**Effectiveness and Cost-effectiveness of the Counselling for Alcohol Problems, a Lay Counsellor Delivered Brief Psychological Treatment for Harmful Drinking in Men: a Randomized Controlled Trial in Primary Care in India.**

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**ABSTRACT**

**Background:** We sought to evaluate the effectiveness and cost-effectiveness of Counselling for Alcohol Problems (CAP), a brief psychological treatment delivered by lay counsellors to patients with harmful drinking attending routine primary health care (PHC) settings.

**Methods:** Individual parallel arm randomized controlled trial ~~in PHC settings~~ in Goa, India with male harmful drinkers defined by an Alcohol Use Disorders Identification Test (AUDIT) score of 12 to 19. Participants were randomized to enhanced usual care (EUC) alone or EUC combined with CAP, in randomly sized blocks stratified by PHC. The primary end-point was remission (AUDIT <8) and mean daily alcohol (gms) consumed in the past 14 days, at 3 months. We used logistic regression and zero-inflated negative binomial regression analyses respectively.

**Results:** 377participants were enrolled; 336 (89.1%) completed the 3-month outcome assessment. There was an intervention effect on remission on the AUDIT (36.0% in CAP vs 25.6% in EUC; aPR=1.50, 95%CI 1.09, 2.07); and on the proportion abstinent in the past 14 days (41.5% vs 18.0%; aOR=3.00; 95%CI 1.76, 5.13); but, no effect on mean daily alcohol consumed in past 14 days among those who reported drinking in this period. There was an effect on percent days abstinent in past 14 days (mean 69.4% vs 54.4%; p<0.001), but no intervention effect on percent days of heavy drinking, impact of drinking, disability scores, days unable to work, suicide attempts, and perpetration of intimate partner violence. The incremental cost per additional remission was $217 (95% CI $50, $1073); paying the monthly minimum wage ($415) per individual in remission, CAP has an 85% chance of being cost effective. There was no significant difference in the number of serious adverse events in the two arms (6 vs 13; p=0.11).

**Discussion:** CAP delivered by lay counsellors is superior to EUC for harmful drinkers in routine primary health care settings, and is likely to be cost effective.

**INTRODUCTION**

Alcohol Use Disorders (AUDs) comprise a range of conditions related to excessive alcohol consumption, with hazardous drinking, harmful drinking and dependent drinking reflecting progressively more serious forms1. AUDs contribute substantially to disability and premature mortality accounting for 7.9% (95% CI 6-10) of Years Lost to Disability and 44·4% (95%CI 29·1–60·0) of Years of Life Lost due to all mental and substance use disorders2. Among males in middle income countries, AUDs are the leading neuropsychiatric cause of disease burden3. In India there are high rates of alcohol-attributable mortality and prevalence of AUDs relative to the per capita volume of alcohol consumed1.

Hazardous (quantity or pattern of alcohol consumption that places individuals at risk for physical or psychological harm) and harmful drinking (quantity or pattern of alcohol consumption that has resulted in physical or psychological harm)4 affect more people than dependent drinking5 (quantity or pattern of alcohol consumption characterised by craving, tolerance, a preoccupation with alcohol and continued drinking in spite of harmful consequences)6, but the policy response to the growing public health problem of AUDs in low and middle income countries (LMIC) remains focused on the latter5. A range of psychosocial interventions is available for the treatment of AUDs and can be broadly summarised as follows. ‘Brief Interventions’ are short, typically a single-session lasting up to 15 minutes, focused psychosocial interventions designed to address alcohol related problems or to reduce heavy drinking in hazardous drinkers7. More severe alcohol problems, such as harmful drinking, require more specialized brief or extended therapies (e.g. behaviour therapy, motivational enhancement therapy, Twelve Step Facilitation)8. Although brief psychological interventions are recommended for harmful drinking by the recent Disease Control Priorities Project9 (a project aimed at compiling and disseminating the most up to date evidence on cost-effective interventions and their delivery for the leading causes of global disease burden), the vast majority of people in LMIC, including India, lack access to such interventions because of the lack of skilled human resources10, and the concerns regarding the contextual appropriateness and generalizability of interventions developed in ‘western’ cultural settings11,12. These barriers could be addressed by developing and testing interventions that have been matched to the context in which they will be offered, and delivering them via non-specialist health workers (NSHW) or counsellors13.

PREMIUM (PRogram for Effective Mental health Interventions in Under-resourced health systeMs), a research program whose goal was to design a methodology for the development and evaluation of scalable psychological treatments (PT) that are culturally appropriate, affordable, and feasible for delivery by NSHWs and to apply this methodology14 for depression (the Healthy Activity Program [HAP]), and harmful drinking (the Counselling for Alcohol Problems [CAP])15,16. In this paper we describe the results of a trial evaluating the effectiveness of the CAP treatment while a companion paper (Patel et al, concurrent submission)17 describes the results of the HAP treatment. The trial described in this paper aimed to evaluate the effectiveness and cost-effectiveness of CAP when used in primary care.

