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# Gatekeeper training for vendors to reduce pesticide self-poisoning in rural Asia – A study protocol for a stepped-wedge cluster randomized controlled trial

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# TITLE PAGE

## Gatekeeper training for vendors to reduce pesticide self-poisoning in rural Asia – A study protocol for a stepped-wedge cluster randomized controlled trial

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## ABSTRACT

**Introduction:** Pesticide self-poisoning kills an estimated 110,000-168,000 people worldwide annually. Data from South Asia indicate that 15-20% of attempted suicides and 30-50% of completed suicides pesticides are purchased shortly beforehand for this purpose. Individuals who are intoxicated with alcohol and/or non-farmers represent 72% of such customers. We have developed a 'gatekeeper' training program for vendors to enable them to identify individuals at high-risk of self-poisoning (gatekeeper function) and prevent such individuals from accessing pesticides (means restriction). The primary aim of the study is to evaluate the effectiveness of the gatekeeper intervention in preventing pesticide self-poisoning in Sri Lanka. Other aims are to identify method substitution and to assess the cost and cost-effectiveness of the intervention.

**Methods and analysis:** A stepped-wedge, cluster randomized trial of a gatekeeper intervention is being conducted in rural Sri Lanka with a population of approximately 2.7 million. The gatekeeper intervention is being introduced into 70 administrative divisions, in random order at each of 31 steps over a 40-month period. The primary outcome is the number of pesticide self-poisoning cases identified from surveillance of hospitals and police stations. Secondary outcomes include: number of self-poisoning cases using pesticides purchased within the previous 24h, total number of all forms of self-harm, and suicides. Intervention effectiveness will be estimated by comparing outcome measures between the pre- and post-training periods across the divisions in the study area. The original study protocol has been adapted as necessary in light of the impact of the COVID-19 pandemic.

**Ethics and dissemination:** Ethical Review Committee of the Faculty of Medicine and Allied Sciences, Rajarata University, Sri Lanka (ERC/2018/30) and ACCORD Medical Research

Ethics Committee, Edinburgh University (18-HV-053) approved the study. Results will be disseminated in scientific peer-reviewed journals.

**Trail Registration:** Sri Lanka Clinical Trail Registry (https://slctr.lk):2019/006. International Clinical Trials Registry Platform (U1111-1220-8046).

## Article Summary

### Strengths and limitations of this study

- This large-scale study will be the first to provide evidence of whether 'gatekeeper' training for pesticide vendors is effective in reducing pesticide self-poisoning.
- The study provides a pragmatic evaluation of the 'gatekeeper' training, which will be introduced more generally if found to be effective.
- A potential limitation of the stepped wedge design is susceptibility to confounding by secular trends in pesticide self-poisoning rates during the study period.
- The observed treatment effect may be diluted if individuals attempt to purchase pesticides from a shop outside of their division of residence (contamination). Such an effect has been incorporated into sample size power calculations.
- The intervention can potentially only prevent a proportion of pesticide self-poisoning cases (15-20% of cases purchasing pesticides for the act), requiring a large study to provide sufficient statistical power to detect a modest total treatment effect.

## INTRODUCTION

Pesticide self-poisoning is one of the most frequently used global means of suicide [1], equaling 15-20% of all global suicides, or an estimated 110,000-168,000 deaths annually [2]. Many of these deaths occur among people living in rural areas of low and middle-income countries (LMIC) [3][4], who may ingest pesticides impulsively in a moment of crisis [5]. Pesticides are often available in the community, meaning they can be accessed and ingested with little thought at moments of crisis or anger [4][6].

In Sri Lanka, pesticide shops are widespread in agricultural areas, making pesticides freely available for over the counter purchase and providing easy access for self-poisoning [7][8]. In South Asia, 14-20% of attempted suicides [6][9][10] and 33-49% of completed suicides involve pesticides [11] and occur shortly after individuals purchase the pesticides from a shop for the specific purpose of self-harm (a 'shop case', Box 1). Several interventions have been tested to prevent suicides involving a range of self-poisoning methods by reducing access to means at the point of sale in different countries - analgesic packaging restrictions [12][13] and physical barriers to purchases of charcoal [14]. However, no interventions have been aimed at pesticide shops to support vendors in preventing individuals from accessing pesticides for self-poisoning.

Over a period of three years, we have designed an intervention following the UK Medical Research Council's guidance on development of complex interventions [15] through a series of studies. We first identified major risk factors for buying pesticides for self-harm using a case control design, noting in particular being intoxicated with alcohol at the time of purchase [odds ratio 36.5; 95% confidence interval 1.7 to 783] or being a non-farmer purchasing pesticides

[odds ratio 13.3; 95% confidence interval 1.8 to 100] as key risk factors - one and/or other of these factors characterized 72.0% of cases [16][17]. We then explored the acceptability of possible interventions with stakeholders including pesticide vendors, and finally tested the most acceptable intervention in a qualitative feasibility study. Focus group and stakeholder discussions favored a vendor-based gatekeeper approach identifying, and refusing to sell to, high-risk individuals [18]. A feasibility study showed good vendor acceptance and provided preliminary evidence that it may prevent self-poisoning [19]. Finally, an ex-ante cost analysis and cost-effectiveness threshold analysis of the gatekeeper program were conducted showing it to have a very high potential of being cost-effective [20]. However, before this approach is further pursued, a large-scale trial is required to determine its effectiveness.

## OBJECTIVE

The main objective of the study is to test the effectiveness of the gatekeeper intervention in preventing pesticide self-poisoning in Sri Lanka. This study, furthermore, aims to identify method substitution and to assess the cost and cost-effectiveness of the intervention.

## METHODS AND ANALYSIS

### Design

This study is a single-blinded, stepped-wedge cluster randomized controlled trial (s-w cRCT) of a public health intervention involving pesticide shops. A stepped-wedge design was selected to provide a pragmatic evaluation of this low-risk intervention. Definitions used in the trial design are presented in Box 1.

### Setting

The study is being carried out in two areas (Zones) populated by about 2.7 million people (Census, 2019) in 70 divisions, primarily from six districts (Anuradhapura 22 divisions, Polonnaruwa 7, Matale 11, Vavuniya 4, Batticaloa 14, and Trincomalee 11) and 1 division (Dehiattakandiya) from Ampara District (figure 1). Divisions are government administrative regions with populations of ~40,000 people.

Our previous research during 2011-16 found the incidence of pesticide self-poisoning in the South-West Mahaweli H section of North Central Province (NCP, Zone 1) to be over 250 per 100,000 person years [3]. This study was originally designed with this case incidence and included 29 NCP divisions (Zone 1 districts: Anuradhapura, Polonnaruwa; population 1.5 million). However, initial case collection over the first six months (April to September 2019) showed a markedly lower incidence of pesticide self-poisoning at around 130/100,000 per year. The study was therefore expanded into a second area including 41 divisions to the north and east of the initial study area (Expansion area, Zone 2 districts: Matale, Batticaloa, Trincomalee, Vavuniya and part of Ampara; population 1.2 million) to allow recruitment of sufficient cases. Because the two zones started at different times, they are run as parallel studies; the data will be combined for analysis at the end of the study.

***Participant enrolment***

No up-to-date and comprehensive record of pesticide shops and vendors is available. We therefore carried out a baseline mapping exercise identifying all shops selling pesticides, including seasonal shops, both registered and non-registered with the Department of Agriculture. This survey identified 669 shops and 1,406 pesticide vendors in the study area. During the study, regular surveys are being carried out to identify shops that close or open, to

ensure an up-to-date list of pesticide shops in the study area. Shops that are missed at initial training in their division will receive training as soon as their presence is noted.

**Inclusion and exclusion criteria**

All pesticide shops and vendors directly involved in pesticide sales in the study area during the study period are eligible for the intervention. It is likely that some people living close to division boundaries cross cluster boundaries to buy pesticides in non-study areas. Therefore, our initial zone 1 design included training of vendors in shops located within 5km of divisional boundaries, outside of the NCP study area. However, after six months of data collection, review of out-of-division purchases revealed that cross-boundary purchases within 5km were minimal (1.3% of all purchases). Since we were expanding the study into contiguous areas, around the north and east study area boundary, a decision was made to discontinue training of vendors outside cluster boundaries. Vendors who are aged under 18 years (<1%) are excluded, as well as cashiers and other store workers in larger pesticide shops who do not directly interact with pesticide-purchasing customers.

**Randomization**

The unit of randomization (cluster) is one or more (usually two) divisions. The intervention is being introduced in each of 31 time periods ("steps" of the stepped wedge design) in the two zones, so training will proceed at each step in two or more divisions (the cluster).

Cross-border contamination, i.e., people crossing into a division with discordant training status from their home division to purchase pesticides, is recognised, particularly where multiple pesticide shops exist along a shared boundary (usually a major road). We therefore identified neighbouring divisions with multiple pesticide shops along such a shared boundary and

combined them into a pair, into which the intervention would be introduced during the same step. We expected this approach to reduce contamination.

Random allocation was conducted by a member (NT) of the study team based outside of Sri Lanka once the mapping of pesticide shops and pairing of divisions had been completed, so ensuring allocation was controlled and intervention staff informed two weeks before the start of training (so that logistic plans could be made and maps updated as required). The clusters have been listed in a randomly generated order (using Stata statistical software: StataCorp, College Station, Texas, 2017), and the intervention rolled out into each cluster in turn following this random sequence.

In Zone 1's 29 divisions, the intervention was initially introduced at 78-day intervals; this was reduced to 67-day intervals following COVID-19 pandemic lockdown in March-June 2020. In Zone 2's 41 divisions, which started later, after the lockdown, the intervention was introduced at 42-day intervals. Zone 2 intervals are shorter to ensure all training is completed by the time that Zone 1 training is complete. Before the first intervention, a monitoring period (160 days in Zone 1, and 61 days in Zone 2) was established, during which a baseline number of pesticide self-poisoning cases was recorded.

Overall, the intervention is being rolled out in 15 steps in Zone 1 over 39 months and in 16 steps in Zone 2 over 23 months (figure 2).

**The intervention**

The intervention is a modified 'gatekeeper' training and involves helping pesticide vendors to identify a person at high-risk of purchasing a pesticide for the purpose of self-poisoning

(gatekeeper function), in order to then refuse to sell pesticides to this individual (means restriction) [19]. We have utilised the Capability, Opportunity, Motivation and Behaviour (COM-B) model of behaviour change to plan our intervention for modified 'gatekeeper' training [21]. Using the findings from our pilot work [19], we developed a theoretical model of the behaviour change (figure 3). The intervention employs seven strategies: education, persuasion, incentivization, training, environmental restructuring, modelling and enablement. The characteristics of the intervention have been detailed and a manual produced.

The intervention consists of a 1-hour discussion with small-groups of vendors (maximum 10 participants) on their experience with self-poisoning clients, followed by a 1-hour interactive presentation and discussion on how to identify and respond to high-risk clients. Vendors are trained to observe customer for any unusual behaviours [8] such as sadness or nervousness, and for intoxication, and to ask questions on agriculture for which farmers would be expected to know the answer. Short training films have been produced to standardise presentation of information and training across different shops (https://vimeo.com/user14558312). The training uses role-plays to aid development of skills learnt in the training. The session is performed at a central location within the cluster and/or at pesticide shops in daytime or in evenings, depending on the vendors' preference for the venue and time, and on travel restrictions during the COVID-19 pandemic. The vendors are ideally trained in groups, to increase vendor interaction and cross-learning; however, this is not always possible and had to be stopped during lockdowns in 2020 and 2021.

The intervention is delivered by experienced trainers with extensive local knowledge, assisted by project staff who coordinate the timing and location of training and follow-up training. The trainers were trained using a Train-the-Trainer model in this specific program by a public health

researcher (MW), based on his pilot work. During the COVID-19 partial lockdowns, teaching was run virtually using video conference calling with a laptop delivered to the shop for a training session, run by MW from home (see below).

Due to a high level of turnover of both shops and vendors, we continuously monitor for new shops and vendors across the study area to arrange catch-up training as require. No financial incentives are provided to participants; however, transportation for the training and a folder of materials are provided.

A sticker providing key messages from the training is provided to each shop, to be pasted onto the cash machine or drawer, invisible to customers. Otherwise, trained shops do not receive documents that can be displayed in shops as these could potentially unblind potential purchasers.

**Follow-up training**

Brief follow-up reminders are provided during the first six months at 1-month intervals to reinforce the skills taught during the training. Contact is provided by telephone calls, short text messages (SMS), or post cards.

**Data collection procedures**

**(a) Intervention data:** Registered pesticide shops are identified based on records maintained by the Office of the Registrar of Pesticides and mapped using GPS. Unregistered shops are identified and surveyed by field researchers through a snow-balling method (an initial group of vendors to nominate, through their social networks, other pesticides vendors nearby) and through discussions with local communities, representatives of farmer organizations, and

pesticide companies, as done in our pilot work [22]. Pesticide shop and vendor information is updated throughout the study. This information is used for cluster allocation and to invite vendors to the training sessions.

We assess pre and post-test knowledge and practice at the beginning and end of the training session and again at 6, 12 and 24 months, using a survey based on our previous work [23], modified for use in this trial. After training, information on compliance assessments is performed using interviews to assess vendors' practices following training.

**(b) Surveillance data:** In Zone 1, surveillance data collection started on 01 April 2019 and will last for 42 months. In Zone 2, data collection started on 01 November 2020 and will last for 24 months. Surveillance researchers record all fatal and non-fatal self-harm cases admitted to the wards of 118 study hospitals across the region (figure 4). Following our previous household pesticide storage study processes [24], researchers prospectively record self-harm patients through frequent visits to small primary hospitals (7 to 80 beds); at least weekly) and by telephone calls from hospital staff when patients are admitted. In secondary and tertiary care hospitals, researchers attend the medical wards daily and other wards at least weekly to identify other (less common) non-poisoning means of self-harm in surgical, paediatric, and intensive care units, as well as morgues. During the study set up, we explored where study area patients presented to hospital and ensured that all accessed hospitals were surveyed, both in and out of the study area.

There are no minimum or maximum age limits for inclusion. Non-residents of the study area will be excluded from the final analysis.

Data collected include demographic data for all self-harm cases (sex, date of birth, place of residence and farming status) and event-specific information (date and time of self-harm event, method of self-harm, whether the individual was alcohol intoxicated at the time of purchase and time of hospital admission, and whether the individual died). For pesticide poisoning cases, additional data are collected on how the individuals accessed pesticides (whether they bought the pesticides from a shop or accessed them from home or nearby). Specific information collected for shop cases includes whether the individual or someone else bought pesticides, the individual's intent at the time of pesticide purchase (self-harm or agricultural purpose), date and time of the pesticide purchase, and the division location of the pesticide shop.

We record all self-harm deaths occurring outside hospital settings through a network of 90 police stations and judicial medical officers. The researchers visit these sources every three months to extract data about self-harm events, namely the home address, method of self-harm, and the source of any pesticide used. Where patients leave hospital before they can be interviewed or non-hospitalized deaths occur, address details are obtained from the hospital or police station and permission requested from the patient and family to interview them in their homes about the source of pesticide used in the poisoning.

Field researchers are supervised by experienced senior research staff (KD, DR, and DA) who have undergone training in research ethics. Both the surveillance team and the patient (or patient's family) are blind to the training status of the pesticide shop from which the pesticide was purchased. The surveillance team is also kept separate from the intervention team carrying out the training of vendors to reduce the risk of unblinding.

**Outcome events**

The primary outcome is the number of pesticide self-poisoning cases (fatal and non-fatal attempts) identified from surveillance of hospitals and police stations. Secondary outcomes include:

- Number of pesticide self-poisoning patients (fatal and non-fatal attempts) presenting to study hospitals and/or police stations using pesticides purchased within 24 hrs of the act.
- Total number of hospital-presenting self-harm cases, all methods
- Total number of suicides, all methods

**Data Management**

Study data are collected and managed using REDCap electronic data capture tools hosted at University of Sydney [25][26]. REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources. Data are collected into REDCap case record form by researcher staff following the same protocol as for the household pesticide storage study [24]. Two REDCap databases are used: intervention and surveillance databases. A data coordinator (SR) is responsible for database maintenance, security, and review of data entry on a weekly basis to identify missing data. The trial manager (MP) reviews a weekly data summary. All databases are password protected. At the end of the study, a final anonymized dataset will be sent to the University of Bristol for analysis and then to the University of Edinburgh for archiving.

**Statistics and data analysis**

***Sample size calculation***

The primary outcome measure is the total number of pesticide self-poisoning cases, whilst the intervention is directed towards a sub-population of "shop cases" who self-poison using pesticides bought for this purpose from a shop in the preceding 24 hours. The subpopulation affected by the intervention is likely to be about 20% of all primary outcome cases. This study is aiming to identify any effect of the intervention amongst all primary outcome events. Calculations were performed by the "stepped-wedge" procedure [27].

Initially, the study was powered taking the mean division population of 15+ year olds to be 35,000, the rate of pesticide self-poisoning without intervention to be 250 cases per 100,000 person years, and the coefficient of variation of pesticide self-poisoning across the divisions to be 0.55 (calculated from our ongoing provincial and study area hospital surveillance). In this case, a stepped wedge design with the intervention introduced into two districts at each of 15 steps separated by 58 days (5562 person-years of follow-up of each district at each step) would detect a true 11.5% reduction to 221 cases per 100,000 person years with 80% power at the 5% significance level. To achieve this 11.5% reduction overall requires a 58% reduction amongst shop cases, assuming shop cases make up 20% of all cases in the absence of the intervention.

However, after six months, the rate of pesticide self-poisoning in the study area was observed to be 130 cases per 100,000 person years. To achieve an acceptable level of statistical power with this lower incidence rate we repeated our sample size calculation with a doubling of the study area and the intervention being introduced into four districts at each of the 16 steps. This calculation indicated that a 11.5% reduction from 130 to 115 pesticide self-poisoning cases per 100,000 person years would be detected with 82% power at the 5% significance level.

### *Data analysis*

A signed and dated statistical analysis plan will be written and made publicly available online before release of the data for analysis.

The division of residence of the patient and date of self-harm event will be used to allocate cases to the correct study condition. The primary analysis will follow the intention-to-treat principle, comparing the observed incidence of pesticide self-poisoning between periods/areas with and without the intervention in place. A Poisson regression model will be used to estimate the intervention effect as an incidence rate ratio, with variation between areas accommodated as a random effect, and any secular or seasonal time trends accommodated as covariates. This approach will be adapted for the secondary event-based outcomes.

