ARTEMIS

Adolescents' Resilience and Treatment Needs for Mental health in Indian Slums

Statistical Analysis Plan

Version: 0.3 (Final)

Date: 24 June 2024

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On behalf of the Management Committee

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Contents

1 Administrative Information

1.1 Study identifiers

- Protocol Version 9.0 22/02/2024
- Clinical Trials Registry – India, Identifier: CTRI/2022/ 02/040307. Registered on 18 February 2022

1.2 Revision History

Version	Date	Details
0.1	25 April 2024	First draft
0.2	21 May 2024	Addressed comments from all authors on first draft and revised tables and shells
0.3	24 June 2024	Finalized SAP

1.3 Contributors to Statistical Analysis Plan

Title and name	Affiliation	Role on study	Contribution to the SAP
Dr Arpita Ghosh	The George Institute for Global Health India	Study statistician	Developed the SAP
Prof Laurent Billot	The George Institute for Global Health	Study statistician	Reviewed and edited every version
Dr Sandhya Kanaka Yatirajula	The George Institute for Global Health India	Project Manager	Implemented the project and is helping with data analysis plan
Prof Graham Thornicroft	King's College London	CoPI	Reviewed and provided critical input to all versions
Prof Pallab Maulik	The George Institute for Global Health India	PI	Reviewed and provided critical input to all versions

2 Approvals

The undersigned have reviewed this plan and approve it as final. They find it to be consistent with the requirements of the protocol as it applies to their respective areas. They also find it to be compliant with ICH-E9 principles and, in particular, confirm that this analysis plan was developed in a completely blinded manner, i.e. without knowledge of the effect of the intervention(s) being assessed.

Doctor Arpita Ghosh

27 June 2024

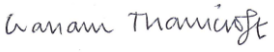
Professor Laurent Billot

26 June 2024

Doctor Sandhya Kanaka Yatirajula

27 June 2024

Professor Graham Thornicroft



26 June 2024

Professor Pallab K. Maulik

27 June 2024

3 Introduction

3.1 Purpose of this document

This statistical analysis plan (SAP) describes the statistical methods and data presentations to be used in the summary and analyses of data from Artemis study. This document is based on Artemis PROTOCOL Version 9.0 dated 22/02/2024. It describes the final analyses for evaluation of intervention at 12 months from randomization. Health economics modelling are not a part of this SAP. The document should be finalised before database lock and unblinding.

3.2 Study Synopsis

The study aims to test clinical effectiveness and effectiveness of implementation strategies to identify and reduce depression, other significant emotional or medically unexplained complaints and suicide risk among adolescents living in urban slums. We hypothesise that:

1. a community-based anti-stigma campaign will lead to significant improvements in community behaviours toward adolescents with depression, other significant emotional or medically unexplained complaints, and increased risk of self-harm/suicide; and

2. a mobile device-based decision support system will improve the treatment of adolescents at high risk of depression, other significant emotional or medically unexplained complaints, and increased risk of self-harm/suicide for this project and lead to higher remission rates from depression and reduced suicide risk.

4 Study Methods

4.1 Trial design

This is two-arm cluster randomised trial across two geographical locations – slums in Delhi and Vijayawada. Slum cluster (constituting 1-5 slums located in the same area) is the unit of randomisation. Each slum cluster has a population of ~8000 and is serviced by at least one primary care doctor.

4.2 Eligibility

4.2.1 Slum cluster eligibility

- Non-contiguous slum clusters, within a radius of 60 km from the field office in both cities, Delhi and Vijayawada, were selected, to get a total adolescent population of around 69600.
- Each slum cluster has a minimum of one community women volunteer/non-physician health worker (NPHW) per 1000 population.

4.2.2 Participant inclusion criteria

All consenting adolescents in the age group of 10 – 19 years were eligible for screening for stress, depression and increased risk of self-harm/suicide to identify both a high-risk and non-high-risk cohort. To be eligible for the high-risk cohort participants must have at least one of the following:

- High risk of depression based on a Patient Health Questionnaire-9 item (PHQ9) score ≥ 10
- Positive response (score ≥2) to the suicide risk question on the PHQ-9

4.2.3 Participant exclusion criteria

- Participants with severe ill-health that would prevent them from giving consent or participating in the study
- Adolescents or their guardians who do not provide informed written consent
- Participants who are temporary residents of the slums

The implementation team ensured reasonable accommodation of adolescents who manifest physical or mental impairment and field investigators were provided training in lines with the Guidelines on Disability Inclusion in Research.