The primary hypothesis was that CAP, in addition to enhanced usual care (EUC), would be superior to EUC alone in improving drinking outcomes at 3 months post-enrolment. Secondary hypotheses were that CAP would be superior to EUC alone in reducing the consequences of alcohol use, disability, suicidal behaviour, and costs of illness. The trial was conducted in alignment with the protocol registered with the International Society for the Registration of Clinical Trials (ISRCTN76465238)18. The trial protocol was approved by the Trial Steering Committee, and approval for the conduct of the trial was obtained from the Institutional Review Boards of the London School of Hygiene and Tropical Medicine, Sangath (the implementing institution in India), and the Indian Council of Medical Research.

**METHODS**

Details of the methods are described in the protocol18 and a summary is presented below. The two trials of the HAP treatment17 and the CAP treatment were conducted concurrently in the same PHCs and over the same period of time, with the same counsellors delivering both treatments according to the trial allocation of the participant.

***Study design, setting and participants:*** We conducted a parallel arm single blind individually randomized controlled trial conducted in primary health centres (PHCs) in Goa, India. Out of the 14 PHCs in the North district of Goa, the Directorate of Health Services gave permission for PREMIUM to operate in 10 PHCs. Screening was started in eight PHCs but, during the course of the trial, two of these were replaced as one had low attendance rates and the other had a large proportion of migrant labourer patient population. So at any given time screening was happening in only eight PHCs, as per protocol. The publicly funded PHC is the first port of call for people seeking health care in the public system in India. The population served generally belongs to lower socio-economic groups.

Participants were 18-65 year~~s~~ old males (females were not eligible as prevalence of any drinking in women in India is low at 1%19) who met the a-priori eligibility criteria and were likely to be harmful drinkers defined as scoring 12-19 on the Alcohol Use Disorders Identification Test (AUDIT)20. Harmful drinkers who screened positive for depression on the Patient Health Questionnaire (PHQ-9) were also included in this trial; those who continued to screen positive for depression at the end of the CAP treatment were offered the HAP treatment. While we did offer persons with alcohol dependence (i.e. men who scored higher than 20) the opportunity to participate in the trial, this was done primarily to enhance the acceptability of the program in the PHCs; as the trial was not powered for outcomes in this opportunistic group, the findings are not reported in this paper. Patients who needed emergency medical treatment and/or in-patient admission, patients who were unable to communicate clearly, and patients who were intoxicated at the time of screening were excluded from screening. Trained ‘health assistants’, independent of the counsellors, screened patients using the AUDIT, and administered a baseline questionnaire to trial participants to collect socio-demographic information (e.g. age, marital status) and data on potential moderators of treatment effect. All outcome interviews were audio-taped (with permission), and the tapes randomly selected for review by the supervisor for quality assurance. Enrolment was conducted between 28th October 2013 and 29th July, 2015 and outcome evaluation was conducted between 29th January 2014 and 30th November 2015 for both the PREMIUM trials. The trial will continue till 30th August 2016 when the 12 month outcome evaluation ends.

***Sample size estimation:*** Based on the assumptions that participants would be randomised within each of the clinics, with one counsellor per PHC at any one time, an intra-cluster correlation (ICC) of 0.04, a loss to follow-up (LTFU) of 15% over 3 months and a 1:1 allocation ratio, a trial size of 400 enrolled participants with harmful drinking had 90% power to detect the hypothesized effects (effect size of 0.45 for mean standard ethanol content consumed; remission rates of 68% vs 40% in favour of CAP) for the primary outcomes, with a 5% Type 1 error.

***Randomization:*** A randomization list in randomly sized blocks (two to six) stratified by PHC, was generated by a statistician independent of the trial. The randomisation code was concealed and allocated at the individual level after completion of the baseline assessments, using sequential numbered opaque sealed envelopes21.

***Interventions:*** Participants were allocated to either of two intervention arms as follows:

*Enhanced Usual Care:* The comparison intervention was usual care (consultation with the PHC physician) enhanced by providing the screening results to the PHC physician, and providing a contextualized version of the WHO Mental Health Gap Action Programme (mhGAP) guidelines22 for harmful drinking, including when and where to refer patients for specialist care.

*Counselling for Alcohol Problems (CAP):* In this arm, participants received the EUC plus the CAP treatment. Details of the development, theoretical orientation, and content of CAP are described in a separate paper15 and are briefly summarised here. CAP is a manualised PT delivered in three phases over a maximum of four sessions (each lasting approximately 30-45 minutes) at weekly to fortnightly intervals: a) ‘Initial phase’ involving detailed assessment followed by personalised feedback, b) ‘Middle phase’ involving helping the patient to develop cognitive and behavioural skills and techniques which include drink refusal skills, handling peer pressure, problem solving skills, and handling difficult emotions, and c) ‘Ending phase’ in which the patient learns how to manage potential or actual relapses using the skills acquired in the ‘middle phase’. The stance adopted by the counsellor is that of Motivational Interviewing (MI)23 and client centred ‘general counselling’ strategies (e.g. open ended questioning, demonstrating empathy). The ‘general counselling’ and ‘problem solving’ strategies were shared between the CAP and HAP treatments. Sessions were typically conducted face-to-face, at the PHC or patient’s home, but telephone sessions were used when necessary. Patients who missed three consecutive scheduled sessions were considered to have dropped out of treatment. The counsellors were adults with no professional training and/or qualification in the field of mental health, had completed at least high school education, and were fluent in the vernacular languages used in the study settings. The selection process comprised interviews with role plays for applicants for the training; for those who cleared this step, an intensive two week classroom training in both the CAP and HAP treatments followed by a competency assessment; for those who graduated this step, a six month internship with supervision of cases by experts; and a final selection through testing of knowledge (multiple choice question exam), and skills (role plays using standardised vignettes and quality ratings of actual CAP sessions delivered). Eleven counsellors participated in the trial. They received weekly peer-led supervision in groups of 4-6 that involved rating randomly selected recorded sessions on the CAP Therapy Quality Scale (TQS)24 and individual supervision twice monthly. Further details of the selection, training, and supervision of the counsellors are described elsewhere24.

