in Uganda). Among AUD screen-positive participants, detection of AUD ranged from 0% in Ethiopia and India to 7.8% in Nepal. Treatment was 0% in all countries aside Nepal, where it was 2.2%.

For probable non-cases, detection of depression ranged from 0/557 (0.0%) in India to 3/74 (4.0%) in Nepal, and detection of AUD ranged from 0/557 (0.0%) in India to 2/74 (2.7%) in Nepal. Treatment was almost entirely absent. (See Table 7)

Table 7. Detection and treatment among probable non-cases in PRIME implementation clinics, 2013-2014.

Country site (# depression and AUD screen-negative and no depression symptoms in 12 months)	**Ethiopia** (n=752)	**India** (n=557)	**Nepal** (n=74)	**South Africa** (n=113)	**Uganda** (n=332)
Depression					
Detected, n (%)	16/752 (2.1)	0/557 (0.0)	3/74 (4.1)	4/113 (3.5)	2/332 (0.6)
Treatment initiated, n (%)	0/752 (0.0)	0/557 (0.0)	0/74 (0.0)	3/113 (2.6)	1/332 (0.3)
Alcohol use disorder					
Detected, n (%)	0/752 (0.0)	0/557 (0.0)	2/74 (2.7)	2/113 (1.8)	1/332 (0.3)
Treatment initiated, n (%)	0/752 (0.0)	0/557 (0.0)	0/74 (0.0)	0/113 (0.0)	1/332 (0.3)

DISCUSSION

This study establishes the magnitude of the detection gap for adults attending primary care in diverse LMIC settings. There were low levels of detection of depression from screen-positive participants in Ethiopia, Nepal, South Africa and Uganda and no detection in India. There was no detection of AUD among screen-positive participants outside Nepal and Uganda. Conversely, there was almost no evidence of mis- or over-diagnosis of depression or AUD among participants who screened negative.

The detection figures observed here are substantially lower than the average figures found by Mitchell et al. for detection of depression (47%) and for AUD (42%) by primary care providers in high income countries.[13,14] As studies of clinical detection in LMIC settings were not available for these meta-analyses, this study fills a key gap in our understanding of the detection gap globally. The consistency of findings across these 5 diverse settings likely provides insight across LMIC settings generally. The health service organisations in this study varied considerably in catchment size, services offered and provider types (Table 1), and facility attendees varied considerably by age, sex, educational attainment and symptom severity (Table 5). Yet detection was consistently poor. These findings provide insight into how the population-level treatment gap in LMIC is at least partially attributable to a facility-level detection gap.

While detection levels were low, the facility-level treatment gap approached 100% in most settings. The treatment outcome definitions used here were broad and included provision of advice or referrals to specialist care, both of which clinicians were able to dispense prior to implementation of the PRIME mental health care plans. The first barrier for providing treatment at the health facility is detection, and, as reported above, across all settings detection levels were extremely low. The findings of this study indicate consistent missed opportunities for providing evidence-based care across these diverse LMIC settings. Improving clinical detection and treatment of depression and AUD by primary care providers remains an area where intervention development is required; the PRIME consortium will evaluate its own interventions – the plans for which have described in detail [34–38] - in follow-ups to this report.

The PRIME Facility Detection study uses widely-validated screening tools to identify probable cases. While diagnostic interviews are the gold standard for identifying cases, screening tools are usable by trained interviewers rather than clinicians, and so the methods

used here are more easily replicable for monitoring and evaluation activities in other LMIC settings. Our outcome data were collected directly from the participants and clinicians rather than from a health management information system, which is also a replicable monitoring method for LMIC settings.

There are several limitations to our study. First, screening tools (PHQ-9 and AUDIT) were used to identify probable cases of depression and AUD; an unknown number of screen-positive cases are actually false positive cases. Further, a 100% detection figure is not a desirable goal, as it indicates diagnosis among false positive cases. Screening misclassification is likely to be similar in the follow-up round, and so the denominators for detection and treatment are equally biased across rounds and allows a valid comparison across time to be made. Second, non-random sampling was used to select patients in some countries. While the samples may not be representative of the facility-attending population, the same sampling plan will be used in follow up rounds, enabling valid comparisons for the study's primary findings. And, given the non-random sampling and use of screening tools it is not appropriate to interpret the proportions of participants who screen positive as prevalence figures for cross-country comparisons. The loss to follow-up for screen-positive participants in Nepal, South Africa and Uganda could result in biased findings, as the diagnostic characteristics of lost participants is unknown.