### Implementation Analysis

We will employ a mixed method approach to evaluate the implementation of the intervention based on the REAIM framework [28]; employing quantitative tools to measure reach, effectiveness, adoption, implementation and maintenance and qualitative tools to identify contextual factors that may help to explain the effectiveness of the intervention.

### Economic evaluation

Cost and cost-effectiveness analyses are being conducted concurrently with the trial to assess the cost-effectiveness of the intervention. The cost-effectiveness of implementing the training program on a national level is also being assessed through modelling. A governmental perspective is adopted for the economic evaluations i.e., only cost and outcomes that impact on government as a third-party funder are included. In the economic evaluation of the

intervention, a three-year time horizon is applied. This time horizon will be expanded to five years when modelling a full national roll-out of the 'gatekeeper' training intervention.

All costs are expressed in US dollars (US$) and measured in real prices for the reference year (2019) using the gross domestic product deflator. If this is not available, the consumer price index will be used. The discounting of costs is undertaken at the recommended real rate of 3% to take into account the timing of costs and health outcomes of the intervention that does not occur in the present [29][30].

All participants recruited in the s-w cRCT will be included in the economic evaluation of the 'gatekeeper' training intervention. When determining the potential cost-effectiveness of the intervention on a national scale, data will be extrapolated to the total Sri Lankan population.

In accordance with the study perspective, all direct costs related to the implementation of the 'gatekeeper' training intervention and to the health care system will be included in the analysis. Effectiveness data, i.e., number of pesticide self-poisoning cases and deaths prevented, will be obtained from the s-w cRCT. Data from the 'gatekeeper' training intervention s-w cRCT are also used as basis for costing the intervention. All costs associated with the implementation, delivery and follow-up on the intervention are included. Research costs associated with the intervention are excluded from the analyses.

All relevant cost and cost offsets are identified, quantified and ascribed a unit cost. The cost components for the intervention are divided into five categories: capital costs, personnel costs, overhead, consumables, and transportation costs. Unit costs and prices will be obtained from

official statistics, health facilities, the Medical Supply Division of the Ministry of Health and the Provincial Department of Health.

One-way sensitivity analyses will be undertaken to assess how variable uncertainties impact on the cost-effectiveness of the strategies, thereby identifying the factors affecting the total cost of implementation [30]. Multivariate sensitivity analyses will also be performed to assess how simultaneous changes of several variables affect the cost-effectiveness ratio. Probabilistic uncertainty analyses will be performed to explore the impact of variability in input variables that can be measured, and input variables for which there is an underlying probability distribution.

## ETHICS AND DISSEMINATION

Ethical approval was granted by the Ethical Review Committee of the Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka (Reference ERC/2018/30) and the ACCORD Medical Research Ethics Committee, University of Edinburgh (Reference 18-HV-053). This study is sponsored by the Academic and Clinical Central Office for Research Development (Ref. AC 18099) at the University of Edinburgh.

Study approval was received from the national Ministry of Health, the Provincial Departments of Health Services and Agriculture in the North Central Province, Eastern Province, Northern Province and Central Province, the Office of the Registrar of Pesticides, and the Pesticide Technical and Advisory Committee (PeTAC) of Sri Lanka.

The study will be published through both scientific peer-reviewed journals. The outcome will be presented to the provincial Departments of Health Services and Agriculture and PeTAC. Opportunities to disseminate the results both nationally and internationally will be taken including presentations at scientific conferences.

**Consent**

Agreement to participate is being sought from each vendor eligible for the training once details of the study have been provided in the vendor's own language. Individuals identified in case finding are invited to provide informed consent for their information to be used in the research. If the patient is too ill to give consent, or underage (less than 12 years old), consent is requested from a relative (or guardian). If the patient is between 12 and 18 years old, consent from both patient and relative/guardian is requested as per standard Sri Lankan practice.

Both vendors and self-harm patients are provided with an information sheet containing an introduction to the research, its objective, the people involved, the benefits and disadvantages of participating, and contact information of the research group. We also seek written agreement from vendors to participate in follow-up assessments. Vendors are under no obligation to practise what they have learned. The participants are free to withdraw from the study at any point.

The main risk of this study is that discussion concerning self-harm might cause distress. We therefore provide contact information for a local counselling service among self-harm patients immediately after interviews. A sensitive data collection technique is used, and ethical issues are being considered throughout the study.

## Data monitoring

An independent Data Monitoring Committee (DMC) has been established to oversee the safety of trial participants and collection of high-quality data. The DMC aims to meet annually.

## Data availability

Anonymized data will be made available after publication of the trial's results upon submission of a request to the Principal Investigator (m.eddleston@ed.ac.uk).

## Patient and public involvement and engagement (PPIE)

While the pilot Safe Storage studies [31][32] were ongoing, we decided to explore whether we could take a complementary approach by working with pesticide vendors.

The design and development of the 'gatekeeper' intervention for pesticide vendors was done based on a series of community engagement studies, which took place over several years. As part of the intervention developing process, we conducted a stakeholder analysis with key stakeholders (farmers, pesticide vendors, pesticide company representatives, agricultural officers, public health experts and general community) to identify the most promising method to prevent access to pesticides from shops for self-poisoning [33].

A separate feasibility pilot study was conducted with pesticides vendors to understand vendors' concerns on the gatekeeper intervention [22]. For the current trial, we offer opportunities for pesticide vendors to give their perspectives, priorities and issues related to research problem and intervention process. We also discuss and collaborate with Department of Agriculture at group meetings to express views on the proposed intervention.

**Modifications due to COVID-19**

Following the outbreak of COVID-19, the Government of Sri Lanka implemented a national curfew and a ban on gatherings and non-essential movements. This led to a suspension of all research activities for a period of nearly 3 months (17th March 2020 to 7th June 2020). This period of 'lockdown' had implications for both the intervention and surveillance elements of the study.

During the lockdown, we were unable to gather people for training sessions and so the intervention was suspended. This delay resulted in the steps for Zone 1 being reduced from 78 days to 67 days. The intervention had not commenced in Zone 2 by the time lockdown started and so was delayed. It is now being delivered in a compressed time frame of 42 days per step. We also developed remote versions of the training, limiting staff numbers and participants to ensure we complied with local public health guidance. As local outbreaks have occurred since June 2020, there have been additional localized restrictions placed on movements.

During the lockdown, access to all Sri Lankan hospitals was severely restricted and research personnel not permitted on site. The surveillance team remained in contact with hospitals where possible to set up systems for continuing surveillance, such as daily logs, telephone interviews and setting aside records for review post-opening up. Once the curfew was lifted, the team gained access to the records and made telephone calls where possible or visits to households to gather data. Continuing local restrictions on access to hospitals have recurred and individualized systems have been developed in each hospital to minimize the disruption to data collection.

**Study dates**

In Zone 1, recruitment started on September 30, 2019 and should be complete on October 27, 2022. In Zone 2, recruitment started on January 18, 2021 and will be completed in November 2022.

**Author Contributions**

Study conception: ME, MW, FK and MP; Study design: ME, MW, FK, MP, DG, SA, KH, MM, SJ, TA, CM and JAS; Data analysis plan: CM and NT; Surveillance: KD, SR, DR, DA, AK and ST; Intervention: CP, RK; Data management: SR; Cost-effectiveness analysis: FK and LBM: Drafting manuscript: MW, ME, FK, MP, CM, and SP; Critical revisions: all authors. All authors read and approved the final version.

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**DATA MONITORING COMMITTEE**:

John Norrie (University of Edinburgh), Saroj Jayasinghe (University of Colombo) and Richard Maude (University of Oxford).

**COMPETING INTERESTS**

KH is joint chair of the Prevention of Pesticide Self-poisoning Special Interest group of the International Association for Suicide Prevention. He declares having received a small grant from Syngenta for a study of safer storage of pesticides in Sri Lanka. DG, FK and ME were

expert advisers to WHO's Consultation on cost-effectiveness of suicide prevention interventions, including pesticide regulation (Geneva, 2019). They provided technical assistance for the development and publication of Preventing Suicide: A Resource Guide for Pesticide Registrars and Regulators (WHO, May–June 2019). DG was a member of the scientific advisory group for a Syngenta-funded study to assess the toxicity of a new paraquat formulation (2002-2006); a member of the scientific advisory group for a pesticide storage project funded by Syngenta (2005-2007); and chaired the DMEC for a Syngenta-funded trial of the medical management of paraquat poisoning (2007-2010); he received travel costs to attend research meetings but no other fees. DG was an expert adviser to WHO's First Consultation on Best Practices on Community Action for safer access to pesticides (Geneva, 2006). ME is a WHO member of the FAO–WHO Joint Meeting on Pesticide Management and received an unrestricted research grant from Cheminova (2012) and travel expenses from Syngenta to attend study meetings (2005–06). ME is affiliated with the Centre for Pesticide Suicide Prevention, which is funded by an Incubator Grant from the Open Philanthropy Project Fund, an advised fund of Silicon Valley Community Foundation, on the recommendation of GiveWell, USA. The other authors declare no competing interests.

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**Box 1**

**Study definitions**

***(i). Shop cases:*** We defined a shop case as an incidence of self-harm which fulfils each of the following criteria with regards to the purchase of the pesticide: 1) the purchase was made by the individual who ingested it, 2) the purchase occurred at a pesticide shop, 3) the purchase was made within 24 hrs of self-poisoning. We also collected data on whether the person bought the pesticide with the intention of ingesting it. However, we did not include intention within the definition of a shop case, as intention is subjective and may be unreliable.

***(ii). Pesticides:*** A pesticide was defined as an agrochemical (herbicide, insecticide, fungicide or rodenticide) used to control agricultural pests, or a chemical used to control domestic pests.

***(iii). Self-harm patient:*** A self-harm patient in the study was defined as a permanent resident, temporary resident or guest/visitor in the study area at the time of the self-harm episode, who was admitted to one of the study hospitals during the study period due to suicide attempt.

***(iv). Pesticide shop:*** Seasonal shops (open only in agricultural season) or non-seasonal shops that are selling pesticides throughout of the year, regardless of whether they hold a government license to sell pesticides.

***(v). Pesticide vendor:*** Either a full-time or part-time vendor who is directly involved in the sale of pesticide to customers in the study area during the study period.

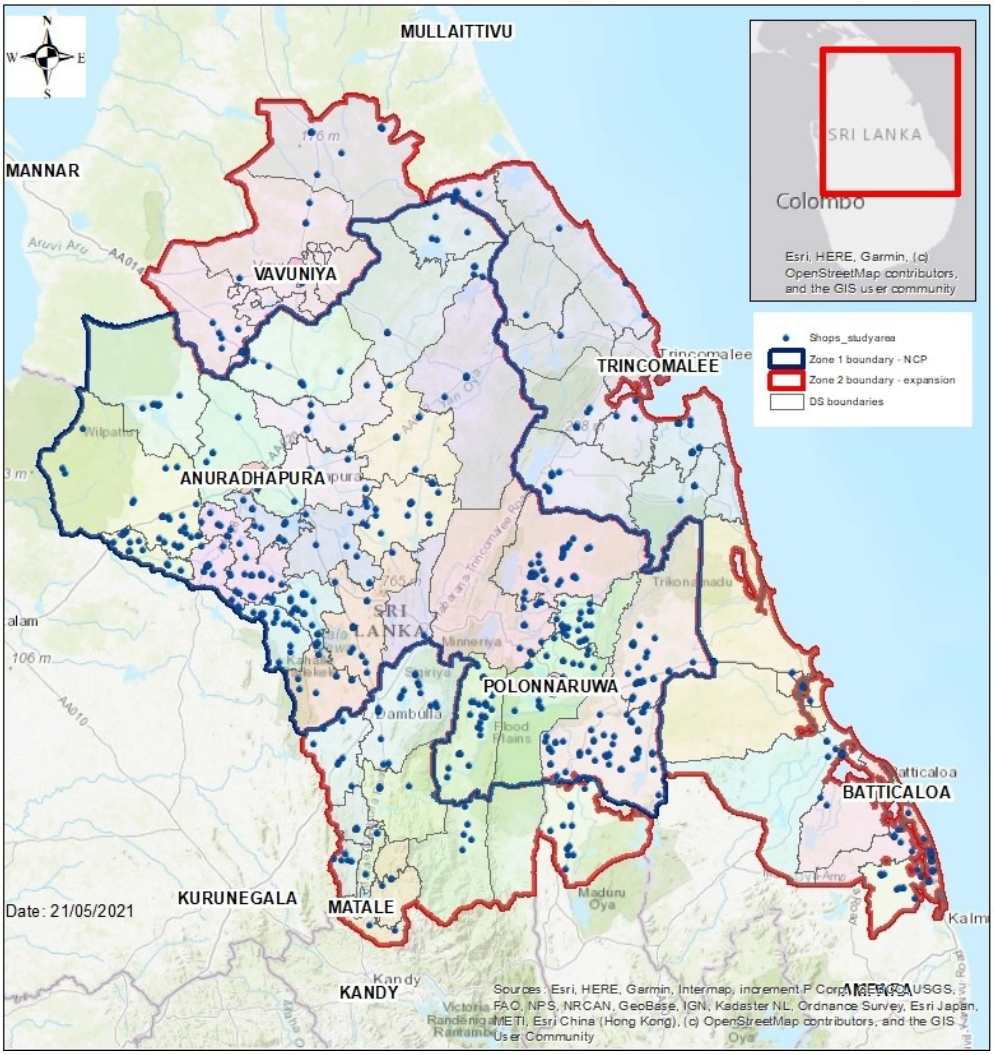


Figure 1: Study area – spatial distribution of pesticide shops across the two Zones

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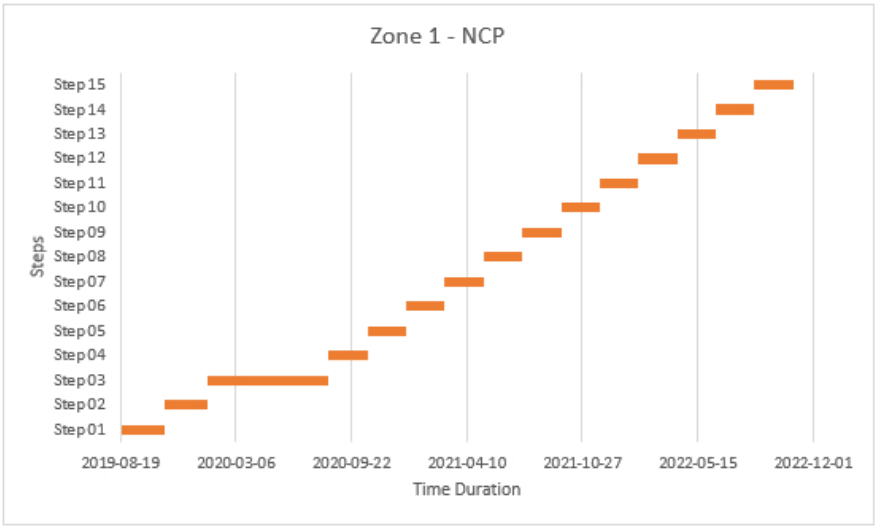


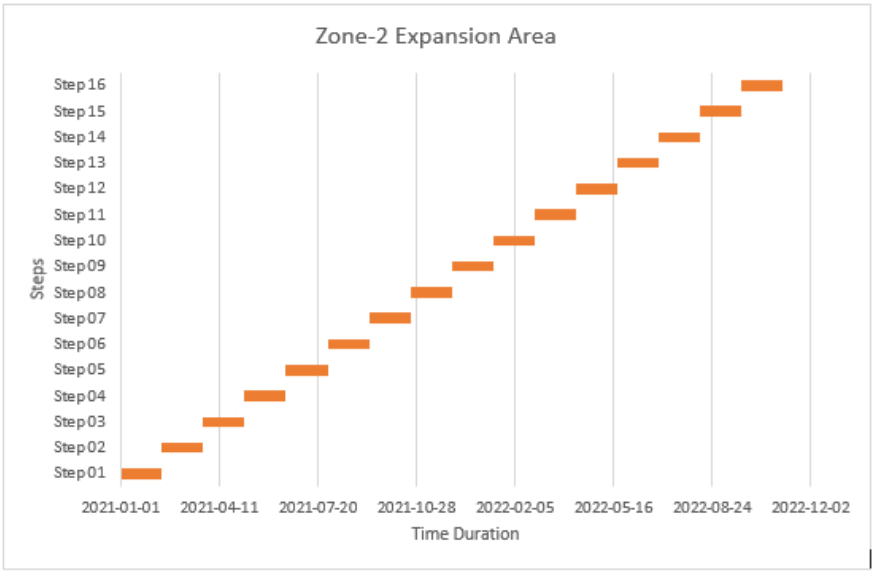


Figure 2: Schematic of the timing of the intervention across the study area and period

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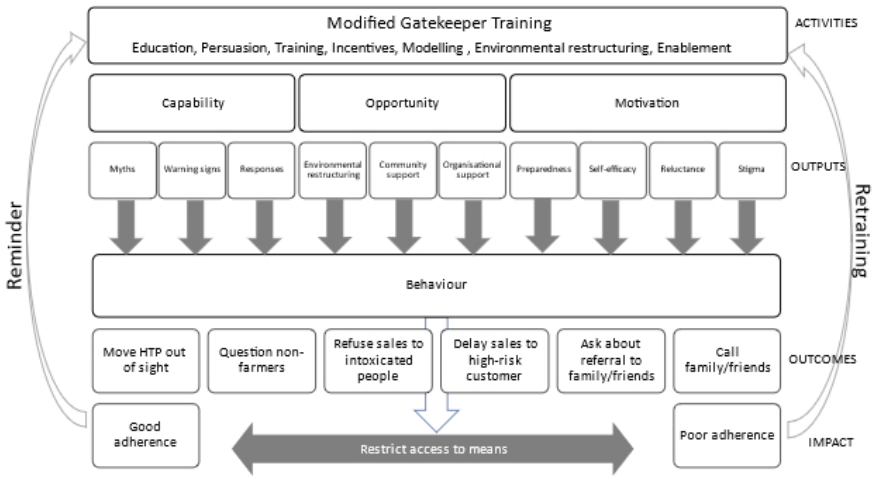


Figure 3: Behaviour change model for the modified 'gatekeeper' training intervention of pesticide vendors in rural Sri Lanka.

