

# Implementing primary health care-based measurement, advice and treatment for heavy drinking and comorbid depression at the municipal level in three Latin American countries: final protocol for a quasi-experimental study (SCALA study)

**Eva Jane Llopis**

Universitat Ramon Llull

**Peter Anderson** (✉ [peteranderson.mail@gmail.com](mailto:peteranderson.mail@gmail.com))

<https://orcid.org/0000-0003-4605-9828>

**Marina Piazza**

Universidad Peruana Cayetano Heredia

**Amy O'Donnell**

Newcastle University Institute for Health and Society

**Antoni Gual**

Hospital Clinic de Barcelona

**Bernd Schulte**

Universitätsklinikum Hamburg-Eppendorf

**Augusto Perez Gomez**

Universidad Nacional de Colombia Facultad de Medicina

**Hein de Vries**

Universiteit Maastricht

**Guillermina Natera Rey**

Instituto Nacional de Psiquiatria Ramon de la Fuente Muniz

**Dasa Kokole**

Universiteit Maastricht

**Ines Bustamente**

Universidad Peruana Cayetano Heredia

**Fleur Braddick**

Hospital Clinic de Barcelona

**Juliana Mejia Trujillo**

Universidad Nacional de Colombia Facultad de Medicina

**Adriana Solovei**

Universiteit Maastricht

**Alejandra Perez de Leon**

Instituto Nacional de Psiquiatria Ramon de la Fuente Muniz

**Eileen Kaner**

Newcastle University Institute for Health and Society

**Silvia Matrai**

Hospital Clinic de Barcelona

**Jakob Manthey**

Technische Universität Dresden

**Liesbeth Mercken**

Universiteit Maastricht

**Hugo Lopez Pelayo**

Hospital Clinic de Barcelona

**Gill Rowlands**

Newcastle University Institute for Health and Society

**Christiane Schmidt**

Universitätsklinikum Hamburg-Eppendorf

**Jurgen Rehm**

Centre for Addiction and Mental Health

---

## Study protocol

**Keywords:** Primary health care, municipal action, heavy drinking, comorbid depression, Institute for Health Care Improvement, implementation, measurement of alcohol consumption, AUDIT-C

**Posted Date:** February 6th, 2020

**DOI:** <https://doi.org/10.21203/rs.2.22734/v1>

**License:**   This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

---

# Abstract

**Background :** While primary health care-based prevention and management of heavy drinking is clinically effective and cost-effective, it remains poorly implemented in routine practice. Systematic reviews and multi-country studies have demonstrated the ability of training and support programmes for healthcare professionals to increase primary health care-based measurement and brief advice activity to reduce heavy drinking. However, gains have been only modest and short term at best. WHO studies have concluded that a more effective uptake could be achieved by embedding primary health care activity within broader municipal-based support. **Methods :** A quasi-experimental study will compare primary health care-based prevention and management of heavy drinking in three intervention municipal areas from Colombia, Mexico and Peru with three comparator municipal areas from the same countries. In the implementation municipal areas, primary health care units will receive training embedded within ongoing supportive municipal action over an 18-month implementation test period. In the comparator municipal areas, half the units will receive training, and the other half will continue with practice as usual. The primary outcome is the proportion of the adult population (aged 18+ years) registered with the unit that has their alcohol consumption measured. Return-on-investment analyses and full process evaluation will be undertaken, coupled with an analysis of potential contextual, financial and political-economy influencing factors. **Discussion :** This multi-country study will test the extent to which embedding primary health care-based prevention and management of heavy drinking within supportive municipal action leads to improved scale-up of more patients having their alcohol consumption measured, and subsequently receiving appropriate advice and treatment.

## Background

This paper outlines the protocol for a quasi-experimental study [1] to test the implementation of primary health care-based measurement, advice and treatment for heavy drinking and comorbid depression at the municipal level in three Latin American countries, Colombia, Mexico and Peru (SCALA study).

Heavy drinking is a cause of considerable disability, morbidity, and mortality [2]. Heavy drinking is a causal factor for some communicable diseases (including TB and HIV/AIDS), for many non-communicable diseases (including cancers, cardiovascular diseases and gastrointestinal diseases) and for many mental and behavioural disorders, including depression, dementias and suicide [3,4].

In PHC settings, two-fifths of people with heavy drinking have depression, with risks of incident depression higher for heavier as opposed to lighter drinkers [5]. In addition to its role in the aetiology of depression, heavy drinking is associated with worsening the depression course, including suicide risk, impaired social functioning and impaired health care utilization [6]. Given the strong comorbidity between heavy drinking and depression, our protocol includes screening for depression for those patients identified as heavy drinkers, with appropriate referral or PHC support for treatment.

A robust and extensive body of literature demonstrates the range of evidence-based strategies that can be implemented to reduce heavy drinking in health care settings [14]. Questionnaire-based measurement and brief advice programmes delivered in PHC are effective [15] and cost-effective [16, 17] in reducing heavy drinking. In addition to brief advice, treatment for heavy drinking includes cognitive behavioural therapy and

pharmacotherapy, both of which are found to be effective in reducing heavy drinking [18]. Were the proportion of eligible patients receiving advice and treatment for heavy drinking to increase to 30% of eligible patients, the prevalence of harmful use of alcohol could decrease by between 10% and 15% across OECD member countries [19]. However, to date, measurement and brief advice and treatment programmes have failed to achieve widespread take-up [19].

Two systematic reviews [20,21] and two multi-country studies [22-24] have demonstrated that the proportion of PHC patients whose alcohol consumption is measured, and of heavy drinking patients given advice can be increased by providing training and support to PHC providers, albeit from very low baseline levels, and with effects not generally sustained over the longer term. Moreover, whilst there has been some previous research in countries of Latin America [25-30], most implementation work to date has been undertaken in high-income countries. The SCALA study will build on previous evidence [31] to fast-track scale-up research and practice in Latin American primary health care settings.

Out of a range of implementation frameworks that include a sequential approach for scale-up, and that provide practical guidance for how to work with organizations, health systems, and communities to implement and scale-up best practices [32-39], we adopt the Institute for Healthcare Improvement's (IHI) Framework for going to Full Scale, which identifies adoption mechanisms and support systems for use across sequential steps, and describes the implementation methods that can be used at each step [40].

The second barrier is that standard cut-off points for the frequently used alcohol measurement instrument, AUDIT-C [46] (commonly a score of five for both men and women, or five for men and four for women) to trigger advice are too low [47], being equivalent to an average daily alcohol consumption of about 20 grams of alcohol (around 2 standard drinks) or less [48]. Practitioners may well find it problematic to give advice at such levels, which would also have huge time implications, with one in three or four patients being eligible for advice in many countries, under this criterion. We have argued to adopt similar models to blood pressure, where cut-off points for managing raised blood pressure are often determined by levels of blood pressure at which treatment has shown to be effective [49, 50]. Similarly, cut-off points for brief advice could be the baseline levels of alcohol consumption found in the randomized controlled trials that have investigated the effectiveness of PHC-delivered brief advice. In the first Cochrane review of the topic that focused on primary health care, mean baseline levels were 313 grams of alcohol per week [51], equivalent to an AUDIT-C cut-off of 8 [48].

In the SCALA study, we implement three interventions (independent variables) for the PHCU:

- i. Training of providers (present, versus absent); and,
- ii. Intensity of clinical package and training (standard, versus short, versus none);
- iii. Community integration and support (municipal action present, versus absent).

The main outcome (dependent variable) is the cumulative proportion of the adult (aged 18+ years) population registered with the PHCU that has their alcohol consumption measured within the 18-month implementation test period (defined as coverage). Three hypotheses are to be tested:

**Hypothesis 1:** Municipal action leads to more sustainable coverage. After 18 months, the difference in coverage between municipal action present and municipal action absent is larger than after 12 months;

**Hypothesis 2:** Training leads to higher coverage than no training; and,

**Hypotheses 3:** In the presence of municipal action, the short clinical package and short training do not lead to less measurement coverage than the standard clinical package and standard training.

## Methods

The study is a quasi-experimental design [1], comparing changes in measurement and assessment for alcohol consumption and comorbid depression, and, if needed, advice and/or referral for treatment between primary health care units (PHCUs) in intervention municipal areas and PHCUs in similar comparator municipal areas. In 2017, prior to a grant application, we published a pre-protocol for a three-country study to test the scale-up of primary health care-based programmes to identify and manage the harmful use of alcohol and comorbid depression [56]. Since the application, and during the grant negotiation and planning phase, the design of the study has changed considerably, essentially moving from a two-arm design to a four-arm design, and changing the primary outcome measure to the proportion of the adult population registered with a PHCU that has their alcohol consumption measured, Supplement Box 1. With all changes approved by the concerned ethics committee, this paper outlines the final protocol for a quasi-experimental study to test the implementation of primary health care-based measurement, advice and treatment for heavy drinking and comorbid depression at the community level in three Latin American countries, Colombia, Mexico and Peru (SCALA study).