A third limitation concerns the outcome definitions for detection and treatment. Given the limitations of using patient- and clinician-reported data, with issues around recall and specificity, we opted to use extremely sensitive yet non-specific thresholds of evidence for coding detection or treatment as having occurred. The detection and treatment figures reported here should therefore be regarded as the upper bound of possibility: some of those coded as having been detected with depression may have other mental health disorders, and some of those coded as having treatment may not have what is considered to be minimally-adequate evidence-based care. Again, the bias due to these misclassifications will be equal in the follow up round. Use of cross-country coding criteria facilitates comparisons across diverse settings, and in future reports each country can use these criteria and/or develop their own more locally-appropriate and specific criteria. This process has been completed in Sodo District, Ethiopia, where detection outcomes have been reported separately for using specific criteria for depression and non-specific criteria for common mental disorder.[39]

We plan to repeat this survey in each of the implementation sites. By comparing the baseline versus follow-up figures within each country, we will be able to determine whether the level of detection and level of initiation of evidence-based treatment for depression and for AUD has increased after implementing mental health care plans. Further to this we will compare the change in detection among probable non-cases (Table 7), which is an indicator of inappropriate diagnosis; district health manager can use two detection figures to recalibrate their training and supervision systems. Also using follow up data, we will also be able to assess whether the improved detection and improved treatment provision is equitable by age, sex and other socio-economic factors. And, with the help of Theory of Change framework and process evaluation data collected over the implementation phase,[17] we will try to explain the reasons for improvement/non-improvement of detection and initiation of treatment for depression and for AUD, along identifying with the factors relating to detection. As each country developed its own Theory of Change framework, it will be possible to contrast five frameworks with five sets of follow-up findings, and then to identify the essential characteristics of an effective strategy to improve detection.

Further research can identify the patient-, clinician- and system-level characteristics associated with detection, as a means of further refining interventions. Some of these characteristics are already potential targets for intervention, and have been identified in previous studies: On the patient level, those who have higher level of perceived need[40] and lower levels of internalized stigma[13,14] are more likely to receive a diagnosis. On the clinician level, detection improves with longer consultation time,[41,42] adequate training, a stronger therapeutic alliance,[13] and with contractual incentives.[43] And on the health-system level, detection is likely to improve with the availability of medications and health providers at PHC level who have the authority to prescribe psychotropic medication, as well as referral pathways to counsellors. Also important are buy-in and support from leadership who give priority to mental health[1], governance and supervisory structures to develop and execute standardized protocols,[44] and a functional health management information system[45] to monitor and feed back on clinical activity. A combination of these patient-, clinician- and system- level characteristics may explain some of the substantially lower detection figures for depression and AUD found here from our LMIC settings compared to those found in meta-analyses by Mitchell et al. in HIC settings.

Conclusion

The findings of this study suggest large detection and treatment gaps for adult primary care patients, which are likely contributors to the population-level mental health treatment gap in LMIC. Primary care centres remain unfulfilled intervention points for reducing the population-level burden of disease in LMIC.

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Competing interests

None declared

Authors contributions

Conceptualization SDR, MJ, IP, FK, JN, CL, AF, RS

Design SDR, TR, GM, NPL, AB, IP, FK, JN, CL, AF, RS

Data acquisition TR, GM, VM, SS, NPL, OS, JS

Data analysis SDR

Data interpretation SDR, CL, RS

Drafting SDR, TR, CL, RS

Critical revision GM, VM, SS, NPL, OS, JS, MJ, AB, IP, FK, JN, CL, AF, RS

Final approval SDR, TR, GM, VM, SS, NPL, OS, JS, MJ, AB, IP, FK, JN, CL, AF, RS

Accountability SDR, TR, GM, VM, SS, NPL, OS, JS, MJ, AB, IP, FK, JN, CL, AF, RS

Data sharing statement: Statistical code (Stata) is available as supplementary material. While we cannot make the dataset publicly available, we will consider all request to provide a minimal dataset to interested researchers via the PRIME consortium Expression of interest form here: **http://www.prime.uct.ac.za/contact-us**.