474x400mm (38 x 38 DPI)

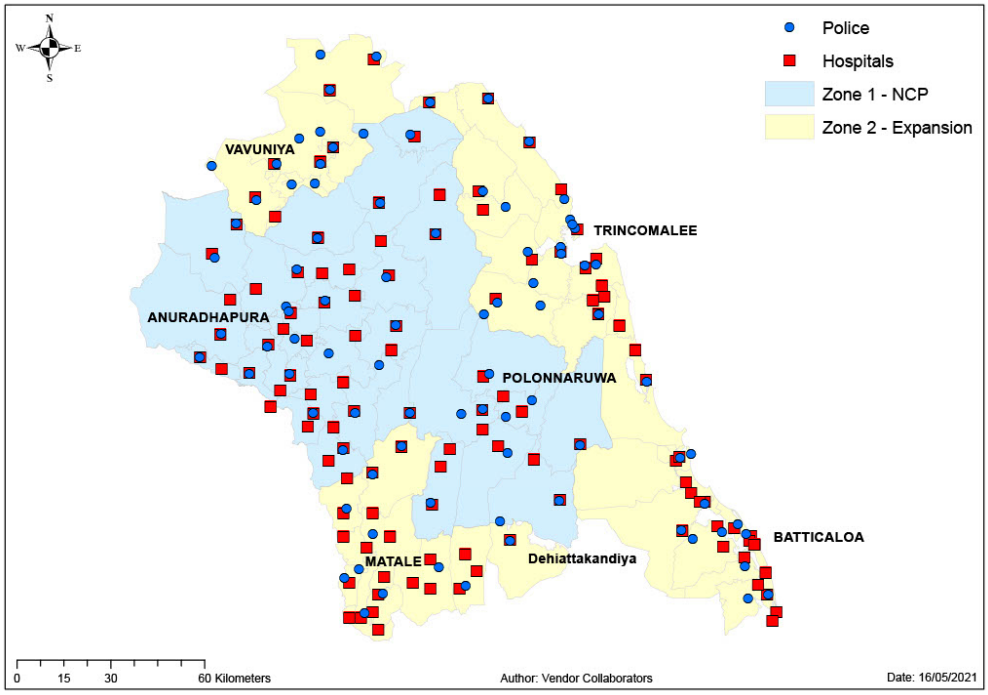


Figure 4: Map of the hospitals and police stations being surveyed across the study area

361x255mm (72 x 72 DPI)

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# Gatekeeper training for vendors to reduce pesticide self-poisoning in rural South Asia – A study protocol for a stepped-wedge cluster randomized controlled trial

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# TITLE PAGE

## Gatekeeper training for vendors to reduce pesticide self-poisoning in rural South Asia – A study protocol for a stepped-wedge cluster randomized controlled trial

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## ABSTRACT

**Introduction:** Pesticide self-poisoning kills an estimated 110,000-168,000 people worldwide annually. Data from South Asia indicate that 15-20% of attempted suicides and 30-50% of completed suicides pesticides are purchased shortly beforehand for this purpose. Individuals who are intoxicated with alcohol and/or non-farmers represent 72% of such customers. We have developed a 'gatekeeper' training program for vendors to enable them to identify individuals at high-risk of self-poisoning (gatekeeper function) and prevent such individuals from accessing pesticides (means restriction). The primary aim of the study is to evaluate the effectiveness of the gatekeeper intervention in preventing pesticide self-poisoning in Sri Lanka. Other aims are to identify method substitution and to assess the cost and cost-effectiveness of the intervention.

**Methods and analysis:** A stepped-wedge, cluster randomized trial of a gatekeeper intervention is being conducted in rural Sri Lanka with a population of approximately 2.7 million. The gatekeeper intervention is being introduced into 70 administrative divisions, in random order at each of 30 steps over a 40-month period. The primary outcome is the number of pesticide self-poisoning cases identified from surveillance of hospitals and police stations. Secondary outcomes include: number of self-poisoning cases using pesticides purchased within the previous 24h, total number of all forms of self-harm, and suicides. Intervention effectiveness will be estimated by comparing outcome measures between the pre- and post-training periods across the divisions in the study area. The original study protocol has been adapted as necessary in light of the impact of the COVID-19 pandemic.

**Ethics and dissemination:** Ethical Review Committee of the Faculty of Medicine and Allied Sciences, Rajarata University, Sri Lanka (ERC/2018/30) and ACCORD Medical Research

Ethics Committee, Edinburgh University (18-HV-053) approved the study. Results will be disseminated in scientific peer-reviewed journals.

**Trial Registration:** Sri Lanka Clinical Trial Registry (https://slctr.lk): SLCTR/2019/006. International Clinical Trials Registry Platform (U1111-1220-8046).

## Article Summary

### Strengths and limitations of this study

- This large-scale study will be the first to provide evidence of whether 'gatekeeper' training for pesticide vendors is effective in reducing pesticide self-poisoning.
- The study provides a pragmatic evaluation of the 'gatekeeper' training, which will be introduced more generally if found to be effective.
- A potential limitation of the stepped wedge design is susceptibility to confounding by secular trends in pesticide self-poisoning rates during the study period.
- The observed treatment effect may be diluted if individuals attempt to purchase pesticides from a shop outside of their division of residence (contamination). Such an effect has been incorporated into sample size power calculations.
- The intervention can potentially only prevent a proportion of pesticide self-poisoning cases (15-20% of cases purchasing pesticides for the act), requiring a large study to provide sufficient statistical power to detect a modest total treatment effect.

## INTRODUCTION

Pesticide self-poisoning is one of the most frequently used global means of suicide [1], equaling 15-20% of all global suicides, or an estimated 110,000-168,000 deaths annually [2]. Many of these deaths occur among people living in rural areas of low and middle-income countries (LMIC) [3][4], who may ingest pesticides impulsively in a moment of crisis [5]. Pesticides are often available in the community, meaning they can be accessed and ingested with little thought at moments of crisis or anger [4][6].

In Sri Lanka, pesticide shops are widespread in agricultural areas, making pesticides freely available for over the counter purchase and providing easy access for self-poisoning [7][8]. In South Asia, 14-20% of attempted suicides [6][9][10] and 33-49% of completed suicides involve pesticides [11] and occur shortly after individuals purchase the pesticides from a shop for the specific purpose of self-harm (a 'shop case', Box 1). To best of our knowledge, no interventions have been aimed at pesticide shops to support vendors in preventing individuals from accessing pesticides for self-poisoning. However, several interventions have been tested to prevent suicides involving a range of other means of self-poisoning methods by reducing access to means at the point of sale in different countries - analgesic packaging restrictions [12][13] and physical barriers to purchases of charcoal [14].

Over a period of three years, we have designed an intervention following the UK Medical Research Council's guidance on development of complex interventions [15] through a series of studies. We first identified major risk factors for buying pesticides for self-harm using a case control design, noting in particular being intoxicated with alcohol at the time of purchase [odds ratio 36.5; 95% confidence interval 1.7 to 783] or being a non-farmer purchasing pesticides [odds ratio 13.3; 95% confidence interval 1.8 to 100] as key risk factors - one and/or other of

these factors characterized 72.0% of cases [16][17]. We then explored the acceptability of possible interventions with stakeholders including pesticide vendors, and finally tested the most acceptable intervention in a qualitative feasibility study. Focus group and stakeholder discussions favored a vendor-based gatekeeper approach identifying, and refusing to sell to, high-risk individuals [18]. A feasibility study showed good vendor acceptance and provided preliminary evidence that it may prevent self-poisoning [19]. Finally, an ex-ante cost analysis and cost-effectiveness threshold analysis of the gatekeeper program were conducted showing it to have a very high potential of being cost-effective [20].

Previous studies have dramatically demonstrated the potential for vendor gatekeeper training to reduce the incidence of pesticide self-poisoning. Because such purchases contribute to many pesticide self-poisoning attempts and deaths cases worldwide, preventing these purchases, as part of a multi-faceted suicide prevention effort, should make a significant contribution to preventing deaths in low-and-middle income countries (LMIC) and to lowering global suicide. However, before this approach is further pursued, a large-scale trial is required to determine its effectiveness.

## OBJECTIVE

The main objective of the study is to test the effectiveness of the gatekeeper intervention in preventing pesticide self-poisoning in Sri Lanka. This study, furthermore, aims to identify method substitution and to assess the cost and cost-effectiveness of the intervention.

## METHODS AND ANALYSIS

### Design

This study is a single-blinded, stepped-wedge cluster randomized controlled trial (s-w cRCT) of a public health intervention involving pesticide shops. A stepped-wedge design was selected to provide a pragmatic evaluation of this low-risk intervention. Definitions used in the trial design are presented in Box 1. This paper complies with the SPIRIT reporting guideline for standard protocol items for clinical trials [21].

**Setting**

The study is being carried out in two areas (Zones) populated by about 2.7 million people (Census, 2019) in 70 divisions, primarily from six districts (Anuradhapura 22 divisions, Polonnaruwa 7, Matale 11, Vavuniya 4, Batticaloa 14, and Trincomalee 11) and 1 division (Dehiattakandiya) from Ampara District (figure 1). Divisions are government administrative regions with populations of ~40,000 people.

Our previous research during 2011-16 found the incidence of pesticide self-poisoning in the South-West Mahaweli H section of North Central Province (NCP, Zone 1) to be over 250 per 100,000 person years [3]. This study was originally designed with this case incidence and included 29 NCP divisions (Zone 1 districts: Anuradhapura, Polonnaruwa; population 1.5 million). However, initial case collection over the first six months (April to September 2019) showed a markedly lower incidence of pesticide self-poisoning at around 130/100,000 per year. The study was therefore expanded into a second area including 41 divisions to the north and east of the initial study area (Expansion area, Zone 2 districts: Matale, Batticaloa, Trincomalee, Vavuniya and part of Ampara; population 1.2 million) to allow recruitment of sufficient cases. Because the two zones started at different times, they are run as parallel studies; the data will be combined for analysis at the end of the study.

***Participant enrolment***

No up-to-date and comprehensive record of pesticide shops and vendors is available. We therefore carried out a baseline mapping exercise identifying all shops selling pesticides, including seasonal shops, both registered and non-registered with the Department of Agriculture. This survey identified 669 shops and 1,406 pesticide vendors in the study area. During the study, regular surveys are being carried out to identify shops that close or open, to ensure an up-to-date list of pesticide shops in the study area. Shops that are missed at initial training in their division will receive training as soon as their presence is noted.

**Inclusion and exclusion criteria**

All pesticide shops and vendors directly involved in pesticide sales in the study area during the study period are eligible for the intervention. It is likely that some people living close to division boundaries cross cluster boundaries to buy pesticides in non-study areas. Therefore, our initial zone 1 design included training of vendors in shops located within 5km of divisional boundaries, outside of the NCP study area. However, after six months of data collection, review of out-of-division purchases revealed that cross-boundary purchases within 5km were minimal (1.3% of all purchases). Since we were expanding the study into contiguous areas, around the north and east study area boundary, a decision was made to discontinue training of vendors outside cluster boundaries. Vendors who are aged under 18 years (<1%) are excluded, as well as cashiers and other store workers in larger pesticide shops who do not directly interact with pesticide-purchasing customers.

**Randomization**

The unit of randomization (cluster) is one or more (usually two) divisions. The intervention is being introduced in each of 30 time periods ("steps" of the stepped wedge design) in the two zones, so training will proceed at each step in two or more divisions (the cluster).

Cross-border contamination, i.e., people crossing into a division with discordant training status from their home division to purchase pesticides, is recognised, particularly where multiple pesticide shops exist along a shared boundary (usually a major road). We therefore identified neighbouring divisions with multiple pesticide shops along such a shared boundary and combined them into a pair, into which the intervention would be introduced during the same step. We expected this approach to reduce contamination.

Random allocation was conducted by a member (NT) of the study team based outside of Sri Lanka once the mapping of pesticide shops and pairing of divisions had been completed, so ensuring allocation was controlled and intervention staff informed two weeks before the start of training (so that logistic plans could be made and maps updated as required). The clusters have been listed in a randomly generated order (using Stata statistical software: StataCorp, College Station, Texas, 2017), and the intervention rolled out into each cluster in turn following this random sequence.

In Zone 1's 29 divisions, the intervention was initially introduced at 78-day intervals; this was reduced to 67-day intervals following COVID-19 pandemic lockdown in March-June 2020. In Zone 2's 41 divisions, the intervention was initially planned to introduce at 66-day intervals. However, Zone 2 started later, after the lockdown, then intervention was introduced at 42-day intervals. Zone 2 intervals are shorter to ensure all training is completed by the time that Zone 1 training is complete. Before the first intervention, a monitoring period (160 days in Zone 1,

and 61 days in Zone 2) was established, during which a baseline number of pesticide self-poisoning cases was recorded.

Overall, the intervention is being rolled out in 15 steps in Zone 1 over 39 months and in 15 steps in Zone 2 over 23 months (figure 2).

**The intervention**

The intervention is a modified 'gatekeeper' training and involves helping pesticide vendors to identify a person at high-risk of purchasing a pesticide for the purpose of self-poisoning (gatekeeper function), in order to then refuse to sell pesticides to this individual (means restriction) [19]. We have utilised the Capability, Opportunity, Motivation and Behaviour (COM-B) model of behaviour change to plan our intervention for modified 'gatekeeper' training [22]. Using the findings from our pilot work [19], we developed a theoretical model of the behaviour change (figure 3). The intervention employs seven strategies: education, persuasion, incentivization, training, environmental restructuring, modelling and enablement. The characteristics of the intervention have been detailed and a manual produced.

The intervention consists of a 1-hour discussion with small-groups of vendors (maximum 10 participants) on their experience with self-poisoning clients, followed by a 1-hour interactive presentation and discussion on how to identify and respond to high-risk clients. Vendors are trained to observe customer for any unusual behaviours [8] such as sadness or nervousness, and for intoxication, and to ask questions on agriculture for which farmers would be expected to know the answer. Short training films have been produced to standardise presentation of information and training across different shops (https://vimeo.com/user14558312). The training uses role-plays to aid development of skills learnt in the training. The session is

performed at a central location within the cluster and/or at pesticide shops in daytime or in evenings, depending on the vendors' preference for the venue and time, and on travel restrictions during the COVID-19 pandemic. The vendors are ideally trained in groups, to increase vendor interaction and cross-learning; however, this is not always possible and had to be stopped during lockdowns in 2020 and 2021.

The intervention is delivered by experienced trainers with extensive local knowledge, assisted by project staff who coordinate the timing and location of training and follow-up training. The trainers were trained using a Train-the-Trainer model in this specific program by a public health researcher (MW), based on his pilot work. During the COVID-19 partial lockdowns, teaching was run virtually using video conference calling with a laptop delivered to the shop for a training session, run by MW from home (see below).

Due to a high level of turnover of both shops and vendors, we continuously monitor for new shops and vendors across the study area to arrange catch-up training as require. No financial incentives are provided to participants; however, transportation for the training and a folder of materials are provided.

A sticker providing key messages from the training is provided to each shop, to be pasted onto the cash machine or drawer, invisible to customers. Otherwise, trained shops do not receive documents that can be displayed in shops as these could potentially unblind potential purchasers.

**Follow-up training**

Brief follow-up reminders are provided during the first six months at 1-month intervals to reinforce the skills taught during the training. Contact is provided by telephone calls, short text messages (SMS), or post cards.

**Data collection procedures**

**(a) Intervention data:** Registered pesticide shops are identified based on records maintained by the Office of the Registrar of Pesticides and mapped using GPS. Unregistered shops are identified and surveyed by field researchers through a snow-balling method (an initial group of vendors to nominate, through their social networks, other pesticides vendors nearby) and through discussions with local communities, representatives of farmer organizations, and pesticide companies, as done in our pilot work [23]. Pesticide shop and vendor information is updated throughout the study. This information is used for cluster allocation and to invite vendors to the training sessions.

We assess pre and post-test knowledge and practice at the beginning and end of the training session and again at 6, 12 and 24 months, using a survey based on our previous work [24], modified for use in this trial. After training, information on compliance assessments is performed using interviews to assess vendors' practices following training.

**(b) Surveillance data:** Self-harm cases are routinely collected at each hospital as part of health information system in Sri Lanka. However, this system has generally been a low priority and no system exist for the vital registration of self-harm cases like for other in-patient data. Therefore, we established a separate prospective surveillance system to identify all in-patient self-harm cases reported to study hospitals and police stations.

In Zone 1, surveillance data collection started on 01 April 2019 and will last for 42 months. In Zone 2, data collection started on 01 November 2020 and will last for 24 months. Surveillance researchers record all fatal and non-fatal self-harm cases admitted to the wards of 118 study hospitals across the region (figure 4). Following our previous household pesticide storage study processes [25], researchers prospectively record self-harm patients through frequent visits to small primary hospitals (7 to 80 beds); at least weekly) and by telephone calls from hospital staff when patients are admitted. In secondary and tertiary care hospitals, researchers attend the medical wards daily and other wards at least weekly to identify other (less common) non-poisoning means of self-harm in surgical, paediatric, and intensive care units, as well as morgues. During the study set up, we explored where study area patients presented to hospital and ensured that all accessed hospitals were surveyed, both in and out of the study area.

There are no minimum or maximum age limits for inclusion. Non-residents of the study area will be excluded from the final analysis.

Data collected include demographic data for all self-harm cases (sex, date of birth, place of residence and farming status) and event-specific information (date and time of self-harm event, method of self-harm, whether the individual was alcohol intoxicated at the time of purchase and time of hospital admission, and whether the individual died). For pesticide poisoning cases, additional data are collected on how the individuals accessed pesticides (whether they bought the pesticides from a shop or accessed them from home or nearby). Specific information collected for shop cases includes whether the individual or someone else bought pesticides, the individual's intent at the time of pesticide purchase (self-harm or agricultural purpose), date and time of the pesticide purchase, and the division location of the pesticide shop.

We record all self-harm deaths occurring outside hospital settings through a network of 90 police stations and judicial medical officers. The researchers visit these sources every three months to extract data about self-harm events, namely the home address, method of self-harm, and the source of any pesticide used. Where patients leave hospital before they can be interviewed or non-hospitalized deaths occur, address details are obtained from the hospital or police station and permission requested from the patient and family to interview them in their homes about the source of pesticide used in the poisoning.

Field researchers are supervised by experienced senior research staff (KD, DR, and DA) who have undergone training in research ethics. Both the surveillance team and the patient (or patient's family) are blind to the training status of the pesticide shop from which the pesticide was purchased. The surveillance team is also kept separate from the intervention team carrying out the training of vendors to reduce the risk of unblinding.