Intervention municipal areas are investigator-selected from Bogotá (Colombia), Mexico City (Mexico) and Callao – Lima (Peru). Comparator municipal areas are investigator-selected in the same cities, on the basis of comparability with the intervention municipal area in terms of socio-economic and other characteristics which impact on drinking, health care and survival, comparable community mental health services, and sufficient geographical separation to minimize spill over effects from the intervention municipal area. Randomized selection of the municipal areas was not feasible due to organizational limitations. Municipal areas are chosen as a scalable implementation unit at mesosystem level that can be replicated as the intervention is scaled-up [40], given their jurisdictional responsibilities for prevention and health care services.

The units of allocation and analysis, i.e., study participants, are primary health care units (PHCUs) and the providers working in them. Within each PHCU, eligible providers include any fully trained health care provider working in the PHCU and involved in medical and/or preventive care. The providers sign an informed consent for their participation. The overall study design is summarized in Figure 1, a CONSORT flow diagram.

For the first six months of an 18-month implementation and test period, a four-arm design is adopted, Figure 2. Within each municipal area, PHCUs are systematically invited to join the study, until nine PHCUs agree. Within the comparator municipal area, four PHCUs are randomly allocated to control (Arm 1), and five PHCUs

to receive short training to implement a short clinical package (Arm 2). Within the intervention municipal area, in which all PHCU receive municipal action, five PHCUs are randomly allocated to receive short training to implement a short clinical package (Arm 3), and four PHCUs to receive standard training to implement a standard clinical package (Arm 4). Random allocation was undertaken using Excel random number generator.

By Month 6, Hypotheses 3, i.e., non-superiority of Arm 4 (longer package with municipal action and training) over Arm 3 (short package with municipal action and training) will be tested. In the presence of clinical equivalence of a relative difference of the primary outcome, i.e., the cumulative coverage of patients whose alcohol consumption is measured, of less than 10%, Arm 4 will be replaced by Arm 3 from month 8 onwards, Figure 3.

The inputs to each of the four arms are summarized in Supplement Tables 1 and 2, and the standard and shorter clinical pathways that are implemented are summarized in Supplement Figures 1 and 2.

## **Data collection and instruments**

### ***Municipal level information***

At the level of the municipal area (or, when not available, at whole city, regional or country level), the following information will be collected from routinely available data on socio-demographic factors, alcohol and mental health data, health system structures, quality of life, sustainable governance and values, Supplement Table 3.

### ***PHCU and provider level information***

All contacted PHCU, including those who did and did not agree to be part of the study, will provide information on:

- Numbers of registered patients, divided into age 0-17 years and 18+ years; and,
- Numbers and professions of provider staff (including physicians, nurses, nurse technicians, midwives, psychologists, social workers, and others).

At recruitment, PHC providers will provide data on their:

- Age;
- Gender;
- Profession (doctor, nurse, practice assistant etc.);
- Time worked in the PHC.

Since we are unable to randomize the municipal areas involved, we will use propensity score matching (PSM) based on data collected at the level of the municipal area and the PHCU, to take into account potential confounding variables between comparator and intervention municipal areas, and minimise bias on account of these.

### ***Provider-based measurement and assessment of alcohol consumption and comorbid depression and record of advice and treatment given (tally sheets)***

Based on the validated methodology of the ODHIN project [22,24], PHC providers will document activity by completing anonymous paper tally sheets that record eligible patients' (aged 18+ years) AUDIT-C scores [57], and, if administered, AUDIT-10 [58], PHQ-2 [59] and PHQ-9 [60] scores, and the advice or treatment given to each patient. The tally sheets will record the age, sex, and educational level of the patient, the latter as a proxy measure of socio-economic status. Data will be collected for the one-month baseline measurement period, and for each calendar month of the 18-month implementation and test period. PHCUs will return data on the number of adult (aged 18+ years) consultations per provider for the one-month baseline measurement period, and for each of the 18 months of the implementation and test period. Monthly data will be collected and reported with accumulation of coverage over time. Formal reporting will be undertaken at baseline, and for coverage achieved by month 12 and by month 18 of the 18-month implementation and test period. Tally sheets will include an identifying code of the provider, PHCU, country and study arm, but no identifying code of the patient. Data will be extracted and sent to the project's data warehouse at Technical University Dresden on a monthly basis.

### ***Extended Tally Sheets***

As part of quality control, in all four Arms at two time points, during the 18-month implementation and test period (months 3 and 15), providers will complete extended tally sheets on two separate days in each month. The extended tally sheets will include an identifying code of the provider but no identifying code of the patient. The extended tally sheet will include: additional information from the patient on alcohol knowledge [61], social norms [62] and health literacy [63] applied to alcohol, as it informs the content of advice given; and, additional information from the provider on contextual characteristics that informed their advice giving. The extended tally sheets will include a consent form for the patient and self-completed additional questions for the patient to complete, once the consultation has ended.

### ***Provider-based attitudes and experiences.***

At recruitment, and at two time points during the 18-month implementation period (months 3 and 13), providers will provide data on their attitudes and experiences to working with patients with heavy drinking and comorbid depression, Supplement Table 4.

Providers will complete a short questionnaire after each of the training and booster sessions that they attended (before baseline assessment and at months 4 and 8). The questionnaires that are adapted based on specific training contents (standard or shorter package), will assess the participants' experience of the training, measuring satisfaction with the components of the training aspects, as well as their perceived utility. Two measures included in the main provider questionnaires, SAAPPQ [64] and self-efficacy [65], will be included in order to assess the specific impact of the training, independent of the effect of the implementation of the intervention.

The specific content, number and timing of the training-related questionnaires will depend on the study arm: Arm 2 and 3 participants will fill in two questionnaires, one after training and one after the booster session; while Arm 4 participants will fill in four questionnaires, one after each of the two training sessions and one after each of the two booster sessions.

### ***Self-completed additional questions by patient***

On two separate days, during months 3 and 13, following the consultation with the extended tally sheet, patients who are able to read and write will be invited to give consent to self-complete additional questions in the waiting room before leaving the PHCU, handing the completed questions to a researcher in attendance. No patient identifying information will be included in the patient questionnaires. Six domains, serving as quality control, will be included:

- i. AUDIT-C [57];
- ii. PHQ-2 [59];
- iii. Experiences of the consultation;
- iv. Views on being asked about alcohol consumption;
- v. Health Literacy [63] as it applies to alcohol; and,
- vi. Exposure to communication and media campaigns on alcohol.

On each day, 270 patient questionnaires will be collected across all PHCUs, with up to 1080 questionnaires completed in total across the four days.

### ***Key informant interviews***

A number of individual or group interviews will be undertaken throughout the project with key stakeholders – providers, user panel members, CAB members, project partners, and any other people involved in the implementation of the SCALA project. Depending on the stakeholder and their involvement in the project, the topics of the interviews will cover topics such as the necessary adaptation to the protocol; the experience of implementing the programme in primary health care practice; and the perception of the municipal support and the community campaigns.

### ***Observations***

The training sessions with the primary health care providers, and the meetings of the CABs will be observed by a neutral observer in order to take note of additional possible barriers in the implementation of the protocol that emerge through the training sessions and meetings. Participant responsiveness will also be observed.

### ***Economic data for return-of-investment analyses***

Within SCALA, we will conduct return-on-investment (RoI) analyses, by assessing for each EURO invested in scaling up delivery of screening and brief interventions in primary health care in Columbia, Mexico, and Peru, how many EUROs will be saved by reductions in future health care utilization. The return of investment will be defined as the [return on investment = (gain from investment – cost of investment) / cost of investment]. For details on the data required for RoI analyses, Supplement Table 5.

For the RoI analyses, the effects of increased coverage of alcohol brief advice among primary health care patients will be modelled using effect sizes from previous meta-analyses [64]. To translate the reduced intake of alcohol into health gains, we will calculate alcohol-attributable fractions for major disease and injury

categories. These fractions will then be applied to the cost data outlined in Supplement Table 5 to estimate the alcohol-attributable costs per disease category.

## **Process evaluation**

As the intervention is embedded in a complex system involving actions and actors at different levels (individual, organisational, municipal), a thorough process evaluation will be carried out to complement and better understand the outcomes. Through the process evaluation, the implementation with its fidelity and adaptation will be assessed, along with the drivers of scale-up and contextual factors influencing the implementation, the drivers, and the outcomes. This will be achieved in four blocks: driver diagram creation; barriers and facilitators analysis; assessment of implementation, mechanisms of impact and context; and, further contextual and policy analysis.

### ***Driver diagrams***

Driver diagrams [65] will be used in order to describe the intervention and its causal assumptions, providing the theory of change through displaying what contributes to intervention aim and what are the relationships between primary drivers, secondary drivers and specific change ideas/activities. The initial general driver diagram, Supplement Figure 3, will be modified based on local contexts and adapted throughout the duration of the project in order to understand how scale up varies in the different cities.