***Outcomes:*** The primary outcomes were measured at three months post-enrolment. As per our pre-specified and approved analysis plan the primary outcomes were: remission defined as an AUDIT score <8; and mean daily alcohol (in gms) in the past 14 days immediately preceding the three-month outcome evaluation. In estimating the sample size, we considered both outcomes and were adequately powered to evaluate each of these independently. For the binary primary outcome, we had 99% power to detect a remission rate of 68% in the CAP arm vs 40% in the EUC arm, and for the continuous primary outcome, we had 93% power to detect an effect size of 0.45. Secondary outcomes were the Short Inventory of Problems (SIP) mean score; WHO-Disability Assessment Scale-II (WHO-DAS) mean disability score; the total days unable to work in the previous month; suicide attempt in the past 3 months; perpetration of intimate partner violence (*‘In the past 3 months, have you slapped, hit, kicked, punched your wife/partner or done something else that did or could have hurt her physically?’*); and resource use and costs of illness estimated from the Client Service Receipt Inventory (CSRI)25. Information on contacts with the counsellor were used to estimate the CAP delivery costs which took into account training, supervision and salary costs. In a joint meeting of the Trial Steering Committee and Data Monitoring and Safety Committee before unblinding, two additional secondary outcomes (percent days abstinent [PDA] and percent days heavy drinking [PDHD] generated from the Timeline Followback [TLFB]) were added to bring the trial into line with recommendations of the National Institute on Alcohol Abuse and Alcoholism (NIAAA)26.

***Masking:*** Physicians providing EUC were masked to allocation status, as were the independent evaluators who conducted the outcome assessments and had no contact with the PHCs or other team members. All authors, apart from the data manager (BB), were masked until the trial results were unblinded.

***Process and Fidelity assessments:*** These were obtained from: treatment completion rates maintained by the counsellors in their clinical records; CAP Therapy Quality Scores (TQS) scores from peer and expert ratings of audio-recordings of sessions during weekly group supervision24; and therapy quality of a random selection of 10% of all sessions by an expert involved in the development of the CAP.

***Statistical methods:*** Statistical analyses were performed using Stata version 14.1. Analyses were on an intention-to-treat basis, with multiple imputation for missing outcome data assuming data were missing at random, assuming predictive mean matching for positively skewed outcomes. Baseline data were summarized by arm. The primary continuous outcome (mean daily ethanol (gm) consumed in the past 14 days) was estimated by multiplying the total standard drinks27 consumed in the past 14 days with 10 (based on the WHO definition of a standard drink as 10 grams of pure ethanol). Zero-inflated negative binomial (ZINB) regression28 was used to estimate the intervention effect for this and other positively skewed over-dispersed outcomes with an excess of zeros. Continuous outcomes with normally distributed residuals were analysed using linear regression. Binary outcomes were analysed using binary logistic regression. All models were adjusted for PHC as a fixed effect to allow for within-PHC clustering, and for baseline AUDIT score. As there were only ten PHCs in the study, it was decided a-priori to adjust for these as fixed effects, as recommended by Kahan (2014) for studies with a small number of centres29. However, sensitivity analysis was conducted using random effects models to adjust for within-PHC clustering. Additionally, post hoc analysis was done allowing for clustered errors using the ‘cluster’ option in Stata. For outcomes analysed using ZINB regression, the intervention effect is estimated for all participants in one model as an adjusted odds ratio (OR) with 95% confidence interval (CI) for proportion with zero (i.e. no reported drinking), and adjusted count ratio among those with non-zero responses, respectively. For other continuous outcomes, the intervention effect was reported as the adjusted mean difference (AMD) and 95%CI. For binary outcomes, the intervention effect was reported as the adjusted prevalence ratio (aPR) and adjusted prevalence difference (aPD) estimated using the marginal standardisation technique with 95%CI for the prevalence ratios estimated using the delta method30. Moderators of treatment effect was assessed for a-priori defined moderators, viz. baseline severity of drinking, readiness to change and expectations of the usefulness of counselling. Sensitivity analyses for linear and logistic regression models included adjustment for counsellor as a random effect, and complete case analysis. Results are described in terms of the strength of evidence rather than statistical significance31 and the consistency of results for related outcomes are examined to interpret findings.