**Outcome events**

This intervention is directed towards a sub-population of "shop cases" who self-poison using pesticides bought for this purpose from a shop in the preceding 24 hours. However, the intervention effectiveness will be estimated by comparing the total number of fatal and non-fatal pesticide self-poisoning attempts identified from surveillance of hospitals and police stations (primary outcome) between the pre- and post-training periods across the divisions in the study area. Secondary outcomes include:

- Number of pesticide self-poisoning patients (fatal and non-fatal attempts) presenting to study hospitals and/or police stations using pesticides purchased within 24 hrs of the act.
- Total number of hospital-presenting self-harm cases, all methods

- Total number of suicides, all methods

## Data Management

Study data are collected and managed using REDCap electronic data capture tools hosted at University of Sydney [26][27]. REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources. Data are collected into REDCap case record form by researcher staff following the same protocol as for the household pesticide storage study [25]. Two REDCap databases are used: intervention and surveillance databases. A data coordinator (SR) is responsible for database maintenance, security, and review of data entry on a weekly basis to identify missing data. The trial manager (MP) reviews a weekly data summary. All databases are password protected. At the end of the study, a final anonymized dataset will be sent to the University of Bristol for analysis and then to the University of Edinburgh for archiving.

## Statistics and data analysis

### *Sample size calculation*

The primary outcome measure is the total number of pesticide self-poisoning cases, whilst the intervention is directed towards a sub-population of "shop cases" who self-poison using pesticides bought for this purpose from a shop in the preceding 24 hours. The subpopulation affected by the intervention is likely to be about 20% of all primary outcome cases. This study is aiming to identify any effect of the intervention amongst all primary outcome events. Calculations were performed by the "stepped-wedge" procedure [28].

Initially, the study was powered taking the mean division population of 15+ year olds to be 35,000, the rate of pesticide self-poisoning without intervention to be 250 cases per 100,000 person years, and the coefficient of variation of pesticide self-poisoning across the divisions to be 0.55 (calculated from our ongoing provincial and study area hospital surveillance). In this case, a stepped wedge design with the intervention introduced into 29 Divisions in two districts at each of 15 steps separated by 78 days (7479 person-years of follow-up of each district at each step) would detect a true 11.5% reduction to 221 cases per 100,000 person years with 90% power at the 5% significance level. To achieve this 11.5% reduction overall requires a 58% reduction amongst shop cases, assuming shop cases make up 20% of all cases in the absence of the intervention. A smaller 10% reduction would be detected with 80% power, all else being equal.

However, after six months, the rate of pesticide self-poisoning in the study area was observed to be 130 cases per 100,000 person years. To achieve an acceptable level of statistical power with this lower incidence rate we decided to approximately double the study area. Assuming for Zone 2 that the intervention would be introduced into 41Divisions in four districts at each of 15 steps each of 66 days duration, then for Zones 1 and 2 combined (with an average 6750 person-years of follow-up of each district during each step) a 11.5% reduction from 130 to 115 pesticide self-poisoning cases per 100,000 person years would be detected with 88% power at the 5% significance level.

***Data analysis***

A signed and dated statistical analysis plan will be written and made publicly available online before release of the data for analysis.

In our previous Safe Storage cRCT [25] in the same context in Sri Lanka, the refusal rate of self-harm patients or their family members for studies is very low (<1%). This level of refusal will not cause bias and does not need to be addressed in the statistical analysis. The division of residence of the patient and date of self-harm event will be used to allocate cases to the correct study condition. The primary analysis will follow the intention-to-treat principle, comparing the observed incidence of pesticide self-poisoning between periods/areas with and without the intervention in place. A Poisson regression model will be used to estimate the intervention effect as an incidence rate ratio, with variation between areas accommodated as a random effect, and any secular or seasonal time trends accommodated as covariates. This approach will be adapted for the secondary event-based outcomes.

The COVID-19 situation in Sri Lanka is still unfolding. Therefore, we will include sensitivity analyses that investigate the impact of COVID-19 measures, taken during the study period, on intervention effectiveness.

**Implementation Analysis**

We will employ a mixed method approach to evaluate the implementation of the intervention based on the REAIM framework [29]; employing quantitative tools to measure reach, effectiveness, adoption, implementation and maintenance and qualitative tools to identify contextual factors that may help to explain the effectiveness of the intervention. REAIM dimension variables and measures are describe in Table 1.

425 **Table 1: REAIM dimension variables and measures**

| Domain | Description | Measures |
|---|---|---|
| REACH | The absolute number, proportion, and representativeness of individuals or settings who are willing to participate in a given initiative. | Exclusion Criteria (% excluded or characteristics)<br>Percent individuals who participate<br>Characteristics of participants compared to non-participants or to target population<br>Reasons contributing to the participation/non-participation of the participants |
| EFFICACY | The impact of an intervention on important outcomes, including potential negative effects, quality of life, and economic outcomes. | Measure of primary outcome<br>Measure of robustness across subgroups (e.g. sex, age, experience, education)<br>Measure of short-term attrition (%) and differential rates by vendor characteristics or shop characteristics<br>Qualitative assessment of contextual factors contributed to the results |
| ADOPTION | The intention, initial decision, or action to try or employ an innovation or evidence-based practice. Adoption also may be referred to as ‘‘uptake.’’ Adoption occurs in the early to mid-implementation stage and is assessed from the setting or staff level. | **Setting Level**<br>Shop Exclusions (% or reasons)<br>Percent of shops approached that participate (valid denominator)<br>Characteristics of shops participating compared to non-participants<br>**Individual Level**<br>Vendor Exclusions (% or reasons)<br>Percent of vendors invited that participated<br>Characteristics of vendors participating vs. non-participating vendors<br>Barriers to adoption<br>Vendor satisfaction with training<br>Trainer feedback |
| IMPLEMENTATION | At the setting level, implementation refers to the intervention agents' fidelity to the various elements of an intervention's protocol. This includes consistency of delivery as intended and the time and cost of the intervention. At the individual level, implementation refers to clients/target populations use of the intervention strategies. | Percent of perfect delivery training (adherence)<br>Adaptations made to intervention during study<br>Cost of intervention (time or money)<br>Consistency of implementation across trainer/time/settings/subgroups<br>Contextual factors linked to the intervention<br>Trainer/vendor attitudes towards the intervention<br>Barriers and facilitators of the intervention |

| | | |
|---|---|---|
| MAINTENANCE | The extent to which a program or policy becomes institutionalized or part of the routine organizational practices and policies. At the individual level, maintenance has been defined as the long-term effects of a program on outcomes after 6 or more months after the most recent intervention contact. | **Individual Level**<br>Measure of training effectiveness immediately following training<br>Robustness data – reassessment of training outcomes at 6 months<br>Measure of long-term attrition (%) and differential rates by shop and vendor characteristics<br>Individual feedback on intervention and assessment of their willingness to maintain adherence in long term.<br>**Setting Level**<br>If and how program was adapted long-term (which elements retained AFTER program completed)<br>Some measure/discussion of alignment to organization mission or sustainability<br>Shop and Vendor feedback on intervention, barriers and facilitators and willingness to maintain change. |

## Economic evaluation

Cost and cost-effectiveness analyses are being conducted concurrently with the trial to assess the cost-effectiveness of the intervention. The cost-effectiveness of implementing the training program on a national level is also being assessed through modelling. A governmental perspective is adopted for the economic evaluations i.e., only cost and outcomes that impact on government as a third-party funder are included. In the economic evaluation of the intervention, a three-year time horizon is applied. This time horizon will be expanded to five years when modelling a full national roll-out of the 'gatekeeper' training intervention.

All costs are expressed in US dollars (US$) and measured in real prices for the reference year (2019) using the gross domestic product deflator. If this is not available, the consumer price index will be used. The discounting of costs is undertaken at the recommended real rate of 3% to take into account the timing of costs and health outcomes of the intervention that does not occur in the present [30][31].

All participants recruited in the s-w cRCT will be included in the economic evaluation of the 'gatekeeper' training intervention. When determining the potential cost-effectiveness of the intervention on a national scale, data will be extrapolated to the total Sri Lankan population.

In accordance with the study perspective, all direct costs related to the implementation of the 'gatekeeper' training intervention and to the health care system will be included in the analysis. Effectiveness data, i.e., number of pesticide self-poisoning cases and deaths prevented, will be obtained from the s-w cRCT. Data from the 'gatekeeper' training intervention s-w cRCT are also used as basis for costing the intervention. All costs associated with the implementation,

delivery and follow-up on the intervention are included. Research costs associated with the intervention are excluded from the analyses.

All relevant cost and cost offsets are identified, quantified and ascribed a unit cost. The cost components for the intervention are divided into five categories: capital costs, personnel costs, overhead, consumables, and transportation costs. Unit costs and prices will be obtained from official statistics, health facilities, the Medical Supply Division of the Ministry of Health and the Provincial Department of Health.

One-way sensitivity analyses will be undertaken to assess how variable uncertainties impact on the cost-effectiveness of the strategies, thereby identifying the factors affecting the total cost of implementation [31]. Multivariate sensitivity analyses will also be performed to assess how simultaneous changes of several variables affect the cost-effectiveness ratio. Probabilistic uncertainty analyses will be performed to explore the impact of variability in input variables that can be measured, and input variables for which there is an underlying probability distribution.

**Patient and public involvement and engagement (PPIE)**

While the pilot Safe Storage studies [32][33] were ongoing, we decided to explore whether we could take a complementary approach by working with pesticide vendors.

The design and development of the 'gatekeeper' intervention for pesticide vendors was done based on a series of community engagement studies, which took place over several years. As part of the intervention developing process, we conducted a stakeholder analysis with key stakeholders (farmers, pesticide vendors, pesticide company representatives, agricultural

officers, public health experts and general community) to identify the most promising method to prevent access to pesticides from shops for self-poisoning [34].

A separate feasibility pilot study was conducted with pesticides vendors to understand vendors' concerns on the gatekeeper intervention [23]. For the current trial, we offer opportunities for pesticide vendors to give their perspectives, priorities and issues related to research problem and intervention process. We also discuss and collaborate with Department of Agriculture at group meetings to express views on the proposed intervention.

## ETHICS AND DISSEMINATION

Ethical approval was granted by the Ethical Review Committee of the Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka (Reference ERC/2018/30) and the ACCORD Medical Research Ethics Committee, University of Edinburgh (Reference 18-HV-053). This study is sponsored by the Academic and Clinical Central Office for Research Development (Ref. AC 18099) at the University of Edinburgh. Before modifications to the protocol will take formal approval from ethics committees.

Study approval was received from the national Ministry of Health, the Provincial Departments of Health Services and Agriculture in the North Central Province, Eastern Province, Northern Province and Central Province, the Office of the Registrar of Pesticides, and the Pesticide Technical and Advisory Committee (PeTAC) of Sri Lanka.

The study will be published through both scientific peer-reviewed journals. The outcome will be presented to the provincial Departments of Health Services and Agriculture and PeTAC.

Opportunities to disseminate the results both nationally and internationally will be taken including presentations at scientific conferences.

**Consent**

Agreement to participate is being sought from each vendor eligible for the training once details of the study have been provided in the vendor's own language. Individuals identified in case finding are invited to provide informed consent for their information to be used in the research. If the patient is too ill to give consent, or underage (less than 12 years old), consent is requested from a relative (or guardian). If the patient is between 12 and 18 years old, consent from both patient and relative/guardian is requested as per standard Sri Lankan practice (Supplementary file 1).

Both vendors and self-harm patients are provided with an information sheet containing an introduction to the research, its objective, the people involved, the benefits and disadvantages of participating, and contact information of the research group (Supplementary file 2). We also seek written agreement from vendors to participate in follow-up assessments. Vendors are under no obligation to practise what they have learned. The participants are free to withdraw from the study at any point.

The main risk of this study is that discussion concerning self-harm might cause distress. We therefore provide contact information for a local counselling service among self-harm patients immediately after interviews. A sensitive data collection technique is used, and ethical issues are being considered throughout the study.

**Data monitoring**

An independent Data Monitoring Committee (DMC) has been established to oversee the safety of trial participants and collection of high-quality data. The DMC aims to meet annually.

**Data availability**

Anonymized data will be made available after publication of the trial's results upon submission of a request to the Principal Investigator (m.eddleston@ed.ac.uk).

**Modifications due to COVID-19**

Following the outbreak of COVID-19, the Government of Sri Lanka implemented a national curfew and a ban on gatherings and non-essential movements. This led to a suspension of all research activities for a period of nearly 3 months (17th March 2020 to 7th June 2020). This period of 'lockdown' had implications for both the intervention and surveillance elements of the study.

During the lockdown, we were unable to gather people for training sessions and so the intervention was suspended. This delay resulted in the steps for Zone 1 being reduced from 78 days to 67 days. The intervention had not commenced in Zone 2 by the time lockdown started and so was delayed. It is now being delivered in a compressed time frame of 42 days per step. Further changes may be required as the COVID-19 situation in Sri Lanka is still ongoing. We also developed remote versions of the training, limiting staff numbers and participants to ensure we complied with local public health guidance. As local outbreaks have occurred since June 2020, there have been additional localized restrictions placed on movements.

During the lockdown, access to all Sri Lankan hospitals was severely restricted and research personnel not permitted on site. The surveillance team remained in contact with hospitals where

possible to set up systems for continuing surveillance, such as daily logs, telephone interviews and setting aside records for review post-opening up. Once the curfew was lifted, the team gained access to the records and made telephone calls where possible or visits to households to gather data. Continuing local restrictions on access to hospitals have recurred and individualized systems have been developed in each hospital to minimize the disruption to data collection.

**Study dates**

In Zone 1, recruitment started on September 30, 2019 and should be complete on October 27, 2022. In Zone 2, recruitment started on January 18, 2021 and will be completed in November 2022. The protocol version is 2.1; 11 Feb 2021.

**Author Contributions**

Study conception: ME, MW, FK and MP; Study design: ME, MW, FK, MP, DG, SA, KH, MM, SJ, TA, CM and JAS; Data analysis plan: CM and NT; Surveillance: KD, SR, DR, DA, AK and ST; Intervention: CP, RK; Data management: SR; Cost-effectiveness analysis: FK and LBM: Drafting manuscript: MW, ME, FK, MP, CM, and SP; Critical revisions: all authors. All authors read and approved the final version.

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**DATA MONITORING COMMITTEE**:

John Norrie (University of Edinburgh), Saroj Jayasinghe (University of Colombo) and Richard Maude (University of Oxford).

## COMPETING INTERESTS

KH is joint chair of the Prevention of Pesticide Self-poisoning Special Interest group of the International Association for Suicide Prevention. He declares having received a small grant from Syngenta for a study of safer storage of pesticides in Sri Lanka. DG, FK and ME were expert advisers to WHO's Consultation on cost-effectiveness of suicide prevention interventions, including pesticide regulation (Geneva, 2019). They provided technical assistance for the development and publication of Preventing Suicide: A Resource Guide for Pesticide Registrars and Regulators (WHO, May–June 2019). DG was a member of the scientific advisory group for a Syngenta-funded study to assess the toxicity of a new paraquat formulation (2002-2006); a member of the scientific advisory group for a pesticide storage project funded by Syngenta (2005-2007); and chaired the DMEC for a Syngenta-funded trial of the medical management of paraquat poisoning (2007-2010); he received travel costs to attend research meetings but no other fees. DG was an expert adviser to WHO's First Consultation on Best Practices on Community Action for safer access to pesticides (Geneva, 2006). ME is a WHO member of the FAO–WHO Joint Meeting on Pesticide Management and received an unrestricted research grant from Cheminova (2012) and travel expenses from Syngenta to attend study meetings (2005–06). ME is affiliated with the Centre for Pesticide Suicide Prevention, which is funded by an Incubator Grant from the Open Philanthropy Project Fund, an advised fund of Silicon Valley Community Foundation, on the recommendation of GiveWell, USA. The other authors declare no competing interests.

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## Figure legends

**Figure 1:** Study area – spatial distribution of pesticide shops across the two Zones

**Figure 2:** Schematic of the timing of the intervention across the study area and period

**Figure 3:** Behaviour change model for the modified 'gatekeeper' training intervention of pesticide vendors in rural Sri Lanka.

**Figure 4:** Map of the hospitals and police stations being surveyed across the study area.

**Box 1**

**Study definitions**

***(i). Shop cases:*** We defined a shop case as an incidence of self-harm which fulfils each of the following criteria with regards to the purchase of the pesticide: 1) the purchase was made by the individual who ingested it, 2) the purchase occurred at a pesticide shop, 3) the purchase was made within 24 hrs of self-poisoning. We also collected data on whether the person bought the pesticide with the intention of ingesting it. However, we did not include intention within the definition of a shop case, as intention is subjective and may be unreliable.

***(ii). Pesticides:*** A pesticide was defined as an agrochemical (herbicide, insecticide, fungicide or rodenticide) used to control agricultural pests, or a chemical used to control domestic pests.

***(iii). Self-harm patient:*** A self-harm patient in the study was defined as a permanent resident, temporary resident or guest/visitor in the study area at the time of the self-harm episode, who was admitted to one of the study hospitals during the study period due to suicide attempt.

***(iv). Pesticide shop:*** Seasonal shops (open only in agricultural season) or non-seasonal shops that are selling pesticides throughout of the year, regardless of whether they hold a government license to sell pesticides.

***(v). Pesticide vendor:*** Either a full-time or part-time vendor who is directly involved in the sale of pesticide to customers in the study area during the study period.