### ***Barriers and facilitators assessment***

Factors influencing the implementation of the SCALA protocol will be assessed before the implementation, as well as monitored throughout. The anticipated barriers and facilitators to implementation will be assessed through development of evaluation tool based on literature review [66-68] and implementation framework [69], with subsequent refinement and adaptation to the local context through focus group discussions and workshops with the CABs. The aim of the tool is to identify the barriers that would have to be addressed and monitored throughout implementation and the facilitators that would incentivize and engage providers and the PHCU unit managers in uptake and scaling up of the SCALA protocol. The experienced barriers and facilitators will be further monitored through meeting observations, provider questionnaires and interviews, as well as interviews with other involved stakeholders (e.g. CAB members, PHCU managers).

### ***Implementation, mechanisms of impact and context***

The factors influencing the progress from scale-up to outcomes will be identified and documented based on UK Medical Research Council guidance [70], analysing factors within five groups: (i) description of intervention and its causal assumptions; (ii) context; (iii) implementation; (iv) mechanisms of impact; and, (v) outcomes. All aspects of the intervention will be taken into consideration: the intervention, intervention tailoring, training, training tailoring, as well as the municipal action, consisting of the CABs and the communication campaign, combining both quantitative and qualitative methods in order to obtain a comprehensive picture of the integration and interaction of included variables. A detailed description of the topics of interest and accompanied methods is presented in Supplement Table 6.

The five groups will be assessed as follows:

- i. *Description of the intervention.* The description of the intervention and its causal assumptions draws from the previously described driver diagram;
- ii. *Implementation.* Delivery of the training will be assessed through document analysis (reports from training), observation and self-reports from the trainers. Delivery of the intervention will be assessed through document analysis, interviews with patients and providers. The areas of focus will be fidelity, adaptation, dose and reach. Implementation of the CAB meetings and community action will be assessed mainly through document analysis, as well as key informant interviews;
- iii. *Mechanisms of impact.* The following three areas will be covered: participant responses to the intervention, mediators and unintended consequences. Mechanisms of impact of intervention delivery will be assessed through patient and providers' questionnaires. The patient interviews will focus on their responsiveness to the intervention, specifically looking at perceived acceptability. In order to evaluate participants' responses to the training, a post-training questionnaire examining satisfaction with the training and perceived utility of training sessions will be applied, triangulated with data from observation and trainers' self-report. Additionally, providers' self-efficacy will be tested as potential mechanism of impact that links the implementation to the outcomes. Mechanisms of impact of the CAB meetings and community action will be examined through key informant interviews and questionnaires. Specific focus will be placed on perceptions and mechanisms of actions of the communication campaign, examining its effect on attitudes and social norms of both providers and patients;
- iv. *Context.* Contextual factors that should be considered in order to better understand the success of the intervention will be assessed through meeting observation, document analysis, and provider questionnaires, as well as stakeholder interviews, with the main focus primarily on individual and organisational level characteristics of the context. For the training evaluation, context will be assessed through observation and trainers' self-report. Context of municipal level actions will be assessed through key informant interviews. Additionally, contextual and policy factors on national and municipal levels will be assessed as described below.
- v. *Outcome.* The data collected through process evaluation will be combined with the outcomes and presented within the RE-AIM framework [71-73], evaluating SCALA's impact across the dimensions of reach, effectiveness, adoption, implementation and maintenance.

### ***Contextual and policy factors***

Based on methodology of Ysa et al [74], contextual and policy factors on national and municipal level will be identified through document analysis and key informant interviews. The main variables considered for contextual analysis will be: (1) available data similar to that of the OECD better life initiative [75]; (2) Sustainable Governance Indicators [76]; and, (3) World Values Survey data [77]. For policy analysis, the information sought will be for a for alcohol policy-related strategies, action plans, legislation and evaluations, both on country and municipal level. The existing contextual and policy factors will be mapped onto the test of the scale-up of the SCALA package to describe and identify those factors on national and municipal level that might influence going to full-scale beyond the tested scalable units.

### **Outcomes**

### ***Primary outcome:***

The primary outcome will be the cumulative proportion of the number of adults (aged 18+ years) registered with the PHCU that have their alcohol consumption measured with a completed AUDIT-C instrument during the study period (coverage). The number of adults registered is provided by the administrative office of the PHCU and includes all adult patients covered by the PHCU, whether or not they consult during the 18-month implementation test period.

### ***Secondary outcomes:***

- **Proportion of consulting patients who have their alcohol consumption measured by AUDIT-C:** Calculated as the number of adults who have their alcohol consumption measured by AUDIT-C divided by the total number of adults who consult the PHCU during the same time period per participating provider and per PHCU;
- **At risk population receiving advice and/or treatment for heavy drinking:** Calculated as the number of adults with an AUDIT-C score of 8+ who receive brief advice and/or referral for their heavy drinking divided by the total number of patients with an AUDIT-C score of 8+ per participating provider and per PHCU. Information will also be collected on the number of patients with an AUDIT-C score of <8 who receive brief advice and/or treatment for their heavy drinking;
- **Proportion of patients with AUDIT-C score of 8+ who receive assessment for depression:** Calculated as the number of consulting adults with an AUDIT-C score of 8+ who complete PHQ-2 divided by the total number of patients with an AUDIT-C score of 8+ per participating provider and per PHCU;
- **At risk population receiving advice and/or treatment for comorbid depression:** Calculated as the number of adults with a PHQ-2 score of 3+ who receive a patient leaflet and/or referral for their depression divided by the total number of patients with a PHQ-2 score of 3+ per participating provider and per PHCU; and,
- **Provider attitudes:** Attitudes of the participating providers will be measured by the short version of the Alcohol and Alcohol Problems Perception questionnaire, SAAPPQ [64]. The responses will be summed within the two scales of role security and therapeutic commitment. Individual missing values for any of the items in a domain will be assigned the mean value of the remaining items of the domain before summation.

### **Statistical tests of key hypotheses**

**Primary study goal:** Multilevel regression analyses will be undertaken at 12 months' time of the implementation test period, using cumulative results at months 1-12, and at 18 months' time using cumulative results months 1-18. Both analyses will include co-variables of country and results during baseline month, analysed at the levels of the PHCU by study arm, taking into consideration the hierarchical nature of the data. For any PHCU that drops out during the study, outcome values for subsequent measurement points will be set at the last value obtained.

### **Hypothesis 1**

### Dependent variables:

- For each PHCU, cumulative results of months 1-18 of number of patients whose alcohol consumption is measured with AUDIT-C per 1,000 registered patients; and cumulative results of months 1-12 per 1,000 registered patients.

### Random effects:

- Country as random intercept (test for inclusion)

### Independent variables:

- Proportion of consulting patients who have their alcohol consumption measured with a completed AUDIT-C instrument during the baseline measurement month
- Conditions:
  - Municipal action (yes vs. no)
  - Training (yes vs. no)

It is postulated that coverage for Arms 3 and 4 will be significantly higher than for Arms 1 and 2.

## **Hypothesis 2**

Training leads to higher coverage than no training. For both months 1-12 and months 1-18, compare cumulative coverage as per primary outcome between Arms 1 and 2 via multilevel regression analyses.

### Dependent variable

- Cumulative results months 1-12, and cumulative results months 1-18 of number of patients whose alcohol consumption is measured with AUDIT-C per 1,000 registered patients with
- PHCU

### Random effects:

- Country as random intercept (test for inclusion)

### Independent variables:

- Conditions:
  - Training (Arm 2 vs. Arm 1)
- Covariates:
  - Proportion of consulting patients who have their alcohol consumption measured with a completed AUDIT-C instrument during the baseline measurement month

It is postulated that coverage for Arm 2 will be significantly higher than for Arm 1.

### Hypotheses 3

In the presence of municipal action, the short clinical package and short training do not lead to less coverage than the standard clinical package and standard training. In the presence of clinical equivalence of a relative difference of cumulative coverage of patients screened by less than 10% by month 6, the difference between Arm 3 and Arm 4 will be assessed with regression analyses. If Arm 4 is not superior to Arm 3, both arms will be collapsed into Arm 3 (shorter package) from month 8 onwards.

#### Dependent variable

- Cumulative results months 1-6 per 1,000 patients

#### Random effects:

- Country as random intercept (test for inclusion)

#### Independent variables

- Condition:
  - Length of clinical package (longer = arm 4 vs. shorter = arm 3)
- Covariates:
  - Proportion of consulting patients who have their alcohol consumption measured with a completed AUDIT-C instrument during the baseline measurement month

It is postulated that Arm 4 is not significantly superior to Arm 3.

### **Sample size calculations for main hypothesis**

As the outcome of the primary study goal is predicted to be Arm3 > Arm2 > Arm1, we compared both Arm 2 > Arm 1, and Arm 3 > Arm 2.