Economic evaluations (comparative analysis of costs and outcomes between intervention and control arms) were performed from the health care system and societal viewpoints. The costs of CAP were estimated by attaching appropriate local Indian unit costs to each resource required to deliver each component of the intervention, including training, supervision, travel and materials. Detailed information was also collected on total counsellor time for all attempted and completed contacts, including travel time and then valued using actual counsellor salary rates. The CSRI was used to record participants’ subsequent contacts with health services, including hospital inpatient and outpatient contacts, and also to document any patient- or family-borne costs, including time out of usual role. Time out of role for patients and their families was valued using relevant published mean wage rates.

Changes in principal outcomes were compared with changes in costs to calculate Incremental Cost Effectiveness Ratios (ICER). Cost per additional remission or non-drinker achieved and QALY gained were calculated. Differences in mean costs were compared using standard parametric tests. QALY scores were derived through transformation of WHO-DAS 12 item scores32. Missing values for QALYs and cost data were imputed and ICERs bootstrapped to derive 95% confidence intervals. Statistical uncertainty around the ICERs was explored through cost-effectiveness acceptability curves (CEAC) showing the likelihood that CAP would be cost-effective at different levels of willingness-to-pay thresholds. All costs are presented in 2015 International Dollars (<http://eppi.ioe.ac.uk/costconversion/>).

***Ethical issues:*** The trial protocol was approved by the Trial Steering Committee, and approval for the conduct of the trial was obtained from the Institutional Review Boards of the London School of Hygiene and Tropical Medicine, Sangath (the implementing institution in India), and the Indian Council of Medical Research. Written (or witnessed, if the participant is illiterate) informed consent was mandatory for enrolment. All consent procedures were audio-taped, with the patient’s approval.

***Role of funding agency:*** The sponsors of the study (the Wellcome Trust) had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The authors had access to the data in the study and had final responsibility for the decision to submit for publication.

VP, HAW, AN, BW, DM, AP and BB had full access to the data. VP and AN had responsibility for submission of the manuscript.

**RESULTS**

***Trial conduct:*** Of 73,887 PHC attenders assessed for eligibility, 16,007 were eligible for screening and 14,773 (92.2%) of these were screened using the AUDIT. Of these, 679 (4.6%) screened positive as harmful drinkers and 377 (55.7%) (188 in the CAP arm and 189 in the EUC arm) consented to participate and were enrolled; this constitutes the intention to treat sample (Figure 1). The leading reasons for ineligibility for screening included age less than 18 or more than 65 years (n=23,453, 40.5%), already been screened within last 3 months (n=10,046, 17.4%), not planning to be resident in the study area for the duration of the study (n=9,835, 17.0%), and resident outside the study catchment areas (n=6,014, 10.4%). Compared to those who declined participation, participants tended to be slightly older (Mean age in years [SD] 41.9 [11.4] vs 40.5 [11.7]; p=0.09), with a higher AUDIT score (Median [IQR]) 14 [13-16] vs 14 [13-16]; p=0.04), and higher PHQ-9 score (Median [IQR]) 4 [1-8] vs 3 [1-6]; p<0.001). There was also significant variation in participation by PHCs (p=0.001), with higher participation rates in some PHCs (>60%) than other PHCs (<60%).

Baseline characteristics were similar by arm (Table 1). Of the 377 participants, 336 (89.1%) were seen at the primary endpoint of 3 months, a figure similar to the number predicted for the sample size estimation. Participants who were lost to follow up (LTFU) tended to be younger with a lower AUDIT score (Web-Table 1). Reasons for LTFU included inability to track down the participant (n=26, 63.5%), refusal (n=12, 29.3%), and death (n=3, 7.3%). Outcome data were imputed for the remaining 41 LTFU participants. The intra-class correlation for ethanol consumption at 3 months within PHCs was 0.04, as predicted. There were no significant differences in the number of serious adverse events in the two arms (Web table 2).

[Table 1 and Figure 1 here]

***Process and fidelity assessments:*** Of the 188 participants in the CAP arm, 131 (69.7%) had a planned discharge and none was referred for specialist care. The mean number of sessions for those who had a planned discharge was 2.8 (95% CI 2.7-3.0), while those who had an unplanned discharge were most likely to drop-out after session 1 (mean sessions 1.1, 95% CI 1.0-1.3). Of the total 434 sessions delivered, 425 (98%) were delivered in face to face format; 33% of all sessions from session 2 onwards (n=257) were delivered at home, and 42/188 (22%)of participants had a significant other involved in at least one session. The mean duration of sessions was 42.4 minutes (95% CI 40.9-43.7). The mean TQS score (range 0-4) based on peer supervisor ratings (n=183) was 2.35 (95%CI 2.29, 2.41), comparable to the expert supervisor ratings (n=183, mean=2.44 (95%CI 2.36, 2.51), and to the mean score of the independent rater for 10% of randomly selected sessions (n=40; mean=2.64; 95% CI 2.42, 2.87), indicating adequate to good therapy quality.