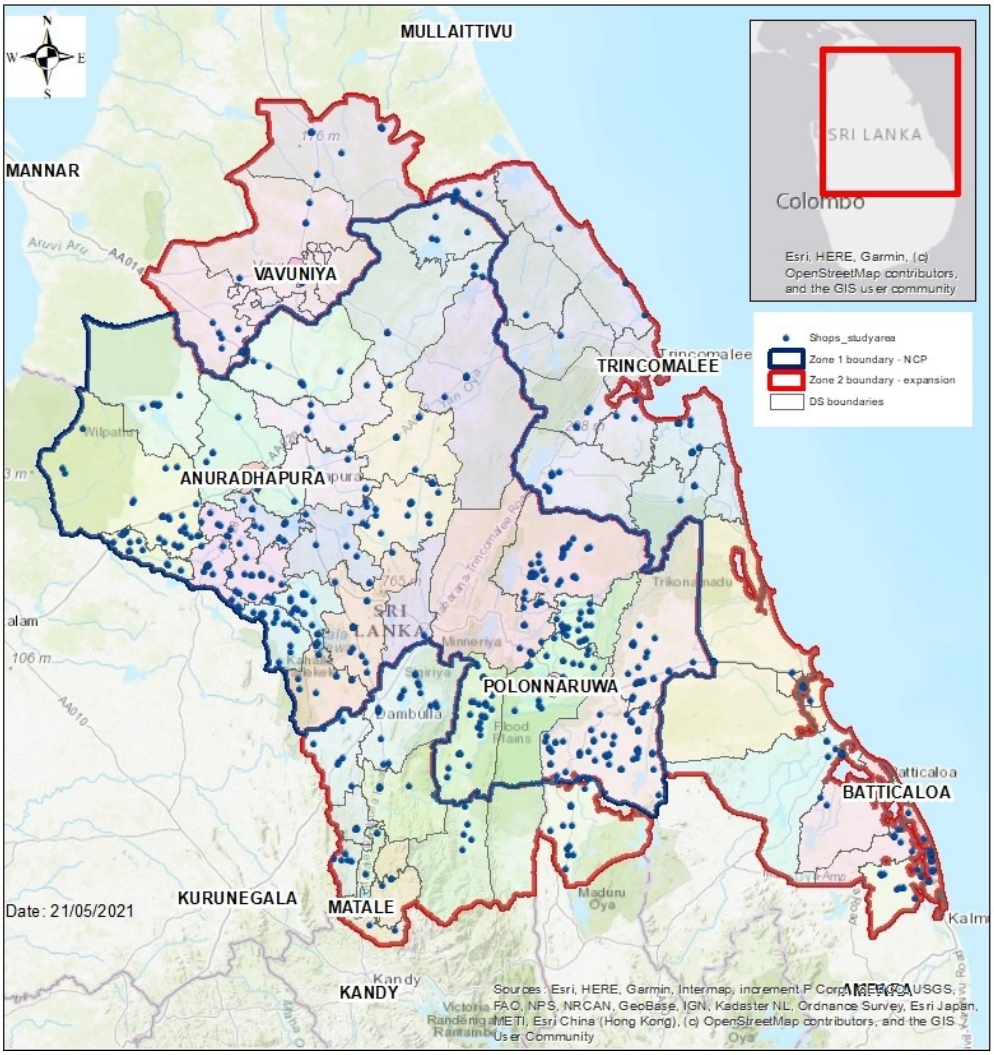
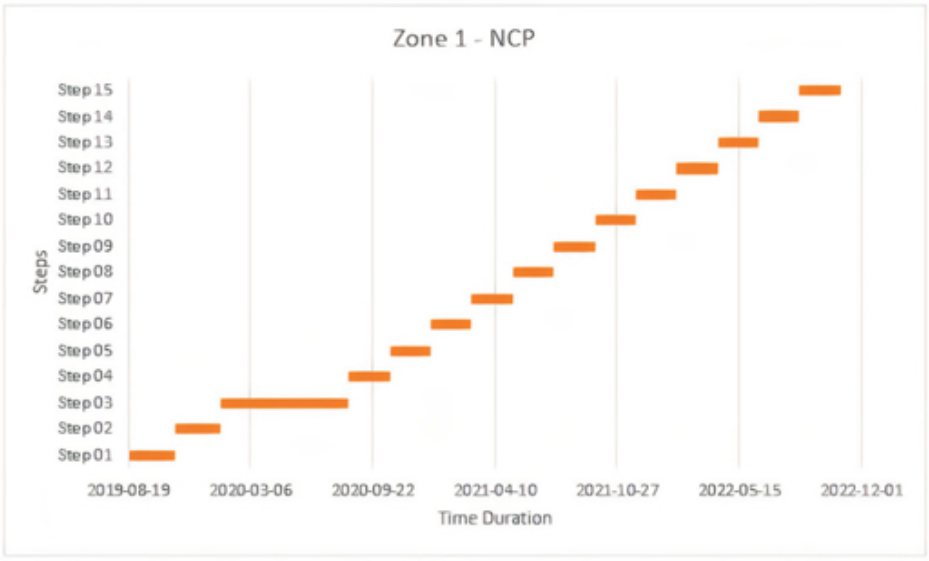



Figure 1: Study area – spatial distribution of pesticide shops across the two Zones

207x218mm (96 x 96 DPI)



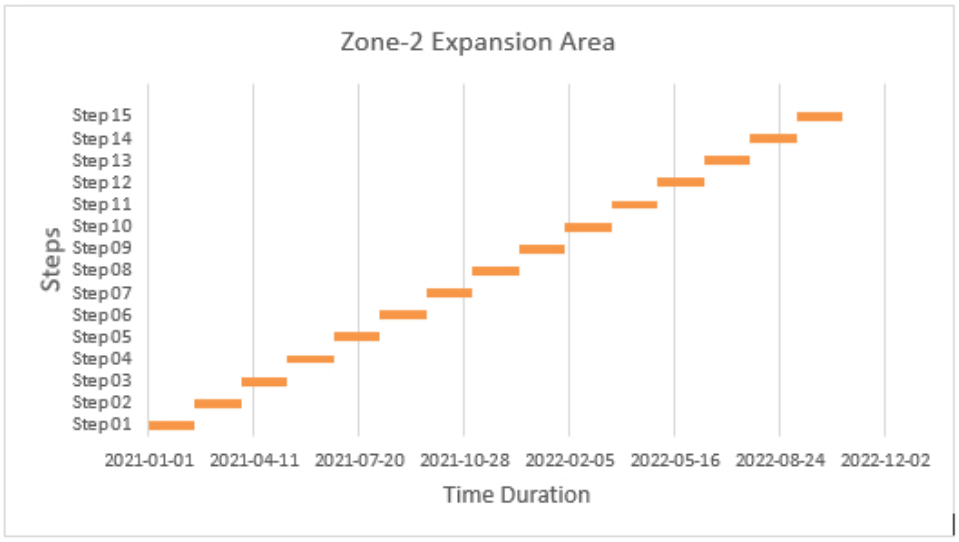




Figure 2: Schematic of the timing of the intervention across the study area and period

291x357mm (47 x 47 DPI)

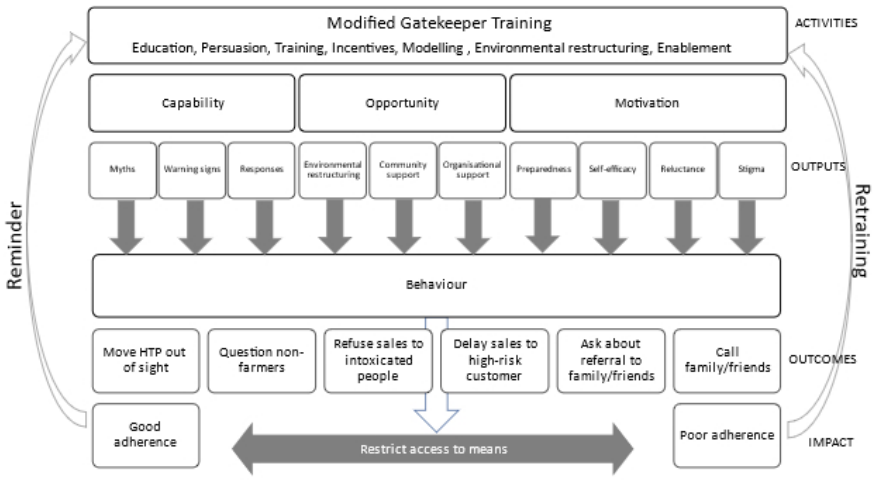



Figure 3: Behaviour change model for the modified 'gatekeeper' training intervention of pesticide vendors in rural Sri Lanka.

474x400mm (38 x 38 DPI)

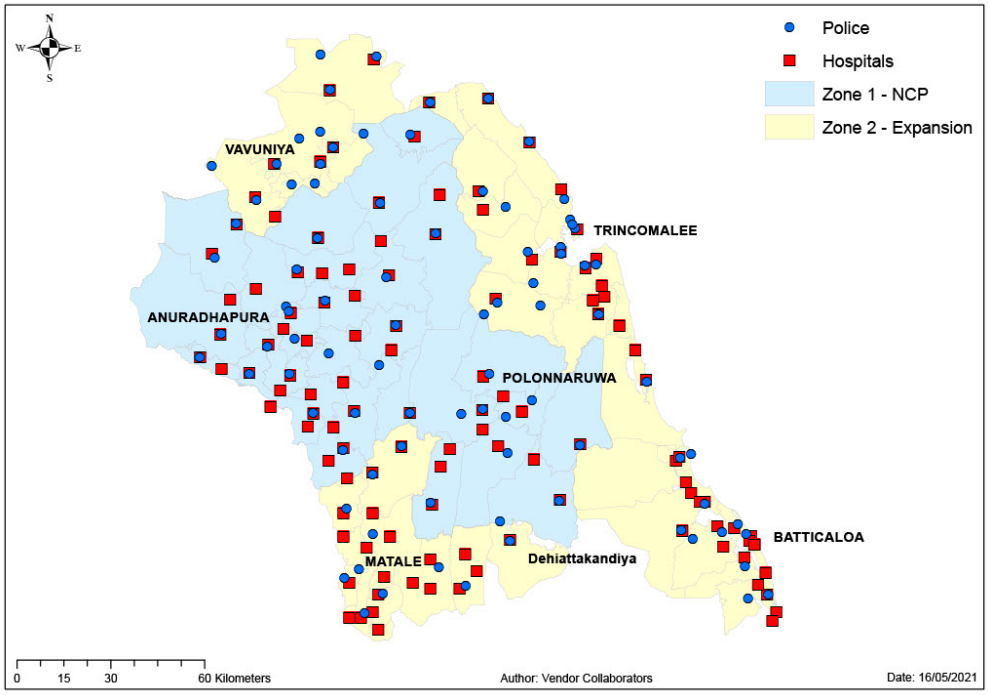



Figure 4: Map of the hospitals and police stations being surveyed across the study area

361x255mm (72 x 72 DPI)

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

| Section/item | Item No | Description | Page(s) / line numbers |
|---|---|---|---|
| **Administrative information** | | | |
| Title | 1 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym | Page 1 / line 2-3 |
| Trial registration | 2a | Trial identifier and registry name. If not yet registered, name of intended registry | Page 5 / line 92-93 |
| | 2b | All items from the World Health Organization Trial Registration Data Set | Page 5 / line 92<br>We have recently submitted the revised registry forms requesting a revision to the Clinical Trial Registry (SLCTR) and still revisions are under consideration.<br>Sri Lanka Clinical Trail Registry (https://slctr.lk): SLCTR/2019/006.<br>International Clinical Trials Registry Platform (U1111-1220-8046). |
| Protocol version | 3 | Date and version identifier | Page 27 / line 561 |
| Funding | 4 | Sources and types of financial, material, and other support | Page 25 / line 570-574 |
| Roles and responsibilities | 5a | Names, affiliations, and roles of protocol contributors | Page 1-2 / line 5-31<br>Page 27 / line 563- 567 |
| | 5b | Name and contact information for the trial sponsor | Page 5 / line 92 (Name and contact information of the trial sponsor is available as part of the trial registry |

| | | | |
|---|---|---|---|
| | | | information) |
| | 5c | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities | Page 27 / line 571-572 |
| | 5d | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) | Page 17 / line 355-368 |
| **Introduction** | | | |
| Background and rationale | 6a | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention | Page 7-8 / line 109-148 |
| | 6b | Explanation for choice of comparators | Page 7 / line 122-125 |
| Objectives | 7 | Specific objectives or hypotheses | Page 8 / line 150-153 |
| Trial design | 8 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) | Page 8-9 / line 155-161 |
| **Methods: Participants, interventions, and outcomes** | | | |
| Study setting | 9 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained | Page 9 / line 163-180 |
| Eligibility criteria | 10 | Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) | Page 10 / line 191-202 |
| Interventions | 11a | Interventions for each group with sufficient detail to allow | Page 12-13 / line 236-276 |

| | | | |
|---|---|---|---|
| | | replication, including how and when they will be administered | |
| | 11b | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) | Page 13 / line 268-271 |
| | 11c | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) | Page 9 / line 172-178<br>Page 10 / line 194-198<br>Page 11/ line 224-228<br>Page 26-27 / line 533-556 |
| | 11d | Relevant concomitant care and interventions that are permitted or prohibited during the trial | In the protocol V2.5 11 FEB 2020 – page 16 |
| Outcomes | 12 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended | Page 16-17 / line 342-353 |
| Participant timeline | 13 | Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) | Figure 2 |
| Sample size | 14 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations | Page 17-18 / line 370--398 |
| Recruitment | 15 | Strategies for achieving adequate participant enrolment to reach target sample size | Page 18 / line 394-398 |
| **Methods: Assignment of interventions (for controlled trials)** | | | |
| Allocation: | | | |
| Sequence generation | 16a | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for | Page 10-11 / line 204-207 |

| | | | |
|---|---|---|---|
| | | stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions | |
| Allocation concealment mechanism | 16b | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned | Page 11 / line 216-222 |
| Implementation | 16c | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions | Page 11 / line 216-219 |
| Blinding (masking) | 17a | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how | Page 16 / line 336-340 |
| | 17b | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial | Page 16 / line 336-340 |
| **Methods: Data collection, management, and analysis** | | | |
| Data collection methods | 18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol | Page 14-16 / line 298-340<br>Data collection forms are available with the protocol |
| | 18b | Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols | Not applicable |
| Data management | 19 | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data | Page 17 / line 355-368 |

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| | | management procedures can be found, if not in the protocol | |
| Statistical methods | 20a | Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol | Page 18-19 / line 400-417<br><br>Overall statistical analysis plan will be written and made publicly available online before release of the data for analysis. |
| | 20b | Methods for any additional analyses (eg, subgroup and adjusted analyses) | Page 19 / line 414-416 |
| | 20c | Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) | Page 18-19 / line 400-417<br><br>Overall statistical analysis plan will be written and made publicly available online before release of the data for analysis. |
| **Methods: Monitoring** | | | |
| Data monitoring | 21a | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed | Page 25-26 / line 525-527 |
| | 21b | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial | No formal stopping rules or interim analyses are planned. However, the data monitoring committee is responsible for safeguarding the interests of trial participants and monitoring the quality of the research. |

| | | | |
|---|---|---|---|
| Harms | 22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct | Page 25 / line 520-523<br>In the protocol V 2.1 11 FEB 2020 - page 21, 11.4. |
| Auditing | 23 | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor | In the protocol V 2.1 11 FEB 2020 - page 21, 11.5. |
| **Ethics and dissemination** | | | |
| Research ethics approval | 24 | Plans for seeking research ethics committee/institutional review board (REC/IRB) approval | Page 24 / line 487-492 |
| Protocol amendments | 25 | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) | Page 24 / line 491-492 |
| Consent or assent | 26a | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) | Page 25 / line 504-523 |
| | 26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable | Not applicable. |
| Confidentiality | 27 | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial | Page 17 / line 364-368 |
| Declaration of interests | 28 | Financial and other competing interests for principal investigators for the overall trial and each study site | Page 28/ line 580=599 |
| Access to data | 29 | Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators | Page 26 / line 529-531 |
| Ancillary and post-trial care | 30 | Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation | Not applicable |
| Dissemination policy | 31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other | Page 24-25 / line 499-502 |

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| | | relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions | |
| | 31b | Authorship eligibility guidelines and any intended use of professional writers | No specific guideline plan for authorship, however those who make a significant contribution to the conception or design of the trial or the acquisition, analysis, interpretation of data and those who work on drafts or review/revise it critically for important intellectual content will be authors in the result paper. |
| | 31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code | Full protocol: Can be download in the trail registration (Page 5 line 92)<br>Participant-level dataset: Page 26 / line 529-531<br>Statistical code: Statistical analysis plan will be written and made publicly available online before release of the data for analysis. |
| **Appendices** | | | |
| Informed consent materials | 32 | Model consent form and other related documentation given to participants and authorised surrogates | Annex 1: “Self-harm patients (≥18-years old)” consent form<br>Annex 2: participant information leaflet |
| Biological specimens | 33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable | Not applicable |

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

# Gatekeeper training for vendors to reduce pesticide self-poisoning in rural South Asia – A study protocol for a stepped-wedge cluster randomized controlled trial



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| | |
|---|---|
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| Primary Subject Heading: | Public health |
| Secondary Subject Heading: | Global health |
| Keywords: | Suicide & self-harm < PSYCHIATRY, PUBLIC HEALTH, TOXICOLOGY |
| | |

# TITLE PAGE

## Gatekeeper training for vendors to reduce pesticide self-poisoning in rural South Asia – A study protocol for a stepped-wedge cluster randomized controlled trial

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## ABSTRACT

**Introduction:** Pesticide self-poisoning kills an estimated 110,000-168,000 people worldwide annually. Data from South Asia indicate that in 15-20% of attempted suicides and 30-50% of completed suicides involving pesticides these are purchased shortly beforehand for this purpose. Individuals who are intoxicated with alcohol and/or non-farmers represent 72% of such customers. We have developed a 'gatekeeper' training program for vendors to enable them to identify individuals at high-risk of self-poisoning (gatekeeper function) and prevent such individuals from accessing pesticides (means restriction). The primary aim of the study is to evaluate the effectiveness of the gatekeeper intervention in preventing pesticide self-poisoning in Sri Lanka. Other aims are to identify method substitution and to assess the cost and cost-effectiveness of the intervention.

**Methods and analysis:** A stepped-wedge, cluster randomized trial of a gatekeeper intervention is being conducted in rural Sri Lanka with a population of approximately 2.7 million. The gatekeeper intervention is being introduced into 70 administrative divisions, in random order at each of 30 steps over a 40-month period. The primary outcome is the number of pesticide self-poisoning cases identified from surveillance of hospitals and police stations. Secondary outcomes include: number of self-poisoning cases using pesticides purchased within the previous 24h, total number of all forms of self-harm, and suicides. Intervention effectiveness will be estimated by comparing outcome measures between the pre- and post-training periods across the divisions in the study area. The original study protocol has been adapted as necessary in light of the impact of the COVID-19.

**Ethics and dissemination:** Ethical Review Committee of the Faculty of Medicine and Allied Sciences, Rajarata University, Sri Lanka (ERC/2018/30) and ACCORD Medical Research

Ethics Committee, Edinburgh University (18-HV-053) approved the study. Results will be disseminated in scientific peer-reviewed journals.