Two cohorts were generated from this screening process.

1. **High-risk cohort** – defined as either: a PHQ-9 score ≥ 10, AND/OR a positive response (≥2) to the suicide risk question on the PHQ-9. Because there was some time delay between screening and randomisation these participants were rescreened to assess if they still met the inclusion criteria prior to randomisation.
2. **Non-high-risk general adolescent cohort**: A second cohort of adolescents per slum cluster not at high risk for stress, depression and self-harm/suicide was identified by selecting a random sample from the remaining screened population stratified by sex (male and female) and age group (10-14 and 15-19 years). This is the 'non-high-risk' cohort.

4.3 Randomization

Slum clusters at each site were randomized to the two arms in a 1:1 allocation ratio using stratified randomization. Four strata of slum clusters were created within each site based on adolescent population size and proportion positive during rescreening, categorized using site-specific median. In one site, there were 2 strata with 8 clusters and 2 with 7 clusters; and in the other site, there were 2 strata with 6 clusters and 2 with 9 clusters. In strata with even number of clusters, half were randomized to one arm and half to the other. In the two strata with 7 clusters, we randomly selected 3 clusters in one stratum and 4 clusters in the other stratum and assign them to one arm; we assign the remaining clusters in the two strata to the other arm. Similarly, we divided the clusters in the strata with 9 clusters into the two arms.

4.4 Sample size

High-risk cohort

Assuming a 50% remission rate in the control arm at 12 months based on published data[1] and 30 clusters per intervention arm, at least 27 subjects per cluster are needed to detect a 15% absolute improvement in the intervention arm (65% intervention vs 50% control) at 12 months with 90% power. This assumes a 2-sided significance level of 0.05 and an intra-class correlation coefficient (ICC) of 0.1 based on pilot data[2] and recent (unpublished) analyses. For secondary outcomes, this sample size will also provide 86% power to detect a standardised mean difference of 0.3 in PHQ-9 scores considering an ICC of 0.1. The hypothesised effect size is consistent to that published in a recent Indian study on provision of mental health services using lay health workers in community settings.[3]

To account for up to 20% of participants lost to follow-up, we will aim to enrol at least 33 participants per cluster for a total sample size of 1980 adolescents (60 clusters × 33 adolescents). We anticipate a prevalence of approximately 3% and will therefore aim to screen about 1,100 adolescents in each cluster. Further assuming that 5% of eligible adolescents will refuse to participate, we aim to screen 1,160 adolescents in each cluster i.e. a total of 69,600 adolescents (60 clusters × 1,160 adolescents).

Non-high-risk cohort

Assuming a conservative ICC of 0.1 (0.01 in our pilot and 0.04 in similar studies)[3, 4], 20% loss to follow-up and a 2-sided significance level of 0.05, 60 clusters and a mean cluster size of 66 per cluster (33 high-risk and 33 non high-risk) will provide more than 90% power to detect a standardised mean difference of 0.3 in mean behaviour scores between the intervention and control arms at 12 months. Assuming baseline mean behaviour scores of 2 (SD 1) and a 20% improvement in the control arm based on pilot and published data,[4] this corresponds to 12-month behaviour scores of 1.6 (20% improvement) and 1.3 (35% improvement) in the control and intervention arms respectively.

The sample has more than 80% power at $2\alpha = 0.05$ to assess sex disaggregated estimates for both the primary outcomes, assuming equal proportion of male and female adolescents in the high-risk and non-high-risk cohorts. Research suggests that among adolescents depression is equally distributed in males and females.

4.5 Framework

We will test for superiority of the primary and secondary outcomes.

4.6 Statistical interim analysis and stopping guidance

No interim analyses were conducted.

4.7 Timing of final analysis

Final analysis for all outcomes will be conducted after 12-month intervention is completed.

4.8 Timing of outcome assessments

The following table shows the timing of the assessments that will be used to define primary and secondary outcomes.

Outcome	Baseline	3-month	6-month	12-month
Combined cohort				
Behaviour score (KAB tool)	x	x	x	x
Knowledge score (KAB tool)	x	x	x	x
Attitude score (KAB tool)	x	x	x	x
Stigma score (BACE tool)	x	x	x	x
High-risk cohort				
PHQ-9 score	x*	x	x	x
Remission at 12 months (PHQ-9 <5, and suicide risk score <2)				x

* Values from rescreening were considered as baseline assessments.