***Effectiveness analyses:*** The proportion with remission on the AUDIT was significantly higher in the CAP arm than the EUC arm [59 (36.0%) vs 44 (25.6%)] scoring less than 8 on AUDIT; aPR=1.50, 95%CI 1.09, 2.07, aPD=12.6% 95%CI 5.9%, 27.1%). Analysis of daily ethanol consumption showed a significantly higher proportion of participants reporting no alcohol consumption in the past 14 days in the CAP arm than the EUC arm [68 (41.5%) vs 31 (18.0%); aOR=3.00; 95%CI 1.76, 5.13], and no difference in consumption among those who reported any drinking in this period (37.0g vs 31.0g; p=0.62). There was a significant intervention effect on PDA in past 14 days (mean 69.4% vs 54.4%; p<0.001) and no evidence of an intervention effect on percent days of heavy drinking, SIP, WHO-DAS, days unable to work, suicide attempts, and perpetration of intimate partner violence (Table 2). There was no statistically significant evidence of effect modification by baseline AUDIT score, readiness to change or expectations of the usefulness of counselling. Results were similar when adjusted for counsellor as a random effect, when using complete case analyses, and allowing for clustered errors.

(Table 2 here)

***Cost-effectiveness analyses:*** From the health system perspective, the total health care cost per person, i.e. including the intervention cost, was significantly higher in the CAP group than in the EUC group (MD= $24; 95% CI 5,44; p=0.014) with no significant difference in QALY scores (MD=-0.001; 95% CI -0.004, 0.001; p=0.29) (Table 3). Excluding intervention costs, there were no significant differences in aggregate health care costs although these were lower in the CAP arm. Medication~~s~~ costs were significantly lower in the CAP arm (MD=$-3, 95% CI -7, 0.6, p=0.017). From a health care system perspective the incremental cost per additional remission was $217 (95% CI $50, $1073); as Figure 3 shows if society is willing to pay up to the monthly minimum wage in Goa ($415)33 per individual in remission, CAP has a 85% chance of being cost effective. Similarly the cost per additional non-drinker was $124 (95% CI -$102, $325) with more than 99% chance of being considered cost effective.

(Table 3 here)

(Figure 3 here)

**DISCUSSION**

This study provides evidence of the effectiveness of Counselling for Alcohol Problems, a brief psychological treatment for harmful drinking delivered by non-specialist health workers (called counsellors) in routine primary care settings. CAP was associated with strong effects on abstinence and remission at three months post-enrolment, but no effects on other alcohol outcomes. The economic analysis indicates that CAP is likely to be cost effective when looking at remission and non-drinking outcomes.

Although the WHO recommends ‘brief counselling’ for the treatment of harmful drinkers34, almost the entire evidence in support of these recommendations are from high income settings7. Our results add to this evidence base by demonstrating that multi-session brief interventions for harmful drinking in primary care attenders can be effective when delivered by well trained and supervised health workers without any previous mental health training35. There are only two published RCTs from LMIC which have tested a NSHW delivered treatment for any form of AUD36,37. However, both these studies targeted hazardous and/or binge drinkers, and only one was based in primary care. Moreover, this is the first study of such an intervention which has included an economic evaluation. Thus the CAP treatment is the first contextually appropriate intervention for harmful drinking developed specifically to be delivered by lay counsellors in primary care settings in a LMIC, and this study provides evidence of effectiveness over enhanced usual care. One can speculate that when wider societal impacts (e.g. domestic violence, law enforcement costs) and savings to the family are considered, the economic case is further strengthened. Although this might strengthen the case for action it would need to be tested in future evaluations.

As described earlier BIs typically involve a brief conversation delivered to hazardous drinkers. For harmful drinkers ‘brief therapies’, focusing on specific behavioural change strategies, including providing clients with skills to deal with alcohol related problems, may be more appropriate38,39. The CAP treatment seeks to do just that. In India, a wide variety of alcoholic beverages are consumed and these include commercial, licit non-commercial and illicit home-brewed alcoholic beverages1. The CAP treatment is designed around assessment, personalised feedback and provision of skills needed to manage behaviours around drinking, irrespective of the specific type of alcohol consumed. The pattern of outcomes suggests that CAP had impacts upon those who chose abstinence as a treatment goal but did not have any effects on those who chose to continue drinking. This finding is congruent with the prevailing beliefs about the nature of alcohol problems in India, which place great importance on abstinence40. CAP did not have any significant effect on the adverse consequence of AUD. One probable reason for this finding is that the severity of harmful drinking is not great enough to register on tools like SIP whose previous use has been primarily for persons with dependent drinking, and consequently any intervention targeting such drinking patterns does not result in observed changes in these tools. Finally, it is possible that changes in outcomes like perpetration of domestic violence might require specific strategies targeting these behaviours and only targeting drinking as a mediating mechanism might not be effective in reducing domestic violence.