Our power calculations are based on the following assumptions: given an average size of a PHCU of approximately 15,000 adults, with an average of 1500 new consultations per month, we expect a cumulative coverage after 12 months of 0.0325 of the registered adult population to have had their alcohol consumption measured in the control condition (Arm 1) (data extrapolated from month 3 and month 9 assessments of control group from ODHIN study [22, 24]; Anderson, personal communication). For the short clinical package and short training (Arm 2), we expect this to increase to 0.075 (data extrapolated from month 3 and month 9 assessments of training group from ODHIN study [22, 24]; Anderson, personal communication). Although the WHO Phase IV study predicts an additional beneficial impact of municipal support [41], precise empirical data is not available – however, we consider an estimate for Arm 3, with municipal support, to be 0.15, a proportion that would need to be achieved to consider municipal support to be worthwhile. To detect the difference between Arm 2 and Arm 1, assuming a design effect of 15 PHCUs (clusters) across the three municipal areas in Arm 2, with 15,000 patients (items), and 12 PHCUs (clusters) in Arm 1, with 15,000 patients (items), with an ICC for PHCUs of 0.03 (data from ODHIN study [22, 24]; Anderson, personal communication) we would have

82% power at a significance level of 5% [78]. For the difference between Arm 3 and Arm 2 (15 PHCUs/clusters in each arm), we would have 96.5% power.

## Discussion

This protocol outlines a quasi-experimental study [1] to test the extent to which embedding PHC-based measurement and brief advice activity within supportive municipal action leads to improved scale-up of an intervention package, with more patients having their alcohol consumption measured, and with heavy drinkers receiving subsequent appropriate advice and treatment.

The study has several features worth mentioning. It:

1. uses a theory-based approach [69, 79, 80] to tailoring clinical materials and training programmes, creating city-based Community Advisory Boards, and user-based User Panels to ensure that tailoring matches user needs, municipal services [81], and co-production of health [82];
2. sets a higher cut-off score for AUDIT-C (8+) than is commonly used to trigger advice-giving, matching definitions of heavy drinking [83, 84], and similar to baseline levels of alcohol consumption in PHC-based trials to reduce heavy drinking [51]. We set the same cut-offs for men and women, based on epidemiological evidence [85], and to minimize unintended consequences of using different cut offs for men and women [86]. We recognize the importance of comorbid depression [87,88] by building in identification, management, and referral mechanisms [89, 90];
3. tests for non-superiority of implementing a standard measurement and 5-minute brief advice intervention with six hours of training, compared with implementing a shorter 1-minute brief advice intervention with three hours of training, taking into account that brief advice is as effective and cost-effective as more extended advice or treatment in reducing heavy drinking [52, 91, 92], and the need for very brief clinical and training programmes for time-constrained providers;
4. tests the added value of embedding and implementing PHC activity within municipal-based adoption mechanisms and support systems [40], and communication campaigns over and above training programmes solely directed to primary health care providers;
5. has a longer time frame (18 months) than is traditionally used in implementation studies [93, 94], to assess longer term impacts; and,
6. gives considerable emphasis to process evaluation [70], developing logic models to document the fidelity of all implementation strategies, and to identify, the drivers and barriers and facilitators to successful implementation and scale-up, and the political and economic contextual factors that might influence scale-up.

There are some limitations to the study design. A trial with random assignment of municipal areas is not feasible due municipal-based political and technical considerations. As we are unable to randomize the involved municipal areas, we adopt a quasi-experimental design [1], trying to optimize comparator municipal areas for confounding, and by using propensity score matching (PSM). While full comparisons via randomization, and thus establishment of causality, are not possible, together with the qualitative evaluation component of the study, we will be able to clearly identify the mechanisms which were crucial in leading to

the outcomes. According to a recent 7-item checklist for classifying quasi-experimental studies for Cochrane reviews [95], our approach is, nevertheless, ranked as a strong design, Supplement Table 7.

Although our focus on embedding PHC activity within supportive municipal actions is hypothesized to increase measurement and brief activity over and above that previously demonstrated, such an approach also brings risks. Municipal and national governments change; and, thus health priorities may change. Although our approach minimizes the need for extra resources (and in some jurisdictions, could be resource saving [19], it is not resource free. Funding constraints could limit future scale-up and sustainability.

We have based our protocol adopted on a model of transdisciplinary research to promote sustainability. Such a model identifies, structures, analyses, and deals with specific problems in a way that grasps the complexity of problems [96]; it takes into account the diversity of real-world and scientific perceptions of problems; and develops knowledge and practices that promote what is generally accepted to be the common good [97]. As such, we include municipalities and health systems as stakeholders to form explicitly orchestrated and managed ecosystems that cross organizational boundaries. Municipal areas and health systems create an engagement platform that provides the necessary environment, including people and resources, for sustainability.

## Abbreviations

CAB  
Community Advisory Board  
PHC  
Primary Health Care  
PHCU  
Primary Health Care Unit

## Declarations

### Ethics approval and consent to participate

The Ethics Committee of the Technical University of Dresden gave final ethical approval for the SCALA project on 12 April 2019, EK90032018. All participating primary health care units and participating primary health care providers sign an informed consent form for participation. Selected patients at two separate time points sign an informed consent form to provide additional anonymized information following a consultation with a primary health care provider.

### Consent for publication

No individual person's data will be published in any form.

### Availability of data and materials

All materials are publicly available on the project website: <https://www.scalaproject.eu/>. According to the SCALA data management plan, by default, all quantitative datasets generated in the course of the SCALA

study will be made openly available through the UK Data Service upon publication of the results (<http://www.data-archive.ac.uk/>). Prior to publication, all data will be formatted to meet UK Data Service requirements.

### **Competing interests**

None declared

### **Funding**

The research leading to these results or outcomes has received funding from the European Horizon 2020 Programme for research, technological development and demonstration under Grant Agreement no. 778048 – Scale-up of Prevention and Management of Alcohol Use Disorders and Comorbid Depression in Latin America (SCALA). Participant organisations in SCALA can be seen at: [www.scalaproject.eu](http://www.scalaproject.eu). The views expressed here reflect those of the authors only and the European Union is not liable for any use that may be made of the information contained therein.

### **Authors' contributions**

All authors contributed to the Grant Application, on which this protocol is based and adapted. EJ-L drafted the first version of the paper, and revised the paper based on author's feedback and comments. PA prepared the paper and material for submission and undertook the submission process. All authors commented on drafts of the manuscript and read and approved the final version. PA undertook random allocation generation. APG and JMT assigned PHCU to arms in Colombia; GNR and APdL assigned PHCU to arms in Mexico; MP and IVB assigned PHCU to arms in Peru.

### **Acknowledgements**

Not applicable

## **References**

01. Shadish WR, Cook TD, Campbell DT: Experimental and quasi-experimental designs for generalized causal inference. 2nd edition. Houghton Mifflin, Michigan, 2002. Reference Source
02. World Health Organization. (2018). Global Status Report on Alcohol and Health 2018. Geneva, Switzerland: WHO Press.
03. Rehm J, Gmel GE, Gmel G et al. The relationship between different dimensions of alcohol use and the burden of disease - an update. *Addiction* 2017 doi:10.1111/add.13757
04. Odlaug BL, Gual A, DeCourcy J, Perry R, Pike J, Heron L, Rehm J. Alcohol dependence, co-occurring conditions and attributable burden. *Alcohol and Alcoholism* 2016 51 201-209.
05. Bellos S, Skapinakis P, Rai D et al. Longitudinal association between different levels of alcohol consumption and a new onset of depression and generalized anxiety disorder: Results from an international study in primary care. *Psychiatry Research* 2016 243 30-34.
06. Boden J. M., Fergusson D. M. Alcohol and depression. *Addiction* 2011; 106: 906–14.
07. Probst C, Roerecke M, Behrendt S, Rehm J. Socioeconomic differences in alcohol-attributable mortality