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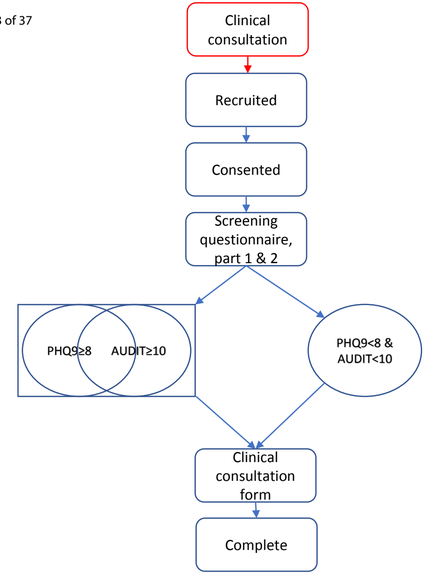
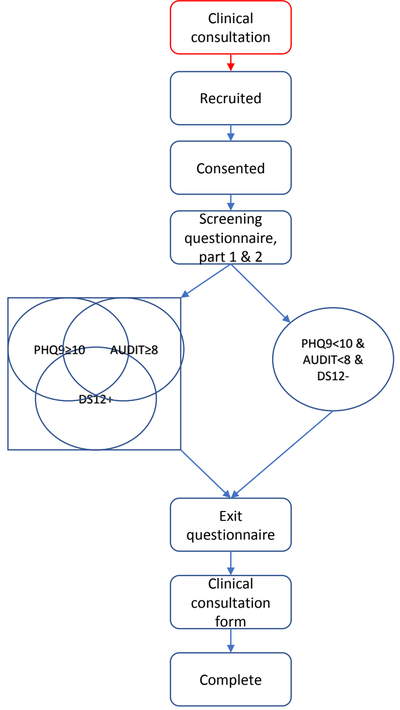
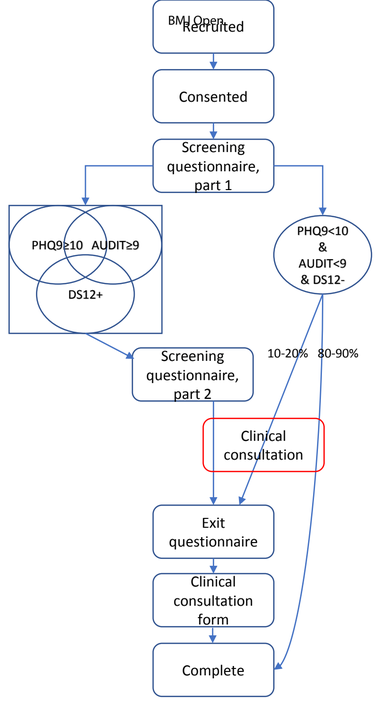
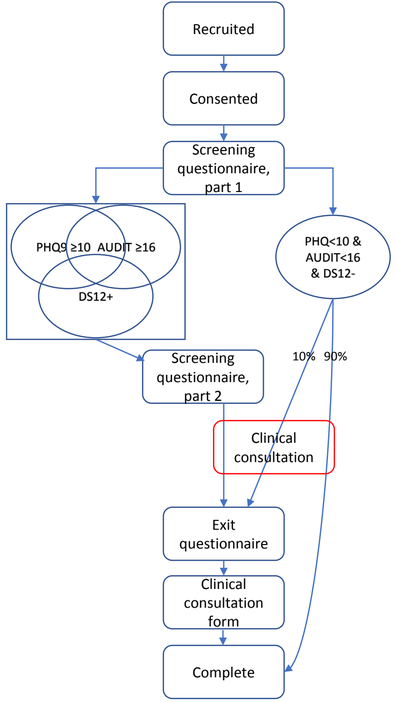
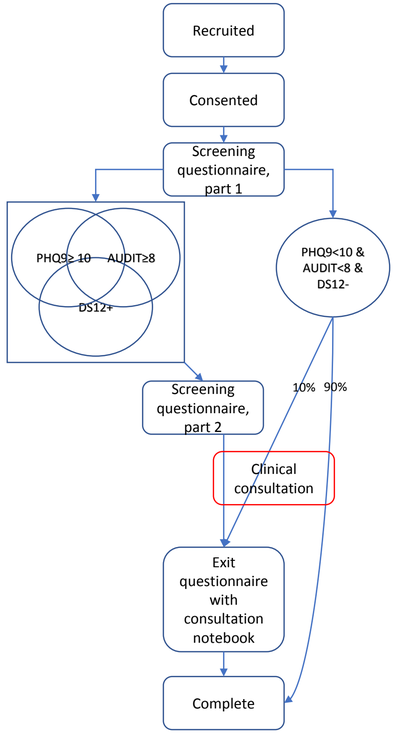

Clinical consultation
Recruited
Consented
Screening questionnaire, part 1 & 2
PHQ9≥8
AUDIT≥10
PHQ9<8 & AUDIT<10
Clinical consultation form
Complete