The limitations of the study are as follows. Reliance on self-reported outcome data entails vulnerability to social desirability bias, and this may have varied by randomised arm41. Reasons for such under-reporting might have included the participant actually believing the information they reported (self-deception), or ‘faking good’ to conform to socially acceptable values, avoid criticism, or gain social approval. However, biomarkers are insensitive to AUD except when severe, and alcohol treatment trials do not find advantages in using collateral reports or other alternatives42. Biomarkers may, in time, be developed for use in clinical trials, though at present the most promising ones available do not accurately and sensitively estimate levels of consumption43. The results in this paper are restricted to the primary end-point outcomes at three months where our interest lies in the response and remission of participants with harmful drinking to our treatment. We intend to assess the sustainability of these outcomes, including recovery from harmful drinking, at a 12 month follow-up. There are no established cost effectiveness thresholds for alcohol outcomes in India; we have conservatively assumed this is no more than the monthly wage for an unskilled worker. The lack of effect on QALYs may be seen in the context of doubt about the capacity of standard measures such as used here to capture improvements in alcohol-related quality of life44. It is also possible that there is a delayed response of reduced drinking or abstinence on QALYs and we could possibly expect to see a differential effect between the two arms at the 12-month outcome evaluation. Finally, it could be argued that our findings would not be generalisable to females as CAP was developed and tested only in males. However, none of the content of CAP is gender specific and there is no reason to believe that CAP would not work in females. Nevertheless, as alcohol consumption and resulting problems are starting to increase in India, albeit from an extremely small base, the demonstration that this treatment also works with female harmful drinkers will be an important task.

The strengths of this trial lie in its design and the rigorous procedures followed in its implementation. The ratings of therapy quality, both independent and by supervisors, and the relatively high levels of treatment completion testify to the acceptability and feasibility of this non-specialist delivered treatment. The high follow-up rates, the strict adherence to masking of the study investigators, a robust and transparent audit trail of data, testify to a high level of internal validity of the trial. Another strength was that intensive assessments were not done at baseline as it has been found that assessment reactivity can be problematic in AUD trials45,46 Considered together with the companion paper (Patel et al, concurrent submission)17, these two PREMIUM trials represent a significant achievement in global mental health for several reasons: first, the interventions are brief, delivered by lay people and provided to primary health care attenders with limited exclusion criteria, thus enhancing their generalizability to routine health care; second, the treatment was delivered by the same counsellors who concurrently delivered the treatment for depression, mimicking the real world where one would have a single counsellor in a health facility simultaneously treating the two leading mental health causes of the global burden of disease; third, the treatments are built around a theoretical orientation which have a strong grounding in the psychological treatment literature; fourth, the conduct of the trials were carried out in complete adherence with the protocol; and finally, they report the first evidence on the cost-effectiveness of psychological treatments for these two common mental health conditions from a LMIC.

In conclusion, this particular trial represents the first-ever publication from any LMIC evaluating the effectiveness and cost-effectiveness of any psychological treatment for harmful drinking in primary care. CAP is the first evidence based intervention for harmful drinking which can be delivered by NSHWs in routine primary care in a global context. Future research should focus on the dissemination and scaling up of CAP and evaluation of its effects on more severe forms of AUD, including as a component of a stepped care intervention for the full range of AUD. Our dissemination efforts for the CAP include the launching of an online platform for those interested to learn the treatment (https://nextgenu.org/login/index.php).

**Research in Context**

**Evidence before this study**

Brief psychological treatments, based on motivational enhancement, have been demonstrated to be effective for the management of harmful drinking and are recommended as first line interventions by WHO’s mhGAP programme for delivery in routine health care settings. However, the existing evidence has limited generalizability to many low and middle income countries (LMIC) where both supply side barriers (low availability of mental health professionals) and demand side barriers (low levels of mental health literacy) lead to large treatment gaps.

**Added value of this study**

This study reports the first findings from any LMIC evaluating the effectiveness and cost-effectiveness of a brief psychological treatment for harmful drinking, delivered by lay counsellors, in primary care. The brief (up to 4 session) psychological treatment (Counselling for Alcohol Problems), based on motivational enhancement, with additional behavioural and cognitive elements, was superior to enhanced usual care on all pre-specified primary clinical outcomes, but there was no effect on social and functional outcomes. The treatment was readily accepted by this treatment naïve population and was highly likely to be cost-effective in this setting.

**Implications of all the available evidence**

Brief psychological treatments for harmful drinking, based on motivational enhancement, are acceptable, feasible, and cost-effective, even when delivered by non-specialist health workers in routine health care settings in treatment naïve populations. Such treatments should be scaled up as one of the key strategies to address the large and rising global burden of alcohol use disorders.

**Conflict of interest**

D. McDaid has received honorariums for lectures not related to this work from Otsuka Pharmaceuticals, Janssen-Cilag Ltd and H Lundbeck A/S in the past two years. None of the other authors have any conflicts of interest.

**Table 1. Baseline characteristics of the trial participants by arm**

|  | **CAP arm (n=188)** | **EUC arm (n=189)** |
| --- | --- | --- |
| **Mean Age in years (SD)** | 42.3 (11.8) | 41.7 (10.9) |
| **Marital status** (n [%])  Married  Single  Separated/Divorced/Widower | 147 (78.2%)  38 (20.2%)  3 (1.6%) | 154 (81.6%)  32 (16.8%)  3 (1.6%) |
| **Occupation** (n [%])  Unemployed  Unskilled manual labour  Skilled manual labour  Clerical & professional | 25 (13.3%)  131 (70.0%)  13 (6.9%)  19 (10.1%) | 28 (14.7%)  135 (71.4%)  12 (6.3%)  14 (7.4%) |
| **Education** (n [%])  No formal education  Completed primary education  Completed secondary education or higher | 41 (21.8%)  90 (47.9%)  57 (30.3%) | 29 (15.3%)  107 (56.6%)  53 (28.0%) |
| **Patient’s expectation of usefulness of counselling** (n [%])  Not useful  A little/somewhat useful  Moderately useful  Very useful | 1 (0.5%)  36 (19.2%)  42 (22.3%)  109 (58.0%) | 2 (1.1%)  39 (20.6%)  38 (20.0%)  110 (57.9%) |
| **Mean AUDIT score** **(SD)** | 14.7 (2.1) | 15 (2.1) |
| **AUDIT score** (median [IQR]) | 14 (13-16) | 15 (13-16.5) |