- compared with all-cause mortality: A systematic review and meta-analysis. *Int J Epidemiol* 2014; 43(4): 1314-27
08. Kontis V, Mathers, CD, Rehm J, Stevens G A, Shield K D, Bonita R, et al. Contribution of six risk factors to achieving the “25×25” NCD mortality reduction target. *Lancet* 2014 [http://dx.doi.org/10.1016/S0140-6736\(14\)60616-4](http://dx.doi.org/10.1016/S0140-6736(14)60616-4).
09. Kontis V, Mathers CD, Bonita R et al. Regional contributions of six preventable risk factors to achieving the 25 × 25 non-communicable disease mortality reduction target: a modelling study. *Lancet Glob Health* 2015; 3: e746–57
10. United Nations General Assembly. Political declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases. <http://www.un.org/en/ga/ncdmeeting2011/> Accessed 01/02/2017
11. GBD 2015 SDG Collaborators. Measuring the health-related Sustainable Development Goals in 188 countries: a baseline analysis from the Global Burden of Disease Study 2015. *Lancet* 2016 388 1813-50.
12. Shield, K.D., Manthey, J., Rylett, M., Probst, C., Wettlaufer, A., Parry, C.D.H. & Rehm, J. (2020). National, regional, and global burdens of disease from 2000 to 2016 attributable to alcohol use. *Lancet Public Health*, 5(1), e51–61. doi: 10.1016/S2468-2667(19)30231-
13. Economic Dimensions of Noncommunicable Diseases in Latin America and the Caribbean: Policy Agenda Considerations 143 George Alleyne. In: [http://iris.paho.org/xmlui/bitstream/handle/123456789/28501/9789275119051\\_eng.pdf?sequence=1&isAllowed=y](http://iris.paho.org/xmlui/bitstream/handle/123456789/28501/9789275119051_eng.pdf?sequence=1&isAllowed=y)
14. Levin C, Chisholm D. Cost-Effectiveness and Affordability of Interventions, Policies, and Platforms for the Prevention and Treatment of Mental, Neurological, and Substance Use Disorders. In Patel, V., D. Chisholm., T. Dua, R. Laxminarayan, and M. E. Medina-Mora, editors. 2015. *Mental, Neurological, and Substance Use Disorders. Disease Control Priorities, third edition, volume 4*. Washington, DC: World Bank. doi:10.1596/978-1-4648-0426-7.
15. O'Donnell, A., Anderson, P., Newbury-Birch, D., Schulte, B., Schmidt, C., Reimer, J. & Kaner, E. The Impact of Brief Alcohol Interventions in Primary Healthcare: A Systematic Review of Reviews. *Alcohol and Alcoholism* doi: 10.1093/alcalc/agt170.
16. Angus C, Thomas C, Anderson P, et al. Estimating the cost-effectiveness of brief interventions for heavy drinking in primary health care across Europe. *Eur J Public Health*. 2017;27:345–351.
17. Rehm J & Barbosa C. (2018) The cost-effectiveness of therapies to treat alcohol use disorders, *Expert Review of Pharmacoeconomics & Outcomes Research*, 18:1, 43-49, DOI: 10.1080/14737167.2018.1392241
18. Rehm, J., Shield, K. D., Gmel, G., Rehm, M. X., & Frick, U. (2013). Modeling the impact of alcohol dependence on mortality burden and the effect of available treatment interventions in the European Union. *European Neuropsychopharmacology*, 23(2), 89–97.
19. Organisation for Economic Co-operation and Development. *Tackling Harmful Alcohol Use: Economics and Public Health Policy*. Paris: Organisation for Economic Co-operation and Development, 2015.
20. Anderson, P., M. Laurant, E. Kaner, M. Wensing and R. Grol (2004). "Engaging general practitioners in the management of hazardous and harmful alcohol consumption: results of a meta-analysis." *J Stud Alcohol* 65(2): 191-199.
21. Keurhorst M, van de Glind I, Bitarello do Amaral-Sabadini M, Anderson P, Kaner E, Newbury-Birch D, Braspenning J, Wensing M, Heinen M, Laurant M (2015) Determinants of successful implementation of

- screening and brief interventions for hazardous and harmful alcohol consumption in primary healthcare. A systematic review and meta-regression analysis. *Addiction* 110:877–900.
22. Anderson, P., Gual, T., Coulton, S., Kaner, E., Bendsten, P., Kłoda, K., Reynolds, J., Keurhorst., M. N., Segura, Wojnar, M., Mierzecki, A., Deluca, P., Newbury-Birch, D., Parkinson, K., Okulicz- Kozaryn, K., Drummond, C., Laurant, M. (2017) Improving the delivery of brief interventions for heavy drinking in primary health care: nine month outcomes of the ODHIN five country cluster randomized factorial trial. *Annals of Family Practice*. In Press.
23. Anderson, P., E. Kaner, S. Wutzke, M. Funk, N. Heather, M. Wensing, R. Grol, A. Gual, L. Pas and W. H. O. B. I. S. Group (2004). "Attitudes and managing alcohol problems in general practice: an interaction analysis based on findings from a WHO collaborative study." *Alcohol Alcohol* 39(4): 351-356.
24. Anderson, P., Bendsten, P., Spak, F., Reynolds, J., Drummond, C., Segura, L., Keurhorst., M. N., Palacio-Vieira, J., Wojnar, M., Parkinson, K., Colom, J., Kłoda, K., Deluca, P., Baena, B., Newbury-Birch, D., Wallace, P., Heinen, M., Wolstenholme, A., van Steenkiste, B., Mierzecki, A., Okulicz- Kozaryn, K., Ronda, G., Kaner, E., Laurant, M., Coulton, S., Gual, T. (2016) 'Improving the delivery of brief interventions for heavy drinking in primary health care: outcome results of the ODHIN five country cluster randomized factorial trial' *Addiction* DOI: 10.1111/add.13476.
25. Carlos Campillo Serrano, Rosa Díaz Martínez, Martha P. Romero Mendoza, Juan Cerrud Sánchez, Jorge Villatoro (1992). La intervención eficaz del médico general en el tratamiento de bebedores cuyo hábito alcohólico representa un riesgo para su salud o ya les ha ocasionado algún daño. (Preliminary results of a prospective double blind clinical trial). *Salud mental*, 15 (2).
26. Hoffman KA, Beltrán J, Ponce J, García-Fernandez L, Calderón M, Muench J, et al. Barreras para implementar el despistaje, intervenciones breves y referencia al tratamiento por problemas de consumo de alcohol y otras drogas en hospitales que atienden personas que viven con el VIH/SIDA en el Perú. *Rev Peru Med Exp Salud Publica*. 2016;33(3):432-7.
27. Lillian Gelberg, Guillermina Natera Rey, Ronald M. Andersen, Miriam Arroyo, Ietza Bojorquez-Chapela, Melvin W. Rico, Mani Vahidi, Julia Yacenda-Murphy, Lisa Arangua & Martin Serota (2017): Prevalence of Substance Use Among Patients of Community Health Centers in East Los Angeles and Tijuana, *Substance Use & Misuse*, 52:3, 359-372
28. Soto-Brandt, G. et al, (2013). Evidencia de validez en Chile del Alcohol, Smoking and Substance Involvement Screening Test (ASSIST). *Adicciones* vol.26 (4).
29. Costa PH, Mota DC, Cruvinel E, Paiva FS, Ronzani TM. (2013). A methodology to implement preventive actions against harmful drug use in the context of primary health care in Latin America *Rev Panam Salud Publica*. 33(5):325-31.
30. Natera R et al., 2014: Final Narrative Report of the bi-national assist screening and quit using drugs intervention trial (quit) Tijuana/Los Angeles. Mexico, National Institute on Psychiatry de la Fuente Muniz.
31. Kaner E. Brief alcohol interventions – time for translational research. *Addiction* 2010; 105: 960-961.
32. Eccles M, Grimshaw J, Walker A, et al.: Changing the behavior of healthcare professionals: the use of theory in promoting the uptake of research findings. *J Clin Epidemiol*. 2005;58(2):107–112. 15680740 10.1016/j.jclinepi.2004.09.002
33. Norton W, Mittman B: Scaling-up Health Promotion/Disease Prevention Programmes in Community Settings: Barriers, Facilitators, and Initial Recommendations. West Hartford, Connecticut, The Patrick and Catherine Weldon Donaghue Medical Research Foundation.2010. Reference Source

34. Woolf SH, Johnson RE: The break-even point: when medical advances are less important than improving the fidelity with which they are delivered. *Ann Fam Med*. 2005;3(6):545–552. 16338919 10.1370/afm.4061466946
35. Massoud R: An approach to rapid scale-up using HIV/AIDS treatment and care as an example. Geneva: World Health Organization;2004. Reference Source
36. Cooley L, Kohl R: Scaling up—from vision to large-scale change: a management framework for practitioners. Washington D.C: Management Systems International;2006. Reference Source
37. Damschroder LJ, Aron DC, Keith RE, et al.: Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci*. 2009;4:50. 19664226 10.1186/1748-5908-4-50 2736161
38. Yamey G: Scaling up global health interventions: a proposed framework for success. *PLoS Med*. 2011;8(6):e1001049. 21738450 10.1371/journal.pmed.1001049 3125181
39. Adamou B: Guide for monitoring scale-up of health practices and interventions: MEASURE evaluation.2013; Accessed 4 November 2016. Reference Source
40. Barker PM, Reid A, Schall MW: A framework for scaling up health interventions: lessons from large-scale improvement initiatives in Africa. *Implement Sci*. 2016;11(1):12. 26821910 10.1186/s13012-016-0374-x 4731989
41. Heather N. editor. WHO Collaborative Project on Identification and Management of Alcohol-related Problems in Primary Health Care – Report to the World Health Organisation on Phase IV: Development of Country-wide Strategies for Implementing Early Identification and Brief Intervention in Primary Health Care. Geneva: World Health Organisation, Department of Mental Health and Substance Abuse: 2006. [http://www.who.int/substance\\_abuse/publications/identification\\_management\\_alcoholproblems\\_phaseiv.pdf](http://www.who.int/substance_abuse/publications/identification_management_alcoholproblems_phaseiv.pdf)
42. Keurhorst M, Heinen M, Colom J et al. Strategies in primary healthcare to implement early identification of risky alcohol consumption: why do they work or not? A qualitative evaluation of the ODHIN study. Keurhorst et al. *BMC Family Practice* (2016) 17:70 DOI 10.1186/s12875-016-0461-8.
43. Babor T, Del Boca F, Bray JW. Screening, brief intervention and referral to treatment: implications of SAMHSA’s SBIRT initiative for substance abuse policy and practice. *Addiction* 2017 112 (Suppl. 2) 110-117.
44. Vendetti J., Gmyrek A., Damon D., Singh M., McRee B., Del Boca F. Screening, Brief Intervention and Referral to Treatment (SBIRT): implementation barriers, facilitators and model migration. *Addiction* 2017; 112 (Suppl. 2), 23–33.
45. Singh M., Gmyrek A., Hernandez A., Damon D., Hayashi S. Sustaining Screening, Brief Intervention and Referral to Treatment (SBIRT) services in health-care settings. *Addiction* 2017; 112 (Suppl. 2), 92–100.
46. Jonas DE, Garbutt JC, Brown JM, Amick HR, Brownley KA, Council CL, et al. Screening, Behavioral Counseling, and Referral in Primary Care to Reduce Alcohol Misuse. Comparative Effectiveness Review No. 64. Rockville, MD: Agency for Healthcare Research and Quality; July 2012. Accessed at [www.ncbi.nlm.nih.gov/books/NBK99199/](http://www.ncbi.nlm.nih.gov/books/NBK99199/) on 16 April 2016.
47. Rehm J, Anderson P, Manthey J, Shield KD, Struzzo P, Wojnar M, Gual A. (2016). Alcohol use disorders in primary health care: what do we know and where do we go? *Alcohol and Alcoholism* 51 422-427.
48. Rubinsky, A.D., Dawson, D.A., Williams, E.C., Kivlahan, D.R. & Bradley, K.A. AUDIT-C Scores as a Scaled Marker of Mean Daily Drinking, Alcohol use disorders Severity, and Probability of Alcohol Dependence in a U.S. General Population Sample of Drinkers. *Alcoholism: Clinical and Experimental Research* 2013 37 1380-1390.