**Trial Registration:** Sri Lanka Clinical Trial Registry (https://slctr.lk):SLCTR/2019/006. International Clinical Trials Registry Platform (U1111-1220-8046).

## Article Summary

### Strengths and limitations of this study

- The study provides a pragmatic evaluation of the 'gatekeeper' training, which will be introduced more generally if found to be effective.
- A potential limitation of the stepped wedge design is susceptibility to confounding by secular trends in pesticide self-poisoning rates during the study period.
- The observed treatment effect may be diluted if individuals attempt to purchase pesticides from a shop outside of their division of residence (contamination).
- The intervention can potentially only prevent a proportion of pesticide self-poisoning cases (15-20% of cases purchasing pesticides for the act), requiring a large study to provide sufficient statistical power to detect a modest total treatment effect.

## INTRODUCTION

Pesticide self-poisoning is one of the most frequently used global means of suicide [1], equaling 15-20% of all global suicides, or an estimated 110,000-168,000 deaths annually [2]. Many of these deaths occur among people living in rural areas of low and middle-income countries (LMIC) [3][4], who may ingest pesticides impulsively in a moment of crisis [5]. Pesticides are often available in the community, meaning they can be accessed and ingested with little thought at moments of crisis or anger [4][6].

In Sri Lanka, pesticide shops are widespread in agricultural areas, making pesticides freely available for over the counter purchase and providing easy access for self-poisoning [7][8]. In South Asia, 14-20% of attempted suicides [6][9][10] and 33-49% of completed suicides involve pesticides [11] and occur shortly after individuals purchase the pesticides from a shop for the specific purpose of self-harm (a 'shop case', Box 1). To the best of our knowledge, no interventions have been aimed at pesticide shops to support vendors in preventing individuals from accessing pesticides for self-poisoning. However, several interventions have been tested to prevent suicides involving a range of other means of self-poisoning methods by reducing access to means at the point of sale in different countries - analgesic packaging restrictions [12][13] and physical barriers to purchases of charcoal [14].

Over a period of three years, we have designed an intervention following the UK Medical Research Council's guidance on development of complex interventions [15] through a series of studies. We first identified major risk factors for buying pesticides for self-harm using a case control design, noting in particular being intoxicated with alcohol at the time of purchase [odds ratio 36.5; 95% confidence interval 1.7 to 783] or being a non-farmer purchasing pesticides [odds ratio 13.3; 95% confidence interval 1.8 to 100] as key risk factors - one and/or other of

these factors characterized 72.0% of cases [16][17]. We then explored the acceptability of possible interventions with stakeholders including pesticide vendors, and finally tested the most acceptable intervention in a qualitative feasibility study. Focus group and stakeholder discussions favoured a vendor-based gatekeeper approach identifying, and refusing to sell to, high-risk individuals [18]. A feasibility study showed good vendor acceptance and provided preliminary evidence that it may prevent self-poisoning [19]. Finally, an ex-ante cost analysis and a cost-effectiveness threshold analysis of the gatekeeper program were conducted, showing it to have a very high potential of being cost-effective [20].

Previous studies have dramatically demonstrated the potential for vendor gatekeeper training to reduce the incidence of pesticide self-poisoning. Because such purchases contribute to many pesticide self-poisoning attempts and deaths cases worldwide, preventing these purchases, as part of a multi-faceted suicide prevention effort, should make a significant contribution to preventing deaths in low-and-middle income countries (LMIC) and to lowering global suicide. However, before this approach is further pursued, a large-scale trial is required to determine its effectiveness.

## OBJECTIVE

The main objective of the study is to test the effectiveness of the gatekeeper intervention in preventing pesticide self-poisoning in Sri Lanka. This study, furthermore, aims to identify method substitution and to assess the cost and cost-effectiveness of the intervention.

## METHODS AND ANALYSIS

### Design

This study is a single-blinded, stepped-wedge cluster randomized controlled trial (s-w cRCT) of a public health intervention involving pesticide shops. A stepped-wedge design was selected to provide a pragmatic evaluation of this low-risk intervention. Definitions used in the trial design are presented in Box 1. This paper complies with the SPIRIT reporting guideline for standard protocol items for clinical trials [21].

**Setting**

The study is being carried out in two areas (Zones) populated by about 2.7 million people (Census, 2019) in 70 divisions, primarily from six districts (Anuradhapura 22 divisions, Polonnaruwa 7, Matale 11, Vavuniya 4, Batticaloa 14, and Trincomalee 11) and 1 division (Dehiattakandiya) from Ampara District (figure 1). Divisions are government administrative regions with populations of ~40,000 people.

Our previous research during 2011-16 found the incidence of pesticide self-poisoning in the South-West Mahaweli H section of North Central Province (NCP, Zone 1) to be over 250 per 100,000 person years [3]. This study was originally designed with this case incidence and included 29 NCP divisions (Zone 1 districts: Anuradhapura, Polonnaruwa; population 1.5 million). However, initial case collection over the first six months (April to September 2019) showed a markedly lower incidence of pesticide self-poisoning at around 130/100,000 per year. The study was therefore expanded into a second area including 41 divisions to the north and east of the initial study area (Expansion area, Zone 2 districts: Matale, Batticaloa, Trincomalee, Vavuniya and part of Ampara; population 1.2 million) to allow recruitment of sufficient cases. Because involvement of the two zones started at different times, they are run as parallel studies; the data will be combined for analysis at the end of the study.

***Participant enrolment***

No up-to-date and comprehensive record of pesticide shops and vendors is available. We therefore carried out a baseline mapping exercise identifying all shops selling pesticides, including seasonal shops, both registered and non-registered with the Department of Agriculture. This survey identified 669 shops and 1,406 pesticide vendors in the study area. During the study, regular surveys are being carried out to identify shops that close or open, to ensure an up-to-date list of pesticide shops in the study area. Shops that are missed at initial training in their division will receive training as soon as their presence is noted.

**Inclusion and exclusion criteria**

All pesticide shops and vendors directly involved in pesticide sales in the study area during the study period are eligible for the intervention. It is likely that some people living close to division boundaries cross cluster boundaries to buy pesticides in non-study areas. Therefore, our initial zone 1 design included training of vendors in shops located within 5km of divisional boundaries, outside of the NCP study area. However, after six months of data collection, review of out-of-division purchases revealed that cross-boundary purchases within 5km were minimal (1.3% of all purchases). Since we were expanding the study into contiguous areas, around the north and east study area boundary, a decision was made to discontinue training of vendors outside cluster boundaries. Vendors who are aged under 18 years (<1%) are excluded, as well as cashiers and other store workers in larger pesticide shops who do not directly interact with pesticide-purchasing customers.

**Randomization**

The unit of randomization (cluster) is one or more (usually two) divisions. The intervention is being introduced in each of 30 time periods ("steps" of the stepped wedge design) in the two zones, so training will proceed at each step in two or more divisions (the cluster).

Cross-border contamination, i.e., people crossing into a division with discordant training status from their home division to purchase pesticides, is recognised, particularly where multiple pesticide shops exist along a shared boundary (usually a major road). We therefore identified neighbouring divisions with multiple pesticide shops along such a shared boundary and combined them into a pair, into which the intervention would be introduced during the same step. We expected this approach to reduce contamination.

Random allocation was conducted by a member (NT) of the study team based outside of Sri Lanka once the mapping of pesticide shops and pairing of divisions had been completed, so ensuring allocation was controlled and intervention staff informed two weeks before the start of training (so that logistic plans could be made and maps updated as required). The clusters have been listed in a randomly generated order (using Stata statistical software: StataCorp, College Station, Texas, 2017), and the intervention rolled out into each cluster in turn following this random sequence.

In Zone 1's 29 divisions, the intervention was initially introduced at 78-day intervals; this was reduced to 67-day intervals following COVID-19 pandemic lockdown in March-June 2020. In Zone 2's 41 divisions, the intervention was initially planned to introduce at 66-day intervals. However, as Zone 2 started later, after the lockdown, the intervention was introduced at 42-day intervals. Zone 2 intervals are shorter to ensure all training is completed by the time that Zone 1 training is complete. Before the first intervention, a monitoring period (160 days in

Zone 1, and 61 days in Zone 2) was established, during which a baseline number of pesticide self-poisoning cases was recorded.

Overall, the intervention is being rolled out in 15 steps in Zone 1 over 39 months and in 15 steps in Zone 2 over 23 months (figure 2).

**The intervention**

The intervention is a modified 'gatekeeper' training and involves helping pesticide vendors to identify a person at high-risk of purchasing a pesticide for the purpose of self-poisoning (gatekeeper function), in order to then refuse to sell pesticides to this individual (means restriction) [19]. We have utilised the Capability, Opportunity, Motivation and Behaviour (COM-B) model of behaviour change to plan our intervention for modified 'gatekeeper' training [22]. Using the findings from our pilot work [19], we developed a theoretical model of the behaviour change (figure 3). The intervention employs seven strategies: education, persuasion, incentivisation, training, environmental restructuring, modelling and enablement. The characteristics of the intervention have been detailed and a manual produced.

The intervention consists of a 1-hour discussion with small-groups of vendors (maximum 10 participants) on their experience with self-poisoning clients, followed by a 1-hour interactive presentation and discussion on how to identify and respond to high-risk clients. Vendors are trained to observe customer for any unusual behaviours [8] such as sadness or nervousness, and for intoxication, and to ask questions on agriculture for which farmers would be expected to know the answer. Short training films have been produced to standardise presentation of information and training across different shops (https://vimeo.com/user14558312). The training uses role-plays to aid development of skills learnt in the training. The session is

performed at a central location within the cluster and/or at pesticide shops in daytime or in evenings, depending on the vendors' preference for the venue and time, and on travel restrictions during the COVID-19 pandemic. The vendors are ideally trained in groups, to increase vendor interaction and cross-learning; however, this is not always possible and had to be stopped during lockdowns in 2020 and 2021.

The intervention is delivered by experienced trainers with extensive local knowledge, assisted by project staff who coordinate the timing and location of training and follow-up training. The trainers were trained using a Train-the-Trainer model in this specific program by a public health researcher (MW), based on his pilot work. During the COVID-19 partial lockdowns, teaching was run virtually using video conference calling with a laptop delivered to the shop for a training session, run by MW from home (see below).

Due to a high level of turnover of both shops and vendors, we continuously monitor for new shops and vendors across the study area to arrange catch-up training as require. No financial incentives are provided to participants; however, transportation for the training and a folder of materials are provided.

A sticker with key messages from the training is provided to each shop, to be pasted onto the cash machine or drawer, not visible to customers. Trained shops do not receive other documents that can be displayed in shops as these could potentially unblind potential purchasers.

**Follow-up training**

Brief follow-up reminders are provided during the first six months at 1-month intervals to reinforce the skills taught during the training. Contact is provided by telephone calls, short text messages (SMS), or postcards.

**Data collection procedures**

**(a) Intervention data:** Registered pesticide shops are identified based on records maintained by the Office of the Registrar of Pesticides and mapped using Global Positioning System (GPS). Unregistered shops are identified and surveyed by field researchers through a snow-balling method (an initial group of vendors to nominate, through their social networks, other pesticides vendors nearby) and through discussions with local communities, representatives of farmer organizations, and pesticide companies, as done in our pilot work [23]. Pesticide shop and vendor information is updated throughout the study. This information is used for cluster allocation and to invite vendors to the training sessions.

We assess pre and post-test knowledge and practice at the beginning and end of the training session and again at 6, 12 and 24 months, using a survey based on our previous work [24], modified for use in this trial. After training, information on compliance assessments is obtained through interviews to assess vendors' practices following training.

**(b) Surveillance data:** Self-harm cases are routinely collected at each hospital as part of health information system in Sri Lanka. However, this system has generally been a low priority and no system exist for the vital registration of self-harm cases as exists for other in-patient data. Therefore, we established a separate prospective surveillance system to identify all in-patient self-harm cases reported to study hospitals and police stations.

In Zone 1, surveillance data collection started on 01 April 2019 and will last for 42 months. In Zone 2, data collection started on 01 November 2020 and will last for 24 months. Surveillance researchers record all fatal and non-fatal self-harm cases admitted to the wards of 118 study hospitals across the region (figure 4). Following our previous household pesticide storage study processes [25], researchers prospectively record self-harm patients through frequent visits to small primary hospitals (7 to 80 beds), at least weekly, and by telephone calls from hospital staff when patients are admitted. In secondary and tertiary care hospitals, researchers attend the medical wards daily and other wards at least weekly to identify patients with other (less common) non-poisoning means of self-harm in surgical, paediatric, and intensive care units, as well as morgues. During the study set up, we explored where study area patients presented to hospital and ensured that all accessed hospitals were surveyed, both in and out of the study area.

There are no minimum or maximum age limits for inclusion. Non-residents of the study area will be excluded from the final analysis.

Data collected include demographic data for all self-harm cases (sex, date of birth, place of residence and farming status) and event-specific information (date and time of self-harm event, method of self-harm, whether the individual was alcohol intoxicated at the time of purchase and time of hospital admission, and whether the individual died). For pesticide poisoning cases, additional data are collected on how the individuals accessed pesticides (whether they bought the pesticides from a shop or accessed them from home or nearby). Specific information collected for shop cases includes whether the individual or someone else bought pesticides, the individual's intent at the time of pesticide purchase (self-harm or agricultural purpose), date and time of the pesticide purchase, and the division location of the pesticide shop.

We record all self-harm deaths occurring outside hospital settings through a network of 90 police stations and judicial medical officers. The researchers visit these sources every three months to extract data about self-harm events, namely the home address, method of self-harm, and the source of any pesticide used. Where patients leave hospital before they can be interviewed or non-hospitalized deaths occur, address details of the individuals are obtained from the hospital or police station and permission requested from the patient or family to interview them in their homes about the source of pesticide used in the poisoning.

Field researchers are supervised by experienced senior research staff (KD, DR, and DA) who have undergone training in research ethics. Both the surveillance team and the patient (or patient's family) are blind to the training status of the pesticide shop from which the pesticide was purchased. The surveillance team is also kept separate from the intervention team carrying out the training of vendors to reduce the risk of unblinding.

**Outcome events**

This intervention is directed towards a sub-population of individuals who self-poison using pesticides bought for this purpose from a shop in the preceding 24 hours ("shop cases"). However, the effectiveness of the intervention will be estimated by comparing the total number of fatal and non-fatal pesticide self-poisoning episodes identified from surveillance of hospitals and police stations (primary outcome) between the pre- and post-training periods across the divisions in the study area. Secondary outcomes include:

- Number of pesticide self-poisoning patients (fatal and non-fatal cases) presenting to study hospitals or identified through police stations who used pesticides purchased within 24 hrs of the act.

- Total number of hospital-presenting self-harm cases involving any method of self-harm
- Total number of suicides involving any method of self-harm

**Data Management**

Study data are collected and managed using REDCap electronic data capture tools hosted at University of Sydney [26][27]. REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources. Data are collected into REDCap case record form by research staff following the same protocol as for the household pesticide storage study [25]. Two REDCap databases are used: intervention and surveillance databases. A data coordinator (SR) is responsible for database maintenance, security, and review of data entry on a weekly basis to identify missing data. The trial manager (MP) reviews a weekly data summary. All databases are password protected. At the end of the study, a final anonymized dataset will be sent to the University of Bristol for analysis and then to the University of Edinburgh for archiving.

**Statistics and data analysis**

***Sample size calculation***

The primary outcome measure is the total number of pesticide self-poisoning cases, whilst the intervention is directed towards a sub-population of "shop cases" who self-poison using pesticides bought for this purpose from a shop in the preceding 24 hours. The subpopulation affected by the intervention is likely to be about 20% of all primary outcome cases. We aim to

identify any effect of the intervention on all primary outcome events. Sample size calculations were conducted using the "stepped-wedge" procedure [28].

Initially, the study was powered taking the mean division population of 15+ year olds to be 35,000, the rate of pesticide self-poisoning without intervention to be 250 cases per 100,000 person years, and the coefficient of variation in rates of pesticide self-poisoning across the divisions to be 0.55 (calculated from our ongoing provincial and study area hospital surveillance). In this case, a stepped wedge design with the intervention introduced into 29 Divisions in two districts at each of 15 steps separated by 78 days (7479 person-years of follow-up of each district at each step) would detect a true 11.5% reduction to 221 cases per 100,000 person years with 90% power at the 5% significance level. To achieve this 11.5% reduction overall requires a 58% reduction amongst shop cases, assuming shop cases make up 20% of all cases in the absence of the intervention. A smaller 10% reduction would be detected with 80% power, all else being equal.

However, after six months, the rate of pesticide self-poisoning in the study area was observed to be 130 cases per 100,000 person years. To achieve an acceptable level of statistical power with this lower incidence rate we decided to approximately double the study area. Assuming for Zone 2 that the intervention would be introduced into 41Divisions in four districts at each of 15 steps each of 66 days duration, then for Zones 1 and 2 combined (with an average 6750 person-years of follow-up of each district during each step) a 11.5% reduction from 130 to 115 pesticide self-poisoning cases per 100,000 person years would be detected with 88% power at the 5% significance level.

***Data analysis***

A signed and dated statistical analysis plan will be written and made publicly available online before release of the data for analysis.

In our previous Safe Storage cluster randomized trial [25] in the same context in Sri Lanka, the refusal rate of self-harm patients or their family members for inclusion in the study was very low (<1%). This level of refusal will not cause bias and does not need to be addressed in the statistical analysis. The division of residence of the patient and date of self-harm event will be used to allocate cases to the correct study condition. The primary analysis will follow the intention-to-treat principle, comparing the observed incidence of pesticide self-poisoning between periods/areas with and without the intervention in place. A Poisson regression model will be used to estimate the intervention effect as an incidence rate ratio, with variation between areas accommodated as a random effect, and any secular or seasonal time trends accommodated as covariates. This approach will be adapted for the secondary event-based outcomes.

The COVID-19 situation in Sri Lanka is still unfolding. Therefore, we will include sensitivity analyses that investigate the impact of COVID-19 measures introduced during the study period on intervention effectiveness.

**Implementation Analysis**

We will employ a mixed method approach to evaluate the implementation of the intervention based on the REAIM framework [29], employing quantitative tools to measure reach, effectiveness, adoption, implementation and maintenance and qualitative tools to identify contextual factors that may help to explain the effectiveness or lack of effectiveness of the intervention. REAIM dimension variables and measures are describe in Table 1.