**Table 2: Effectiveness results for the CAP trial for harmful drinking**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Outcome** | **CAP arm1**  **(n=164)** | **EUC arm1**  **(n=172)** | **Intervention effect (95% CI)2** | **p-value** |
| **Primary outcomes** | | | | |
| Remission (AUDIT<8) (n [%]) | 59 (36.0%) | 44 (25.6%) | aPR=1.50 (1.09, 2.07) | 0.01 |
| Daily standard ethanol consumed in the past 14 days3 |  |  |  |  |
| - Non-drinkers (n [%]) | 68 (41.5%) | 31 (18.0%) | aOR=3.00 (1.76, 5.13) | <0.001 |
| - Ethanol consumption among drinkers (g) (mean (SD)) | 37g (44.2) | 31g (27.8) | Count ratio=1.08 (0.79, 1.49) | 0.62 |
| **Secondary outcomes** | | | | |
| Percent of days abstinent (mean (SD)) | 69.4% (37.3%) | 54.4% (36.3%) | AMD=16.0% (8.1%, 24.1%) | <0.001 |
| Percent days of heavy drinking (mean (SD)) | 9.5% (2.5%) | 10.0% (2.4%) | AMD=-0.4% (-5.7%, 4.9%) | 0.88 |
| Short inventory of problems (SIP) (mean (SD)) | 7.9 (9.1) | 8.2 (8.9) | AMD=-0.03, (-1.93, 1.86) | 0.97 |
| WHO-DAS score (mean (SD)) | 4.4 (6.2) | 3.5 (5.3) | AMD=0.62 (-0.62, 1.87) | 0.32 |
| Days unable to work3  - None (n [%])  - Days unable to work when >1 day reported (mean (SD)) | 109 (67.3%)  11.5 (10.4) | 117 (68.0%)  11.2 (10.1) | aOR=1.02 (0.61, 1.69)  Count ratio = 0.92 (0.59, 1.43) | 0.95  0.70 |
| Number of suicide attempts (n [%]) | 0 (0%) | 3 (1.7%) | aOR=0  aPR=1.8% (-2.4%, 6.0%) | 0.25 |
| Perpetration of intimate partner violence4 (n [%]) | 12/127 (9.5%) | 16/140 (11.4%) | aOR=0.81 (0.39, 1.67)  aPR=3.0% (-10.4%, 4.4%) | 0.57 |

1 Among those with observed data at 3 months

2 Including imputed outcome data for those with missing data

3 Analysed with a zero-inflated negative binomial model which fits two parameters in one model i.e. the proportion with response of zero (e.g. no drinking in 14 days; or no days unable to work), and the mean count (e.g. ethanol consumption or days unable to work) among people with a non-zero (positive) response

4 Among married participants only

**Table 3: Costs per person and cost-effectiveness analyses at 3 months (2015 International $)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | | |  |  |
| **Type of Cost** | **CAP arm**  **(n=188)** | **EUC arm (n=189)** | **Mean Difference**  **(95% CI)** | **p-value** |
| **Health System Costs** | | | | |
| PHC Doctor Consultations (SE) | 7 (0.9) | 9 (1) | -2 (-5, 0.5) | 0.11 |
| Hospital Doctor Consultations (SE) | 3 (0.9) | 3 (0.7) | -0.3 (-2, 1.8) | 0.77 |
| Hospital Admissions (SE) | 13 (7) | 13 (4) | 0 (-16, 14) | 0.89 |
| Laboratory Tests (SE) | 4 (0.6) | 6 (1.5) | -3 (-6, 0.4) | 0.08 |
| Medicines (SE) | 4 (0.7) | 7 (1.3) | -3 (-7, 0.6) | 0.02 |
| Total Public Health Care Costs (SE) | 30 (7) | 38 (5) | -8 (-26, 11) | 0.4 |
| CAP Treatment (SE) | 33 (2) | 0 | 33 (2, 38) | <0.001 |
| **Productivity Costs** | | | | |
| Time costs to service users and families (SE) | 23 (3) | 19 (2) | 4 (-6, 9) | 0.8 |
| Productivity losses (SE) | 53 (8) | 64 (9) | -11 (-37, 9) | 0.24 |
| **Total Costs** |  |  |  |  |
| Health system perspective (SE) | 64 (8) | 39 (6) | 24 (5, 44) | 0.01 |
| Societal perspective (SE) | 139 (15) | 122 (12) | 20 (-18, 59) | 0.3 |
| **Cost effectiveness analyses** | | | | |
| QALYs gained (SE) | 0.220  (0.001) | 0.221  (0.001) | -0.001 (-0.004, 0.001) | 0.29 |
| **Health system perspective** | | | **Societal perspective** | |
|  |  | |  | |
| Cost per remission | 217 (50, 1073) | | 150 (-216, 1051) | |
| Cost per non-drinker | 124 (-102, 325) | | 86 (29, 265) | |
| Cost per QALY gained (95% CI) | -17,710 (-220,368, 141,383) | | -12,267 (-104,070, 133,648) | |