49. National Clinical Guideline Centre (2011). The clinical management of primary hypertension in adults. 2011 <https://www.nice.org.uk/guidance/cg127/evidence/cg127-hypertension-full-guideline3> (accessed 1 December 2016).
50. Rehm, J., Anderson, P., Arbesu Prieto, J.A., Armstrong, I., Aubin, H.-J., Bachmann, M., Bastida Bastús N, Brotons, C., Burton, R., Cardoso, M., Colom, J., Duprez, D., Gmel, G., Gual, A., Kraus, L., Kreutz, R., Liira, H., Manthey, J., Møller, L., Okruhlica, L., Roerecke, M., Scafato, E., Schulte, B., Segura-Garcia, L., Shield, K.D., Sierra, C., Vyshinskiy, K., Wojnar, M., & Zarco, J. (2017). Towards new recommendations to reduce the burden of alcohol-induced hypertension in the European Union. *BMC Medicine*, 15, 173. doi: 10.1186/s12916-017-0934-1.
51. Kaner EF, Beyer FR, Dickinson HO, et al.: Effectiveness of brief alcohol interventions in primary care populations. *Cochrane Database Syst Rev*. 2007; (2): CD004148.
52. Platt L, Melendez-Torres GJ, O'Donnell A, et al.: How effective are brief interventions in reducing alcohol consumption: do the setting, practitioner group and content matter? Findings from a systematic review and meta-regression analysis. *BMJ Open*. 2016;6(8):e011473. 27515753 10.1136/bmjopen-2016-011473 4985973
53. Kaner, E., Bland, M., Cassidy, P., Coulton, S., Dale, V., Deluca, P., ... & Newbury-Birch, D. (2013). Effectiveness of screening and brief alcohol intervention in primary care (SIPS trial): pragmatic cluster randomised controlled trial. *Bmj*, 346, e8501. doi: 10.1136/bmj.e8501
54. Bray, J. W., Zarkin, G. A., Hinde, J. M., & Mills, M. J. (2012). Costs of alcohol screening and brief intervention in medical settings: a review of the literature. *Journal of studies on alcohol and drugs*, 73(6), 911-919. doi: 10.15288/jsad.2012.73.911
55. Groves, P., Pick, S., Davis, P., Cloudesley, R., Cooke, R., Forsythe, M., & Pilling, S. (2010). Routine alcohol screening and brief interventions in general hospital in-patient wards: acceptability and barriers. *Drugs: education, prevention and policy*, 17(1), 55-71. doi: 10.3109/09687630802088208
56. Anderson P, O'Donnell A, Kaner E et al. Scaling-up primary health care-based prevention and management of alcohol use disorder at the municipal level in middle-income countries in Latin America: Background and pre-protocol for a three-country quasi-experimental study. *F1000Research* 2017, 6:311 (doi: 10.12688/f1000research.11173.1).
57. SAMHSA. AUDIT-C. [https://www.integration.samhsa.gov/images/res/tool\\_auditc.pdf](https://www.integration.samhsa.gov/images/res/tool_auditc.pdf)
58. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG AUDIT: The Alcohol Use Disorders Identification Test Guidelines for Use in Primary Care (second edition). [https://www.who.int/substance\\_abuse/publications/audit/en/](https://www.who.int/substance_abuse/publications/audit/en/)
59. US Preventive Service task Force. Patient Health Questionnaire PHQ-9. <https://www.uspreventiveservicestaskforce.org/Home/GetFileByID/218>
60. Center for Quality Assessment and Improvement in Mental Health Patient Health Questionnaire PHQ-2. [http://www.cqaimh.org/pdf/tool\\_phq2.pdf](http://www.cqaimh.org/pdf/tool_phq2.pdf)
61. Rosenberg G, Bauld L, Hooper L et al. New national alcohol guidelines in the UK: public awareness, understanding and behavioural intentions. *Journal of Public Health*, 2018 40, 549–556,
62. Chung A, Rimal RN: Social norms: A review. *Review of Communication Research*. 2016;4:1–29. 10.12840/issn.2255-4165.2016.04.01.008
63. Sørensen K, Van den Broucke S, Pelikan JM, et al.: Measuring health literacy in populations: illuminating the design and development process of the European Health Literacy Survey Questionnaire (HLS-EU-Q). *BMC Public Health*. 2013;13:948. 24112855 10.1186/1471-2458-13-948 4016258

64. Anderson P, Clement S: The AAPPQ revisited: the measurement of general practitioners' attitudes to alcohol problems. *Br J Addict.* 1987;82(7):753–9. 3478065 10.1111/j.1360-0443.1987.tb01542.x
64. Kaner EF, Dickinson HO, Beyer FR, Campbell F, Schlesinger C, Heather N, Saunders JB, Burnand B, Pienaar ED. Effectiveness of brief alcohol interventions in primary care populations. *Cochrane Database of Systematic Reviews* 2007, Issue 2. Art. No.: CD004148. DOI: 10.1002/14651858.CD004148.pub3.
65. Svoronos T, Mate KS: Evaluating large-scale health programmes at a district level in resource-limited countries. *Bull World Health Organ.* 2011;89(11):831–837. 22084529 10.2471/BLT.11.088138 3209726
65. Schaufeli WB, Shimazu A, Hakanen J, Salanova M, De Witte H. An Ultra-Short Measure for Work Engagement: The UWES-3 Validation Across Five Countries. *European Journal of Psychological Assessment* 2017
66. Derges, J., Kidger, J., Fox, F., Campbell, R., Kaner, E., & Hickman, M. (2017). Alcohol screening and brief interventions for adults and young people in health and community-based settings: A qualitative systematic literature review. *BMC Public Health*, 17(1), 1–12. <https://doi.org/10.1186/s12889-017-4476-4>
67. Johnson, M., Jackson, R., Guillaume, L., Meier, P., & Goyder, E. (2011). Barriers and facilitators to implementing screening and brief intervention for alcohol misuse: A systematic review of qualitative evidence. *Journal of Public Health*, 33(3), 412–421. <https://doi.org/10.1093/pubmed/fdq095>
68. O'Donnell, A., Wallace, P., & Kaner, E. (2014). From efficacy to effectiveness and beyond: What next for brief interventions in primary care? *Frontiers in Psychiatry*, 5(AUG), 1–8. <https://doi.org/10.3389/fpsy.2014.00113>
69. Flottorp SA, Oxman AD, Krause J, et al.: A checklist for identifying determinants of practice: a systematic review and synthesis of frameworks and taxonomies of factors that prevent or enable improvements in healthcare professional practice. *Implement Sci.* 2013;8:35. 23522377 10.1186/1748-5908-8-35 3617095
70. Moore GF, Audrey S, Barker M, et al.: Process evaluation of complex interventions: Medical Research Council guidance. *BMJ.* 2015;350:h1258. 25791983 10.1136/bmj.h1258 4366184
71. Glasgow RE, Vogt TM, Boles SM: Evaluating the public health impact of health promotion interventions: the RE-AIM framework. *Am J Public Health.* 1999;89(9):1322–7. 10474547 10.2105/AJPH.89.9.1322 1508772
72. Glasgow RE, Klesges LM, Dziewaltowski DA, et al.: Evaluating the impact of health promotion programs: using the RE-AIM framework to form summary measures for decision making involving complex issues. *Health Educ Res.* 2006;21(5):688–694. 16945984 10.1093/her/cyl081
73. Harden SM, Gaglio B, Shoup JA, et al.: Fidelity to and comparative results across behavioral interventions evaluated through the RE-AIM framework: a systematic review. *Syst Rev.* 2015;4:155. 26547687 10.1186/s13643-015-0141-0 4637141
74. Ysa T, Colom J, Albareda A, et al.: Governance of Addictions. *European Public Policies.* Oxford University Press,2014. Reference Source
75. OECD: Compendium of OECD well-being indicators. *OECD Better Life Initiative.*2011; (Accessed 18 December 2016). Reference Source
76. Bertelsmann Stiftung. [website].2016; (Accessed 18 December 2016). Reference Source
77. Inglehart R, Welzel C: *Modernization, Cultural Change and Democracy.* New York: Cambridge University Press,2005. Reference Source
78. PASS16 sample size software. <https://www.ncss.com/software/pass/>: Donner, A. and Klar, N. 2000. *Design and Analysis of Cluster Randomization Trials in Health Research.* Arnold. London.