Clinical consultation
Recruited
Consented
Screening questionnaire, part 1 & 2
PHQ9≥10
AUDIT≥8
DS12+
PHQ9<10 & AUDIT<8 & DS12-
Exit questionnaire
Clinical consultation form
Complete


Recruited
Consented
Screening questionnaire, part 1
PHQ9≥10
AUDIT≥9
DS12+
PHQ9<10 & AUDIT<9 & DS12-
Screening questionnaire, part 2
10-20%
80-90%
Clinical consultation
Exit questionnaire
Clinical consultation form
Complete


Recruited
Consented
Screening questionnaire, part 1
PHQ9 ≥10
AUDIT ≥16
DS12+
PHQ<10 & AUDIT<16 & DS12-
Screening questionnaire, part 2
10%
90%
Clinical consultation
Exit questionnaire
Clinical consultation form
Complete


Recruited
Consented
Screening questionnaire, part 1
PHQ9≥ 10
AUDIT≥8
DS12+
PHQ9<10 & AUDIT<8 & DS12-
Screening questionnaire, part 2
10%
90%
Clinical consultation
Exit questionnaire with consultation notebook
Complete

```
*****************************
*** Baseline FDS & Methods ***
*****************************
use "C:\PRIME\FDS\UCT\FDS.dta" if round==1, clear
	keep country cname idate _screenexit _dxtx ///
		age sex educ_3c emp ///
		phq? totalphq phqpos dephis aud? aud10 totalaud audpos aud_5c ///
		detect_* treat_* medname*

	drop if mi(sex)
	table country, c(N idate min idate max idate)

	bysort country: alpha phq?, item
	mvencode aud1-aud10, mv(.=0) over
	bysort country: alpha aud1-aud10, item

***************
*** TABLE 1 ***
***************
	* Number of FDS clinics per country
	bysort country: distinct cname
	* Drop Nepal clinics which got training before baseline
	drop if cname==36 | cname==37

***************
*** TABLE 2 ***
***************
	* Age
	tabstat age, by(country) col(stat) stat(n p50 p25 p75) f(%9.3g)
	* % Female
	tab sex country, col
	* Education
	tab educ_3c country, col
	* Employment - propose using unemployed/non-income/income
	* tab emp country, col nolabel
```

```
**********
*** TABLE 6 ***
**********
	* DEPRESSION
	* Median PHQ9 score
	tabstat totalphq, by(country) col(stat) stat(n p50 p25 p75) f(%9.3g)
	* PHQ9+ screening cut off score
	table country phqpos, c(min totalphq max totalphq)
	* PHQ9+ proportion
	table country, c(n phqpos sum phqpos mean phqpos) f(%9.3g)
	tab country dephis, row
	* PHQ9+ proportion and 95% CI
	* prop phqpos, over(country)
	* Retained for exit interview
	tab country _screenexit if phqpos, m
	* Dx Tx for PHQ9+
	foreach var of varlist detect_dd treat_dd {
		tab country `var'  if phqpos==1 & _screenexit!=1, row
		prop `var' if phqpos==1 & _screenexit!=1, over(country)
		}
	* ALCOHOL
	* Mean AUDIT
	tabstat totalaud, by(country) col(stat) stat(n p50 p25 p75) f(%9.3g)
	* AUDIT cut off score
	table country audpos, c(min totalaud max totalaud)
	* AUDIT+ proportion
	table country, c(n audpos sum audpos mean audpos) f(%9.3g)
	* Abstinent and dependent proportions
	tab aud_5c country, col
	* AUDIT+ proportion and 95% CI
	* prop audpos, over(country)
	* Retained for exit interview
	tab country _screenexit if audpos, m
	* Dx Tx for AUDIT+
	table country if audpos==1 & _screenexit!=1, c(freq sum detect_aud mean detect_aud sum treat_aud mean treat_aud) f(%9.3g)
	prop detect_aud treat_aud if audpos==1 & _screenexit!=1, over(country)
```

```
****************
*** TABLE 7 ***
****************
        * Screen negatives
        mrtab phqpos dephis audpos, by(country) incl
        foreach var of varlist detect_dd treat_dd detect_aud treat_aud {
                tab country `var' if phqpos!=1 & audpos!=1 & dephis!=1, row
                }
```

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	11
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	15
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	11
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	16
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	16
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	16
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	19
		(b) Give reasons for non-participation at each stage	18
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	17
		(b) Indicate number of participants with missing data for each variable of interest	18
Outcome data	15*	Report numbers of outcome events or summary measures	19
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	19
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	22
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	23
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	22
Generalisability	21	Discuss the generalisability (external validity) of the study results	22
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	24

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.