**Figure 1: Counselling for Alcohol Problems trial flow chart**

**Screening and recruitment**

**3-Month Outcome**

**Treatment Allocation**

**Assessed for eligibility:**

N= 73,887

**Total screened on AUDIT:**

N= **14773 (92.2%)**

**AUDIT score 12 to 19**

**N= 679 (4.6%)**

* **AUDIT score <12**: n= **13888 (94.0%)**
* **AUDIT score 20+** n= **206 (1.4%)**

Total n=14094

**Allocated to CAP arm**

**N = 188 (49.9%)**

* Not met inclusion criteria: n = **57880** (**78.3%**)

**Allocated to EUC arm**

**N= 189 (50.1%)**

* Declined to participate: n=**301 (44.3%)**

**Eligible for screening:**

N= **16007 (21.7%)**

Refused: n= **1234** (**7.7%**)

3-month FU

**N=164 (87.2%)**

3-month FU

**N=172 (91.0%)**

**Consultation with PHC doctor**

**Informed consent and randomised**:

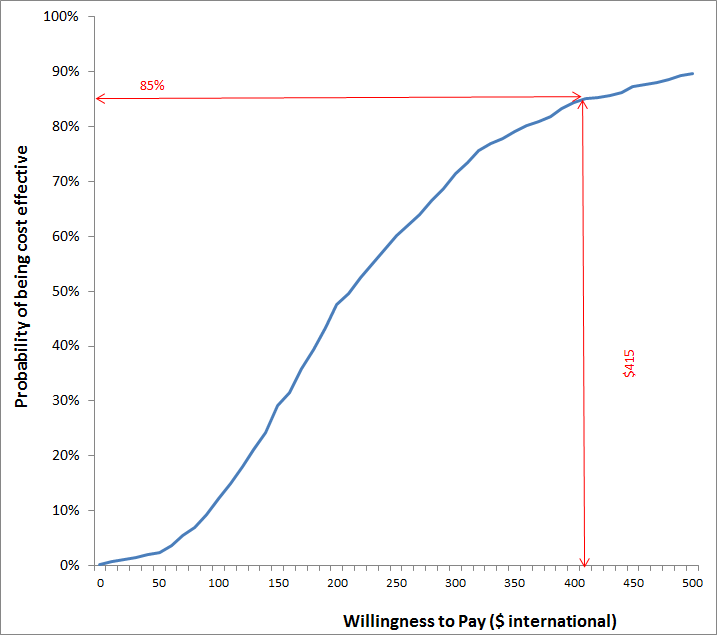
N= **377 (55.7%)**

**Figure 2: Ethanol consumption at 3 months by baseline AUDIT score**

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**Figure 3:** **Cost-effectiveness acceptability curve: willingness to pay per remission achieved from CAP from a health system perspective.**



**Web-table 1: Comparison of participants who were followed up and LTFU at 3 months**

|  | **Lost before 3 month evaluation**  **(n=41; 11%)** | **Completed 3 month outcome evaluation (n=336; 89%)** | **p-value** |
| --- | --- | --- | --- |
| Age (years) (mean [SD]) | 38.5 (12.7) | 42.4 (11.2) | 0.04 |
| **Marital status** (n [%])  Married  Single  Separated/Divorced  Widowed | 28 (68.3%)  12 (29.3%)  1 (2.4%)  0 (0%) | 273 (81.3%)  58 (17.3%)  1 (0.3%)  4 (1.2%) | 0.07 |
| **Occupation** (n [%])  Unemployed  Unskilled manual labour  Skilled manual labour  Clerical & professional | 2 (4.9%)  34 (82.9%)  3 (7.3%)  2 (4.9%) | 51 (15.2%)  232 (69.1%)  22 (6.6%)  31 (9.2%) | 0.20 |
| **Patient’s expectation of counselling** (n [%])  No/a little/somewhat useful  Moderately or very useful | 4 (9.8%)  37 (90.2%) | 74 (22.0%)  262 (77.8%) | 0.07 |
| **AUDIT score** (median [IQR]) | 14 (13-16) | 15 (13-17) | 0.34 |
| **AUDIT score** (mean (SD)) | 14.6 (1.9) | 14.9 (2.1) | 0.32 |
| **AUDIT category** (n [%])  Score 12-15  Score 16-19 | 30 (73.2%)  11 (26.8%) | 207 (61.6%)  129 (38.4%) | 0.17 |

**Web-Table 2: Serious adverse events by trial arm**

| **Type of SAE** | **CAP**  N | **EUC**  N | **p-value** |
| --- | --- | --- | --- |
| Any SAE | 6 | 13 | 0.11 |
| Death | 0 | 3[[1]](#footnote-1) | 0.25 |
| Suicide attempt | 0 | 3 | 0.25 |
| Unplanned hospitalisation | 6 | 7 | 1.00 |

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