5 Statistical Principles

5.1 Confidence intervals and P values

All statistical tests will be 2-sided and will be performed using a 5% significance level. We have two primary outcomes, but they are assessing different components of the intervention, and they apply to different cohorts. No multiplicity adjustments will be made.

5.2 Adherence and Protocol deviations

In the combined cohort, individuals in the intervention arm will be expected to participate at least once in all components of the anti-stigma campaign (pamphlets and brochures; multi-media resources e.g. videos of people with mental disorders talking about their conditions; and street plays a about mental disorders, which was performed live or shown as a video). In the high-risk cohort, individuals in the intervention arm will be expected to be seen by a doctor at least once during the intervention phase.

5.3 Analysis populations

All analyses will be based on the principle of intention-to-treat (ITT), i.e. by analysing subjects according to the group they were randomised to and regardless of whether they received the intervention as intended. The intention will be to include all subjects; however, some might be excluded from analyses due to missing data and may be subject to sensitivity analyses e.g. imputations (see Section 7.3 for details about missing data handling).

'Per-protocol' and 'as-treated' analyses will not be part of main analyses and will be conducted post-hoc as secondary analyses/separate publications.

6 Trial Population

6.1 Recruitment

CONSORT diagram comprising the number of people screened, rescreened, randomised, and followed-up follow-up will be presented.

6.2 Withdrawal/lost to follow-up

All withdrawals/lost to follow-up will be listed.

6.3 Baseline patient characteristics

Participants will be described with respect to their background characteristics such as age, sex, education, marital status, occupation, behavioural risk factors, medical history, treatment history, family history of any mental health problem, experience of domestic violence and intimate partner violence, any stressful event in last one year, and receipt of social support, separately for the two arms. Categorical data will be summarised by numbers and percentages. Continuous data will be summarised by mean, SD, median, IQR, and range. Tests of statistical significance will not be undertaken for baseline characteristics.

Slum cluster characteristics such as adolescent population size, proportion found to be positive upon screening, proportion found to be positive upon rescreening, and slum adversity index will be presented for the two arms.

7 Analysis

7.1 Outcome definitions

1. Anti-stigma component (combined high- and non-high-risk cohorts)
Primary
Behaviour score at 12 months
Secondary
Knowledge, attitude and stigma scores at 12 months

2. mHealth component (high-risk cohort)
Primary
Proportion of high-risk adolescents achieving remission (defined as all of the following: PHQ-9 <5, and suicide risk score <2) at 12 months.
Secondary
PHQ-9 scores at 12 months

In protocol, doctor visits were mentioned as a secondary outcome. However, since the m-health component is about ensuring that adolescents at high risk of depression and increased risk of self-harm/suicide visit a doctor, this will be used as a measure of intervention fidelity rather than a secondary outcome. Details of doctor visits in both arms will be presented but no tests will be conducted.

7.2 Analysis methods

7.2.1 Main analysis of primary outcomes

7.2.1.1 Behavior score in combined cohort

The behaviour score will be derived by summing the ordinal responses (with disagree strongly, disagree slightly, neither disagree nor agree, agree slightly and agree strongly scored as 1, 2, 3, 4 and 5, respectively) to the behaviour questions in the KAB scale – *I would be willing to live with someone with a mental health problem, I would be willing to work with someone with a mental health problem, I would be willing to live nearby someone with a mental health problem, I would be willing to continue a relationship with a friend who developed a mental health problem*. 'Don't know' will be coded as neither disagree nor agree (i.e., 3) for the purposes of determining a total score (see Appendix 1).[5]

The behaviour score will be analysed using a repeated measure linear mixed model.[6] The outcome (dependent variable) will include the behaviour score at 3, 6 and 12 months. Fixed covariates will include the baseline behaviour score, the intervention, the visit (3, 6 or 12 months), the intervention by visit interaction, and variables used for stratified randomization:[7] slum adolescent population size and proportion positive during rescreening. The stratification variables will be treated as continuous variables and a linear relationship with the outcome will be modelled. To model within-cluster correlations, the cluster will be included as a random effect. Correlations between repeated measures on the same subject will be handled by specifying that residual errors are correlated and will be modelled using unstructured covariance. The effect of the intervention will be estimated as

the adjusted mean difference at 12 months together with its 95% confidence interval. The effects at 3 and 6 months will be estimated from the same longitudinal model utilizing data from all visits and 3- and 6-month estimates will be presented as part of additional analyses (please see section 7.4.3). This analysis will include all subjects with a baseline behaviour score and at least one post-baseline behaviour score. This main analysis model will be valid in case of data missing at random. Sensitivity analyses which make different assumptions about the missing data mechanism are described in Section 7.3.