424 **Table 1: REAIM dimension variables and measures**

| Domain | Description | Measures |
|---|---|---|
| REACH | The absolute number, proportion, and representativeness of individuals or settings who are willing to participate in a given initiative. | Exclusion Criteria (% excluded or characteristics)<br>Percent individuals who participate<br>Characteristics of participants compared to non-participants or to target population<br>Reasons contributing to the participation/non-participation of the participants |
| EFFICACY | The impact of an intervention on important outcomes, including potential negative effects, quality of life, and economic outcomes. | Measure of primary outcome<br>Measure of robustness across subgroups (e.g. sex, age, experience, education)<br>Measure of short-term attrition (%) and differential rates by vendor characteristics or shop characteristics<br>Qualitative assessment of contextual factors contributed to the results |
| ADOPTION | The intention, initial decision, or action to try or employ an innovation or evidence-based practice. Adoption also may be referred to as ‘‘uptake.’’ Adoption occurs in the early to mid-implementation stage and is assessed from the setting or staff level. | **Setting Level**<br>Shop Exclusions (% or reasons)<br>Percent of shops approached that participate (valid denominator)<br>Characteristics of participating shops compared to non-participating shops<br>**Individual Level**<br>Vendor Exclusions (% or reasons)<br>Percent of vendors invited that participated<br>Characteristics of vendors participating vs. non-participating vendors<br>Barriers to adoption<br>Vendor satisfaction with training<br>Trainer feedback |
| IMPLEMENTATION | At the setting level, implementation refers to the intervention agents' fidelity to the various elements of an intervention's protocol. This includes consistency of delivery as intended and the time and cost of the intervention. At the individual level, implementation refers to clients/target populations use of the intervention strategies. | Percent of shops which completed training (adherence)<br>Adaptations made to intervention during study<br>Cost of intervention (time or money)<br>Consistency of implementation across trainer/time/settings/subgroups<br>Contextual factors linked to the intervention<br>Trainer/vendor attitudes towards the intervention<br>Barriers and facilitators of the intervention |

| | | |
|---|---|---|
| MAINTENANCE | The extent to which a program or policy becomes institutionalized or part of the routine organizational practices and policies. At the individual level, maintenance has been defined as the long-term effects of a program on outcomes after 6 or more months after the most recent intervention contact. | **Individual Level**<br>Measure of training effectiveness immediately following training<br>Robustness data – reassessment of training outcomes at 6 months<br>Measure of long-term attrition (%) and differential rates by shop and vendor characteristics<br>Individual feedback on intervention and assessment of their willingness to maintain adherence in long term.<br>**Setting Level**<br>If and how the program was adapted long-term (which elements retained AFTER program completed)<br>Some measure/discussion of alignment to organization mission or sustainability<br>Shop and Vendor feedback on intervention, barriers and facilitators, and willingness to maintain change. |

## Economic evaluation

Cost and cost-effectiveness analyses are being conducted concurrently with the trial to assess the cost-effectiveness of the intervention. The cost-effectiveness of implementing the training program on a national level is also being assessed through modelling. A governmental perspective is adopted for the economic evaluations i.e., only cost and outcomes that impact on government as a third-party funder are included. In the economic evaluation of the intervention, a three-year time horizon is applied. This time horizon will be expanded to five years when modelling a full national roll-out of the 'gatekeeper' training intervention.

All costs are expressed in US dollars (US$) and measured in real prices for the reference year (2019) using the gross domestic product deflator. If this is not available, the consumer price index will be used. The discounting of costs is undertaken at the recommended real rate of 3% to take into account the timing of costs and health outcomes of the intervention that does not occur in the present [30][31].

All participants recruited in the s-w cRCT will be included in the economic evaluation of the 'gatekeeper' training intervention. When determining the potential cost-effectiveness of the intervention on a national scale, data will be extrapolated to the total Sri Lankan population, taking into account the population at risk in rural and urban populations.

In accordance with the study perspective, all direct costs related to the implementation of the 'gatekeeper' training intervention and to the health care system will be included in the analysis. Effectiveness data (i.e., number of pesticide self-poisoning cases and deaths prevented) will be identified through the trial. Data from the 'gatekeeper' training intervention will also be used as basis for costing the intervention. All costs associated with the implementation, delivery and

follow-up of the intervention will be included. Research costs associated with the trial will be excluded from the analyses.

All relevant cost and cost offsets are being identified, quantified and ascribed a unit cost. The cost components for the intervention are divided into five categories: capital costs, personnel costs, overhead, consumables, and transportation costs. Unit costs and prices will be obtained from official statistics, health facilities, the Medical Supply Division of the Ministry of Health and the Provincial Department of Health.

One-way sensitivity analyses will be undertaken to assess how variable uncertainties impact on the cost-effectiveness of the strategies, thereby identifying the factors affecting the total cost of implementation [31]. Multivariate sensitivity analyses will also be performed to assess how simultaneous changes of several variables affect the cost-effectiveness ratio. Probabilistic uncertainty analyses will be performed to explore the impact of variability in input variables that can be measured, and input variables for which there is an underlying probability distribution.

**Patient and public involvement and engagement (PPIE)**

While the pilot Safe Storage studies [32][33] were ongoing, we decided to explore whether we could take a complementary approach by working with pesticide vendors. The design and development of the 'gatekeeper' intervention for pesticide vendors was done based on a series of community engagement studies, which took place over several years. As part of the intervention developing process, we conducted a stakeholder analysis with key stakeholders (farmers, pesticide vendors, pesticide company representatives, agricultural officers, public

health experts and general community) to identify the most promising method to prevent access to pesticides from shops for self-poisoning [34].

A separate feasibility pilot study was conducted with pesticides vendors to understand any concerns they had about the gatekeeper intervention [23]. For the current trial, we have offered opportunities for pesticide vendors to express their perspectives, priorities and issues related to the research problem and intervention process. We also discuss and collaborate with Department of Agriculture at group meetings to allow them to express views on the proposed intervention.

## ETHICS AND DISSEMINATION

Ethical approval was granted by the Ethical Review Committee of the Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka (Reference ERC/2018/30) and the ACCORD Medical Research Ethics Committee, University of Edinburgh (Reference 18-HV-053). This study is sponsored by the Academic and Clinical Central Office for Research Development (Ref. AC 18099) at the University of Edinburgh.

Study approval was received from the national Ministry of Health, the Provincial Departments of Health Services and Agriculture in the North Central Province, Eastern Province, Northern Province and Central Province, the Office of the Registrar of Pesticides, and the Pesticide Technical and Advisory Committee (PeTAC) of Sri Lanka.

The study will be published through both scientific peer-reviewed journals. The outcome will be presented to the provincial Departments of Health Services and Agriculture and PeTAC.

Opportunities to disseminate the results both nationally and internationally will be taken including presentations at scientific conferences.

**Consent**

Agreement to participate is being sought from each vendor eligible for the training once details of the study have been provided in the vendor's own language. Individuals identified through case finding are asked to provide informed consent for their information to be used in the research. If the patient is too ill to give consent, or under age (less than 12 years old), consent is requested from a relative (or guardian). If the patient is between 12 and 18 years old, consent from both patient and relative/guardian is requested as per standard Sri Lankan practice (Supplementary file 1).

Both vendors and self-harm patients are provided with an information sheet containing an introduction to the research, its objective, the people involved, the benefits and disadvantages of participating, and contact information of the research group (Supplementary file 2). We also seek written agreement from vendors to participate in follow-up assessments. Vendors are under no obligation to practise what they have learned. The participants are free to withdraw from the study at any point.

The main risk of this study is that discussion concerning self-harm might cause distress. We therefore provide contact information for a local counselling service to the self-harm patients immediately after their interviews. A sensitive data collection technique is used, and ethical issues are being considered throughout the study.

**Data monitoring**

An independent Data Monitoring Committee (DMC) has been established to oversee the safety of trial participants and collection of high-quality data. The DMC aims to meet annually.

**Data availability**

Anonymized data will be made available after publication of the trial's results upon submission of a request to the Principal Investigator (m.eddleston@ed.ac.uk).

**Modifications due to COVID-19**

Following the outbreak of COVID-19, the Government of Sri Lanka implemented a national curfew and a ban on gatherings and non-essential movements. This led to a suspension of all research activities for a period of nearly 3 months (17th March 2020 to 7th June 2020). This period of 'lockdown' had implications for both the intervention and surveillance elements of the study.

During the lockdown, we were unable to gather people for training sessions and so the intervention was suspended. This delay resulted in the steps for Zone 1 being reduced from 78 days to 67 days. The intervention had not commenced in Zone 2 by the time lockdown started and so was delayed. It is now being delivered in a compressed time frame of 42 days per step. Further changes may be required as the COVID-19 situation in Sri Lanka is still ongoing. We also developed remote versions of the training, limiting staff numbers and participants to ensure we complied with local public health guidance. As local outbreaks have occurred since June 2020, there have been additional localized restrictions placed on movements.

During the lockdown, access to all Sri Lankan hospitals was severely restricted and research personnel not permitted on site. The surveillance team remained in contact with hospitals where

possible to set up systems for continuing surveillance, such as daily logs, telephone interviews and setting aside records for review post-opening up. Once the curfew was lifted, the team gained access to the records and made telephone calls where possible or visits to households to gather data. Continuing local restrictions on access to hospitals have recurred and individualized systems have been developed in each hospital to minimize the disruption to data collection.

**Study dates**

In Zone 1, recruitment started on September 30, 2019 and should be complete on October 27, 2022. In Zone 2, recruitment started on January 18, 2021 and will be completed in November 2022. The protocol version is 2.1; 11 Feb 2021.

**Author Contributions**

Study conception: ME, MW, FK and MP; Study design: ME, MW, FK, MP, DG, SA, KH, MM, SJ, TA, CM and JAS; Data analysis plan: CM and NT; Surveillance: KD, SR, DR, DA, AK and ST; Intervention: CP, RK; Data management: SR; Cost-effectiveness analysis: FK and LBM: Drafting manuscript: MW, ME, FK, MP, CM, and SP; Critical revisions: all authors. All authors read and approved the final version.

**FUNDING STATEMENT**

The work is supported by the American Foundation of Suicide Prevention (IIG-0-002-17); the funder is not involved in the conduct of the research nor in the decision to publish the results. DG is supported by the NIHR Biomedical Research Centre at University Hospitals Bristol and Weston NHS Foundation Trust and the University of Bristol, England.

**DATA MONITORING COMMITTEE**:

John Norrie (University of Edinburgh), Saroj Jayasinghe (University of Colombo) and Richard Maude (University of Oxford).

**COMPETING INTERESTS**

KH is joint chair of the Prevention of Pesticide Self-poisoning Special Interest group of the International Association for Suicide Prevention. He declares having received a small grant from Syngenta for a study of safer storage of pesticides in Sri Lanka. DG, FK and ME were expert advisers to WHO's Consultation on cost-effectiveness of suicide prevention interventions, including pesticide regulation (Geneva, 2019). They provided technical assistance for the development and publication of Preventing Suicide: A Resource Guide for Pesticide Registrars and Regulators (WHO, May–June 2019). DG was a member of the scientific advisory group for a Syngenta-funded study to assess the toxicity of a new paraquat formulation (2002-2006); a member of the scientific advisory group for a pesticide storage project funded by Syngenta (2005-2007); and chaired the DMEC for a Syngenta-funded trial of the medical management of paraquat poisoning (2007-2010); he received travel costs to attend research meetings but no other fees. DG was an expert adviser to WHO's First Consultation on Best Practices on Community Action for safer access to pesticides (Geneva, 2006). ME is a WHO member of the FAO–WHO Joint Meeting on Pesticide Management and received an unrestricted research grant from Cheminova (2012) and travel expenses from Syngenta to attend study meetings (2005–06). ME is affiliated with the Centre for Pesticide Suicide Prevention, which is funded by an Incubator Grant from the Open Philanthropy Project Fund, an advised fund of Silicon Valley Community Foundation, on the recommendation of GiveWell, USA. The other authors declare no competing interests.

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## Figure legends

**Figure 1:** Study area – spatial distribution of pesticide shops across the two Zones

**Figure 2:** Schematic of the timing of the intervention across the study area and period

**Figure 3:** Behaviour change model for the modified 'gatekeeper' training intervention of pesticide vendors in rural Sri Lanka.

**Figure 4:** Map of the hospitals and police stations being surveyed across the study area.

**Box 1**

**Study definitions**

***(i). Shop cases:*** We defined a shop case as an incidence of self-harm which fulfils each of the following criteria with regards to the purchase of the pesticide: 1) the purchase was made by the individual who ingested it, 2) the purchase occurred at a pesticide shop, 3) the purchase was made within 24 hrs of self-poisoning. We also collected data on whether the person bought the pesticide with the intention of ingesting it. However, we did not include intention within the definition of a shop case, as intention is subjective and may be unreliable.

***(ii). Pesticides:*** A pesticide was defined as an agrochemical (herbicide, insecticide, fungicide or rodenticide) used to control agricultural pests, or a chemical used to control domestic pests.

***(iii). Self-harm patient:*** A self-harm patient in the study was defined as a permanent resident, temporary resident or guest/visitor in the study area at the time of the self-harm episode, who was admitted to one of the study hospitals during the study period due to suicide attempt.

***(iv). Pesticide shop:*** Seasonal shops (open only in agricultural season) or non-seasonal shops that are selling pesticides throughout of the year, regardless of whether they hold a government license to sell pesticides.

***(v). Pesticide vendor:*** Either a full-time or part-time vendor who is directly involved in the sale of pesticide to customers in the study area during the study period.

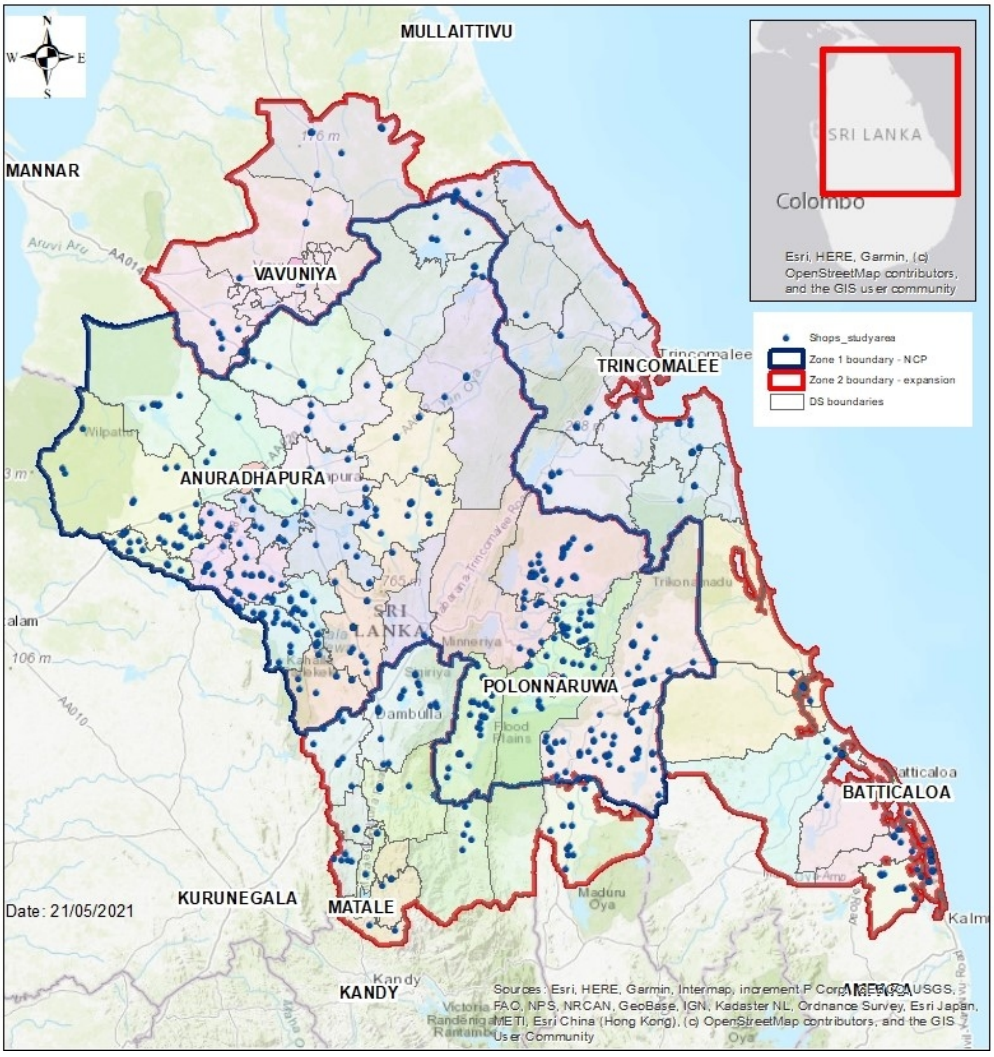
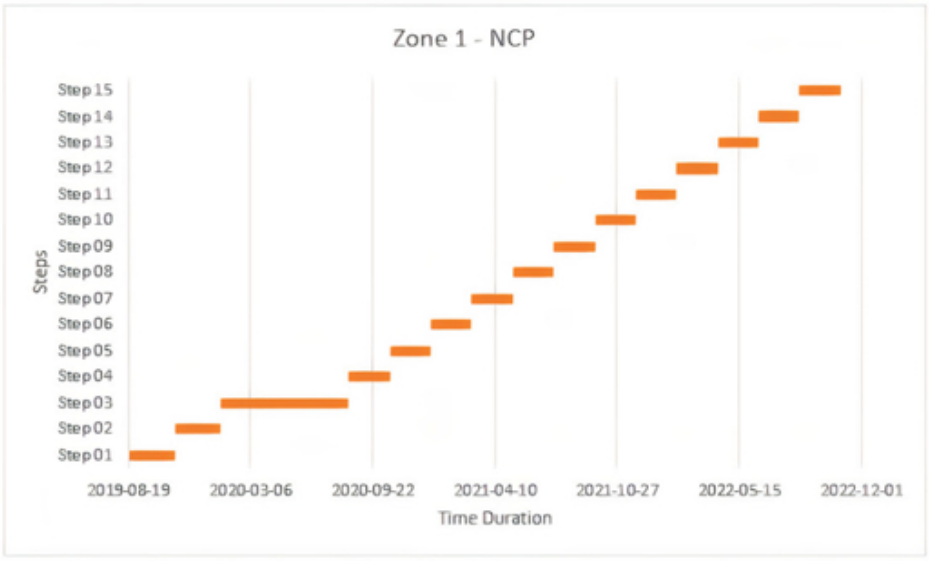