79. Wensing M, Oxman A, Baker R, et al.: Tailored Implementation For Chronic Diseases (TICD): a project protocol. *Implement Sci.* 2011;6:103. 21899753 10.1186/1748-5908-6-103 3179734
80. Wensing M, Huntink E, van Lieshout J, et al.: Tailored Implementation of Evidence-Based Practice for Patients with Chronic Diseases. *PLoS One.* 2014;9(7):e101981. 25003371 10.1371/journal.pone.0101981 4087017
81. Dietz WH, Solomon LS, Pronk N, et al.: An Integrated Framework For The Prevention And Treatment Of Obesity And Its Related Chronic Diseases. *Health Aff (Millwood).* 2015;34(9):1456–1463. 26355046 10.1377/hlthaff.2015.0371
82. Palumbo R: Contextualizing co-production of health care: a systematic literature review. *Int J Public Se Manage.* 2016;29(1):72–90. 10.1108/IJPSM-07-2015-0125
83. Rehm J, Room R, Monteiro M, et al.: Alcohol Use. In: Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Ezzati M et al. (eds), Geneva, Switzerland: World Health Organization.2004;959–1109. Reference Source
84. European Medicines Agency: Guideline on the development of medicinal products for the treatment of alcohol dependence.2010. Reference Source
85. Rehm J, Lachenmeier DW, Room R: Why does society accept a higher risk for alcohol than for other voluntary or involuntary risks? *BMC Med.* 2014;12:189. 25424648 10.1186/s12916-014-0189-z 4203927
86. Cunningham JA: Unintended impact of using different inclusion cut-offs for males and females in intervention trials for hazardous drinking. *Addiction.* 2017. 28168847 10.1111/add.13760
87. Wilson GB, Wray C, McGovern R, et al.: Intervention to reduce excessive alcohol consumption and improve comorbidity outcomes in hypertensive or depressed primary care patients: two parallel cluster randomized feasibility trials. *Trials.* 2014;15:235. 24947447 10.1186/1745-6215-15-235 4076249
88. Lai HM, Cleary M, Sitharthan T, et al.: Prevalence of comorbid substance use, anxiety and mood disorders in epidemiological surveys, 1990–2014: A systematic review and meta-analysis. *Drug Alcohol Depend.* 2015;154:1–13. 26072219 10.1016/j.drugalcdep.2015.05.031
89. Linde K, Sigterman K, Kriston L, et al.: Effectiveness of psychological treatments for depressive disorders in primary care: systematic review and meta-analysis. *Ann Fam Med.* 2015;13(1):56–68. 25583894 10.1370/afm.1719 4291267
90. Gilbody S, Whitty P, Grimshaw J, et al.: Educational and organizational interventions to improve the management of depression in primary care: a systematic review. *JAMA.* 2003;289(23):3145–3151. 12813120 10.1001/jama.289.23.3145
91. Aldridge A, Dowd W, Bray J: The relative impact of brief treatment versus brief intervention in primary health-care screening programs for substance use disorders. *Addiction.* 2017;112(Suppl 2):54–64. 28074568 10.1111/add.13653
92. Barbosa C, Cowell A, Dowd W, et al.: The cost-effectiveness of brief intervention versus brief treatment of screening, brief intervention, and referral to treatment (SBIRT) in the United States. *Addiction.* 2017;112(Suppl 2):73–81. 28074567 10.1111/add.13658
93. Anderson P, Kaner E, Keurhorst M, et al.: Attitudes and Learning through Practice Are Key to Delivering Brief Interventions for Heavy Drinking in Primary Health Care: Analyses from the ODHIN Five Country Cluster Randomized Factorial Trial. *Int J Environ Res Public Health.* 2017;14(2): pii: E121. 28134783 10.3390/ijerph14020121 5334675
94. Funk M, Wutzke S, Kaner E, et al.: A multicountry comparator led trial of strategies to promote

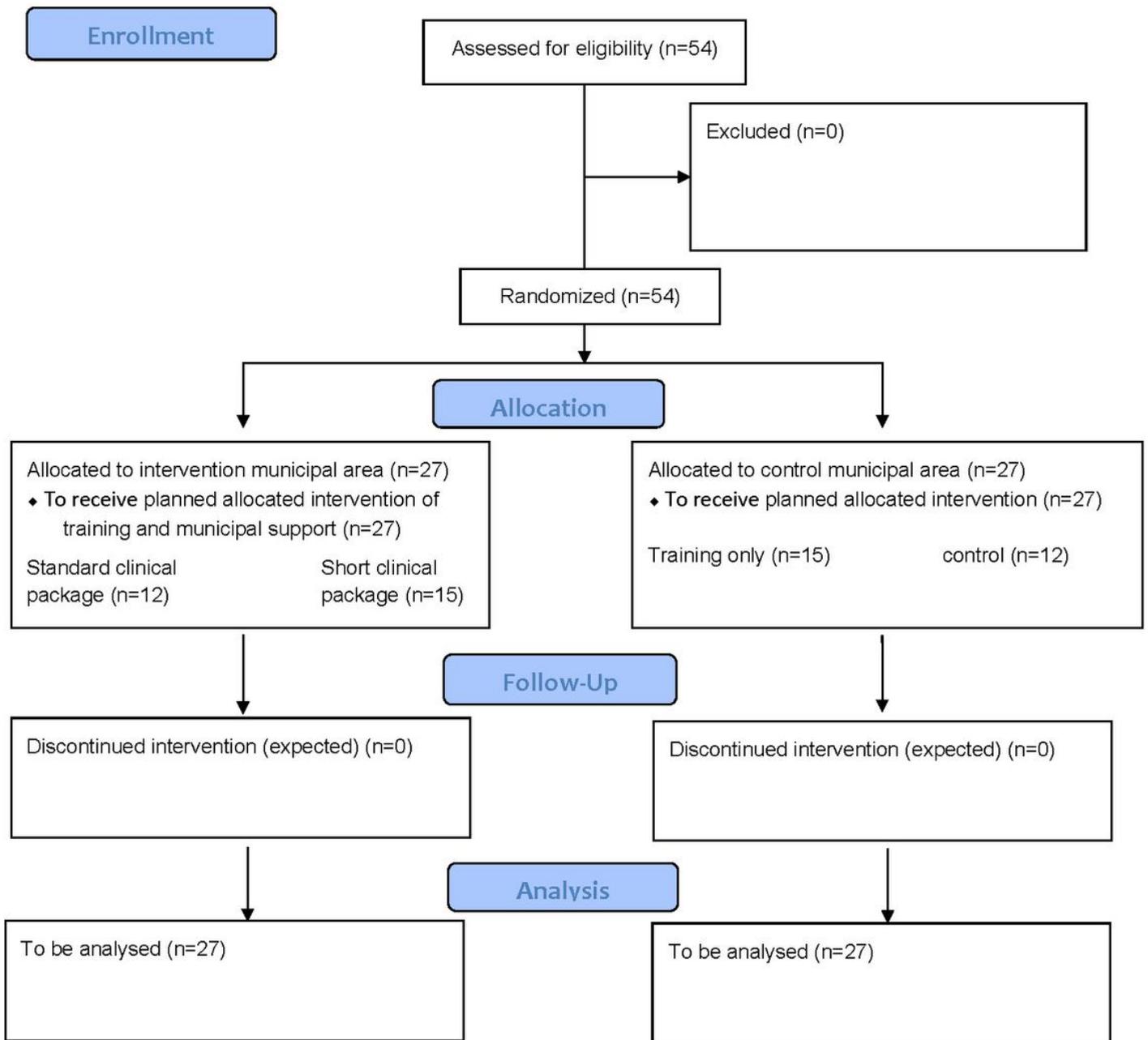
dissemination and implementation of brief alcohol intervention in primary health care: findings of a World Health Organization collaborative study. *J Stud Alcohol*. 2005;66(3):379–388. 16047527  
10.15288/jsa.2005.66.379