Figure 1: Study area – spatial distribution of pesticide shops across the two Zones

207x218mm (96 x 96 DPI)



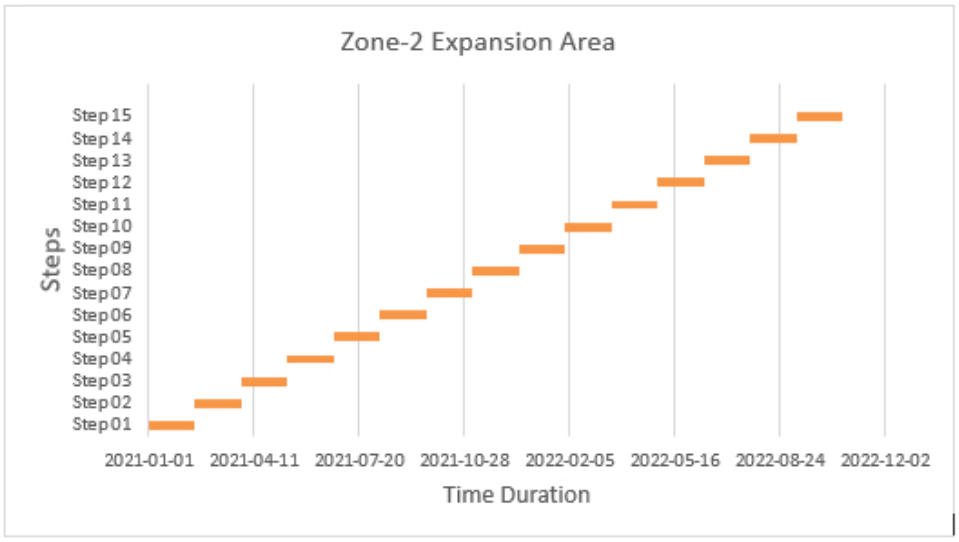




Figure 2: Schematic of the timing of the intervention across the study area and period

291x357mm (47 x 47 DPI)

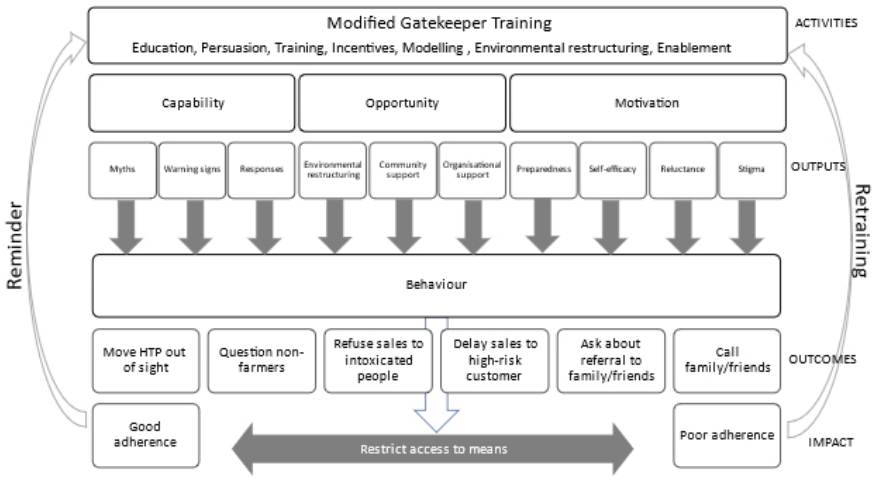



Figure 3: Behaviour change model for the modified 'gatekeeper' training intervention of pesticide vendors in rural Sri Lanka.

474x400mm (38 x 38 DPI)

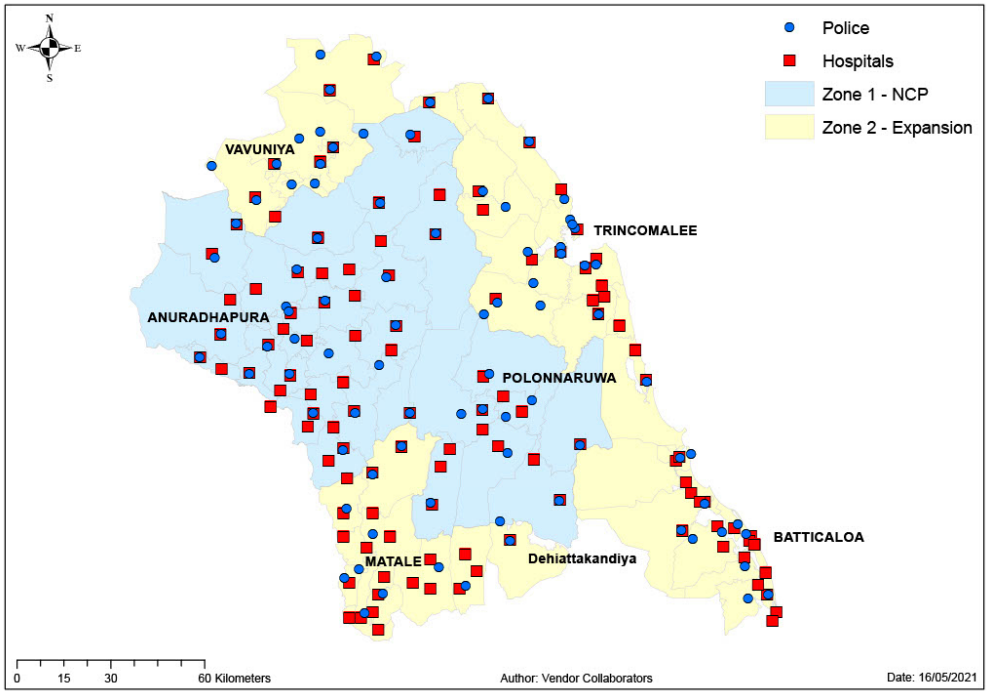



Figure 4: Map of the hospitals and police stations being surveyed across the study area

361x255mm (72 x 72 DPI)

Adult patient consent for Vendor cRCT
Version 0.5 25 SEP 2018

DEPARTMENT OF COMMUNITY MEDICINE
FACULTY OF MEDICINE AND ALLIED SCIENCES
RAJARATA UNIVERSITY OF SRI LANKA

# PARTICIPANT'S CONSENT FORM – ADULT PATIENTS (≥18 YEARS)

## STUDY ON WHETHER PESTICIDE VENDOR TRAINING CAN REDUCE PESTICIDE SELF-POISONING IN RURAL SRI LANKA

| Investigator | Telephone number | Address |
|---|---|---|
| Manjula Weerasinghe | 077 3230888 | Department of Community Medicine, Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka |

Please affirm with your initials

I have read the Patient information sheet version 0.5 (25 SEP 2018) ☐

I have had the opportunity to ask questions and discuss the study. ☐

I have received satisfactory answers to the questions I asked about the project ☐

Who explained the study to you? .....

I understand that I am free to leave the study without giving any reason. ☐

I agree to take part on my own wishes ☐

I understand that the information I give is confidential. ☐

I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from the Sponsors (the University of Edinburgh) where it is relevant to my taking part in this research. I give permission for those individuals to have access to my records ☐

I give my consent to take part in the study and this will include:

| | | |
|---|---|---|
| Interviews | Yes / No | ☐ |

Name ..... Person taking consent .....

Signature ..... Signature .....

Date ..... Date .....

Adult patient consent for Vendor cRCT
Version 0.5 25 SEP 2018


Original (x1) to be retained in site file. Copy (x1) to be included in patient notes. Copy (x1) to be retained by the participant.

**If you have any complaints about this research or its conduct, please contact:**

Secretary,
Ethics Review Committee,
Faculty of Medicine and Allied Sciences,
Rajarata University of Sri Lanka

Phone number: +94(0) 25 2053633 (please contact during working hrs 8 am – 4 pm)
E-mail: ethicsreviewcommittee@gmail.com

**or**

the University of Edinburgh's Research Governance team via email at: resgov@accord.scot

**DEPARTMENT OF COMMUNITY MEDICINE**
**FACULTY OF MEDICINE AND ALLIED SCIENCES**
**RAJARATA UNIVERSITY OF SRI LANKA**

# PARTICIPANT INFORMATION SHEET FOR PATIENTS

## STUDY ON WHETHER PESTICIDE VENDOR TRAINING CAN REDUCE PESTICIDES SELF-POISONING IN RURAL SRI LANKA

*We would like to invite you (on behalf of your relative or your child) to participate in a research project. Please read this leaflet carefully, and if you have any questions about the study do not hesitate to ask from the research assistant. Feel free to discuss the project with your family or friends before you make a decision on whether to participate.*

### What is the purpose of the study?

This is a study about whether pesticide vendor training can reduce pesticides self-poisoning in rural Sri Lanka. This research project is a collaborative project with several Universities including: Rajarata University of Sri Lanka, University of Edinburgh, Northeastern University, University of Bristol, University of Oxford, University of Kelaniya and University of Copenhagen. This research project has been funded by the American Foundation for Suicide Prevention and the study has been approved by the Research Ethics Committee of Rajarata University of Sri Lanka.

### Why have I been invited?

You have been selected for this study because you (or your relative / child) have (has) admitted to a study hospital following a self-harm attempt in or just outside of the boundary of the North Central Province.

### Must I take part?

No. Participation is entirely voluntary. There is no obligation for you to take part, and if you do not want to take part, this will have no effect on your or your relative's / child's medical care or affect you or them in any way. It is also possible for you (or your relative / child) to withdraw from the interview or withdraw data at any point without giving any reasons and without any penalty. As we are conducting this research to test the pesticide vendor training reduces pesticide self-poisoning in rural Sri Lanka, we would greatly appreciate your (or your relative's / child's) participation.

### What will the research involve?

You (your relative /child) will be asked to take part in an interview. One of our trained research assistants will interview you (or your child) to obtain some of the information about your (or your relative's / child's) self-harm event. We will collect information such as address, divisional secretariat, source (access point) of pesticides, method of self-harm, the ingested poison, and

- if the person bought the pesticide - the shop's name and location. We will use your phone and contact details to monitor location. The interview will take about 20 minutes of your time.

We would like to keep your name and address on record and to then contact you again in the future. We will do this to assess the effects of any poison you may have ingested over the next few years. You do not need to do this - you can just complete the interview and ask us not to contact you again.

**Are there any risks?**

We do not envisage any harm from this study. However, it is likely that engaging with this research may encourage you to consider your (or your relative's / child's) circumstances in detail. We hope that this will be a positive experience but we cannot rule out any negative feelings that may occur. All your contributions will be kept confidential.

**Are there any benefits?**

There will be no direct benefits for participating. However, this will be an opportunity to share your (or your relative's / child's) experiences and to contribute to the study. Studying whether pesticide vendor training reduces pesticides self-poisoning might benefit many people in future in rural Sri Lanka and across South Asia. Therefore, we believe that this will be an interesting opportunity for you (or your relative / child).

**Will may or my child taking part in the study be kept confidential?**

Yes, all information you give is strictly confidential. The information you give may be used for a research report or publications, but it will not be possible to identify you (or your relative / child) in any way from this.

**Consent**

The study researchers can answer any questions you may have about the study. They will take your consent for the interview and follow-up. You will have about 60 min to make a decision about whether to have the interview. Please do take the opportunity to discuss it with your family and friends.

**If you have any further questions, please ask:**

Investigator: Manjula Weerasinghe Telephone: 077 3230888

If you would like to discuss this study with someone independent of the study team please contact:

Dr Janaka Pushpakumara on telephone: 0094 077 3565144 or email janakatechno@gmail.com

**If you have any complaints about this research or its conduct, please contact:**

Secretary, Ethics Review Committee, Faculty of Medicine and Allied Sciences,
Rajarata University of Sri Lanka. Phone number: +94(0)25 2053633 (please contact during working hrs 8 am – 4 pm). E-mail: ethicsreviewcommittee@gmail.com
**or**

the University of Edinburgh's Research Governance team via email at: resgov@accord.scot

Patient PIS for Vendor cRCT
Version 0.5 25 SEP 2018


**Data protection**

The University of Edinburgh is the sponsor for this study based in Sri Lanka. We will use information from you and/or your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The sponsor will keep identifiable information about you for 10 years after the study has finished.

As a university, we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

| Section/item | Item No | Description | Page(s) / line numbers |
|---|---|---|---|
| **Administrative information** | | | |
| Title | 1 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym | Page 1 / line 2-3 |
| Trial registration | 2a | Trial identifier and registry name. If not yet registered, name of intended registry | Page 5 / line 92-93 |
| | 2b | All items from the World Health Organization Trial Registration Data Set | Page 5 / line 92<br>We have recently submitted the revised registry forms requesting a revision to the Clinical Trial Registry (SLCTR) and still revisions are under consideration.<br>Sri Lanka Clinical Trail Registry (https://slctr.lk): SLCTR/2019/006.<br>International Clinical Trials Registry Platform (U1111-1220-8046). |
| Protocol version | 3 | Date and version identifier | Page 27 / line 561 |
| Funding | 4 | Sources and types of financial, material, and other support | Page 25 / line 570-574 |
| Roles and responsibilities | 5a | Names, affiliations, and roles of protocol contributors | Page 1-2 / line 5-31<br>Page 27 / line 563- 567 |
| | 5b | Name and contact information for the trial sponsor | Page 5 / line 92 (Name and contact information of the trial sponsor is available as part of the trial registry |

| | | | |
|---|---|---|---|
| | | | information) |
| | 5c | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities | Page 27 / line 571-572 |
| | 5d | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) | Page 17 / line 355-368 |
| **Introduction** | | | |
| Background and rationale | 6a | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention | Page 7-8 / line 109-148 |
| | 6b | Explanation for choice of comparators | Page 7 / line 122-125 |
| Objectives | 7 | Specific objectives or hypotheses | Page 8 / line 150-153 |
| Trial design | 8 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) | Page 8-9 / line 155-161 |
| **Methods: Participants, interventions, and outcomes** | | | |
| Study setting | 9 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained | Page 9 / line 163-180 |
| Eligibility criteria | 10 | Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) | Page 10 / line 191-202 |
| Interventions | 11a | Interventions for each group with sufficient detail to allow | Page 12-13 / line 236-276 |

| | | | |
|---|---|---|---|
| | | replication, including how and when they will be administered | |
| | 11b | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) | Page 13 / line 268-271 |
| | 11c | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) | Page 9 / line 172-178<br>Page 10 / line 194-198<br>Page 11/ line 224-228<br>Page 26-27 / line 533-556 |
| | 11d | Relevant concomitant care and interventions that are permitted or prohibited during the trial | In the protocol V2.5 11 FEB 2020 – page 16 |
| Outcomes | 12 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended | Page 16-17 / line 342-353 |
| Participant timeline | 13 | Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) | Figure 2 |
| Sample size | 14 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations | Page 17-18 / line 370--398 |
| Recruitment | 15 | Strategies for achieving adequate participant enrolment to reach target sample size | Page 18 / line 394-398 |
| **Methods: Assignment of interventions (for controlled trials)** | | | |
| Allocation: | | | |
| Sequence generation | 16a | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for | Page 10-11 / line 204-207 |

| | | | |
|---|---|---|---|
| | | stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions | |
| Allocation concealment mechanism | 16b | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned | Page 11 / line 216-222 |
| Implementation | 16c | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions | Page 11 / line 216-219 |
| Blinding (masking) | 17a | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how | Page 16 / line 336-340 |
| | 17b | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial | Page 16 / line 336-340 |
| **Methods: Data collection, management, and analysis** | | | |
| Data collection methods | 18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol | Page 14-16 / line 298-340<br>Data collection forms are available with the protocol |
| | 18b | Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols | Not applicable |
| Data management | 19 | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data | Page 17 / line 355-368 |

| | | | |
|---|---|---|---|
| | | management procedures can be found, if not in the protocol | |
| Statistical methods | 20a | Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol | Page 18-19 / line 400-417<br><br>Overall statistical analysis plan will be written and made publicly available online before release of the data for analysis. |
| | 20b | Methods for any additional analyses (eg, subgroup and adjusted analyses) | Page 19 / line 414-416 |
| | 20c | Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) | Page 18-19 / line 400-417<br><br>Overall statistical analysis plan will be written and made publicly available online before release of the data for analysis. |
| **Methods: Monitoring** | | | |
| Data monitoring | 21a | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed | Page 25-26 / line 525-527 |
| | 21b | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial | No formal stopping rules or interim analyses are planned. However, the data monitoring committee is responsible for safeguarding the interests of trial participants and monitoring the quality of the research. |

| | | | |
|---|---|---|---|
| Harms | 22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct | Page 25 / line 520-523<br>In the protocol V 2.1 11 FEB 2020 - page 21, 11.4. |
| Auditing | 23 | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor | In the protocol V 2.1 11 FEB 2020 - page 21, 11.5. |
| **Ethics and dissemination** | | | |
| Research ethics approval | 24 | Plans for seeking research ethics committee/institutional review board (REC/IRB) approval | Page 24 / line 487-492 |
| Protocol amendments | 25 | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) | Page 24 / line 491-492 |
| Consent or assent | 26a | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) | Page 25 / line 504-523 |
| | 26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable | Not applicable. |
| Confidentiality | 27 | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial | Page 17 / line 364-368 |
| Declaration of interests | 28 | Financial and other competing interests for principal investigators for the overall trial and each study site | Page 28/ line 580=599 |
| Access to data | 29 | Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators | Page 26 / line 529-531 |
| Ancillary and post-trial care | 30 | Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation | Not applicable |
| Dissemination policy | 31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other | Page 24-25 / line 499-502 |

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| | | relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions | |
| | 31b | Authorship eligibility guidelines and any intended use of professional writers | No specific guideline plan for authorship, however those who make a significant contribution to the conception or design of the trial or the acquisition, analysis, interpretation of data and those who work on drafts or review/revise it critically for important intellectual content will be authors in the result paper. |
| | 31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code | Full protocol: Can be download in the trail registration (Page 5 line 92)<br>Participant-level dataset: Page 26 / line 529-531<br>Statistical code: Statistical analysis plan will be written and made publicly available online before release of the data for analysis. |
| **Appendices** | | | |
| Informed consent materials | 32 | Model consent form and other related documentation given to participants and authorised surrogates | Annex 1: “Self-harm patients (≥18-years old)” consent form<br>Annex 2: participant information leaflet |
| Biological specimens | 33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable | Not applicable |

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.