95. Reeves BC, Wells GA, Waddington H: Quasi-experimental study designs series-paper 5: classifying studies evaluating effects of health interventions-a taxonomy without labels. *J Clin Epidemiol*. 2017; pii: S0895-4356(17)30288-3. 28351692 10.1016/j.jclinepi.2017.02.016

96. Jantsch E: Inter- and Transdisciplinary University: A systems approach to education and innovation. *Policy Sciences*. 1970;1(1):403–428. 10.1007/BF00145222

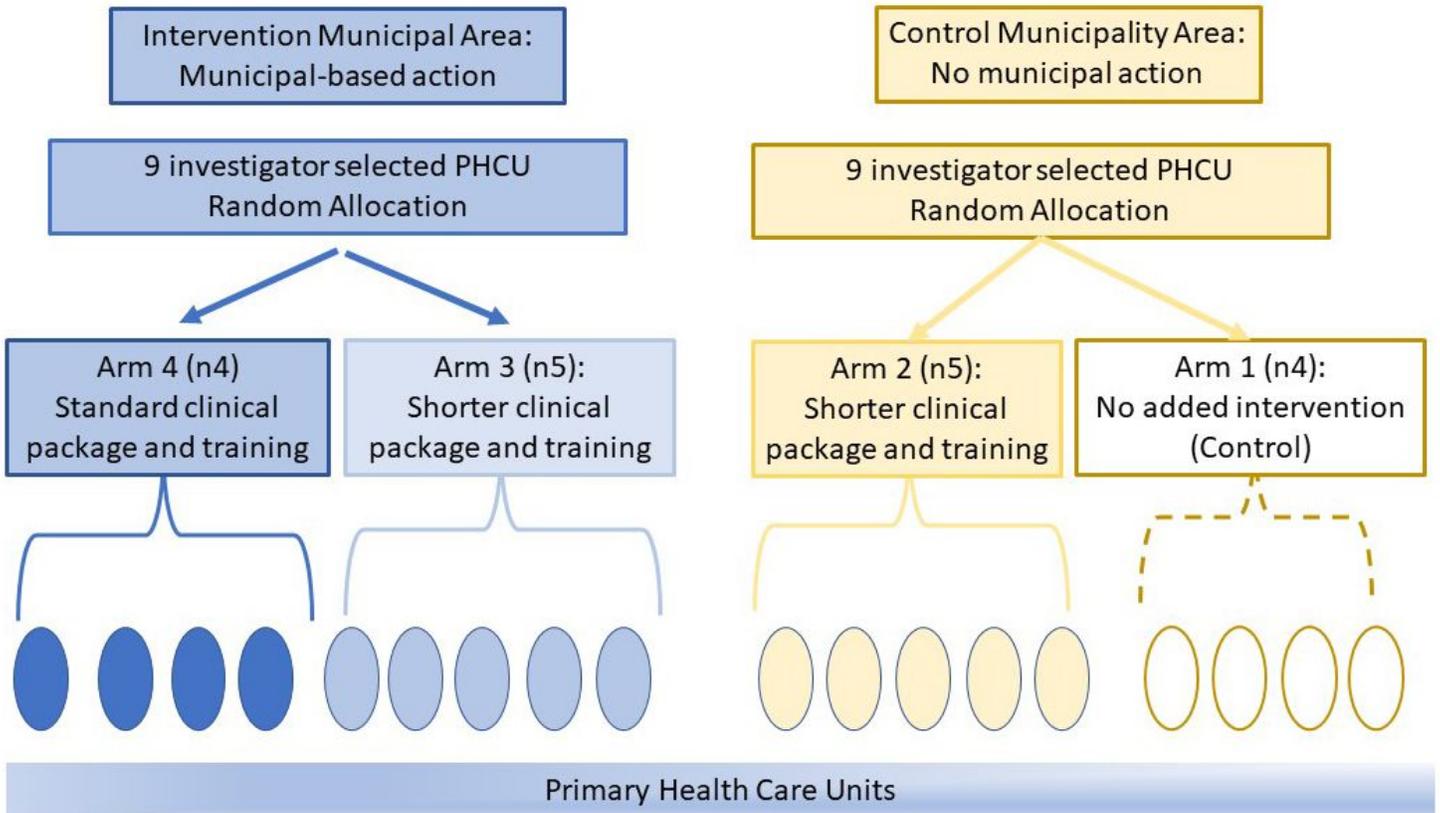
97. Pohl C, Hirsch Hadorn G: Principles for Designing Transdisciplinary Research. proposed by the Swiss Academies of Arts and Sciences. München: oekom Verlag.2007.

## Figures



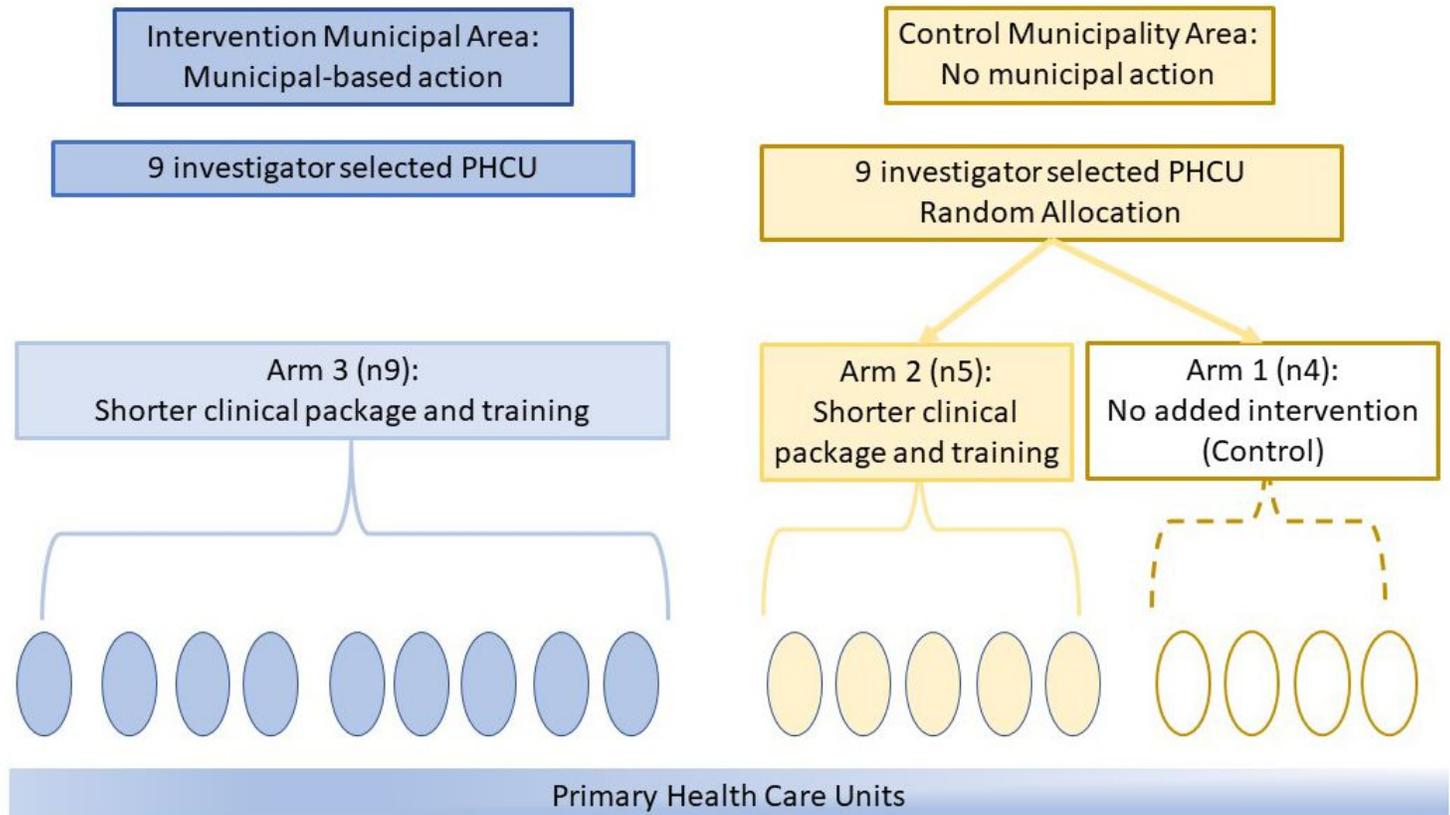
**Figure 1**

CONSORT flow diagram



**Figure 2**

Study design for the first six months of the 18-month implementation period



### Figure 3

Study design from month 8 onwards, assuming no superiority of Arm 4 over Arm 3 during first six months of implementation.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SCALACONSORT2010Checklist.docx](#)
- [SCALAProtocolSupplementR4.docx](#)