7.2.1.2 Remission at 12 months in high-risk cohort

For the high-risk cohort, remission between randomization and end of trial will be defined as PHQ-9 score <5 and suicide risk score <2 at 12 months. It will be analyzed using mixed effects logistic regression with remission as a binary outcome, treatment group and stratification variables as fixed effects and slum clusters as random effects. The effect of the intervention will be estimated as the odds ratio together with its 95% confidence interval. The main model will be run with no baseline covariates. A second model will be fitted by adding the baseline PHQ-9 score as a continuous covariate. Risk difference along with 95% CI will be estimated using the Gaussian distribution, under both marginal approach (generalized estimating equations) and conditional approach (linear mixed model) (https://www.sciencedirect.com/science/article/pii/S0398762023001815).[8]

7.2.2 Analysis of secondary outcomes

7.2.2.1 Knowledge and attitude scores in combined cohort

Mean difference at 12 months in knowledge and attitude scores in the combined non-high-risk and high-risk cohort will be analysed using the same approach as the one used for behaviour score (see Section 7.2.1.1) i.e. using repeated measure linear mixed model with the corresponding baseline score, the intervention, the visit (3, 6 or 12 months), the intervention by visit interaction and the stratification variables as fixed covariates. As with the behaviour score analysis, slum-level random effects will be included and unstructured covariance will be used to model correlations between repeated measures within subjects. Knowledge and attitude scores will be derived by summing over the responses to corresponding questions in KAB scale, following the same approach as used to construct the behaviour score (see Appendix 1).

7.2.2.2 Stigma score in combined cohort

Mean difference at 12 months in stigma perceptions as assessed by Barriers to Access to Care Evaluation- Treatment Stigma Subscale (see Appendix 1) in the combined cohort will be analysed using the same approach as the one used for behaviour score (see Section 7.2.1.1).

7.2.2.3 PHQ-9 score in high-risk cohort

Mean difference in PHQ-9 score (see Appendix 1 for instrument) at 12 months in high-risk cohort will be assessed using a similar approach as the one used for behaviour score in combined cohort i.e. using repeated measure linear mixed model with PHQ-9 scores in high-risk cohort participants at 3, 6 and 12 months as the outcome (dependent) variable and the corresponding baseline score, the intervention, the visit (3, 6 or 12 months), the intervention by visit interaction, and the stratification variables as fixed covariates and slum clusters as random effects. Unstructured covariance will be used to model correlations between repeated measures within subjects.

7.3 Missing data

The main analysis for behaviour score (a repeated-measure linear mixed model) makes valid inference under the missing at random (MAR) assumption. In case of more than 5% of subjects in combined cohort with missing behaviour scores at 12 months, we will perform controlled multiple imputation using the approach described by Cro et al.[9]

As a starting point, we will first run an imputation model under the missing at random (MAR) assumption. This MAR imputation model will use fully conditional specification (FCS)[10, 11] and will include the following variables: behaviour score at baseline, months 3, 6 and 12, a variable indicating the cluster, a variable indicating the intervention, a variable indicating the cohort (high-risk vs not high-risk) and all key socio-demographic, clinical and medical baseline variables (e.g. sex, age, occupation and medical history) collected for both the high-risk and non-high-risk cohort participants. Behaviour score and other missing continuous variables will be imputed using linear regression while categorical variables will be imputed using either a logistic model (for binary variables) or a discriminant function method (for nominal variables). One hundred sets of imputed data will be created and analysed using the models described in Section 7.2.1.1. Estimates of the treatment effect and its standard errors will be combined to obtain a pooled common adjusted mean difference and 95% CI.

Using the same 100 sets of imputed data as our base, we will then assume different behaviour scores for subjects who had missing data at follow-up visits and had their scores imputed. We will start by assuming that those with a missing behaviour score were more likely to have a poorer outcome than those with a non-missing behaviour score and will therefore subtract 3 from the imputed behaviour score (with a minimum score of 4) in the 100 sets of imputed data. We will then analyse the 100 modified-imputed datasets and combine the results using the same strategy as for the base set of imputed data.

A similar strategy will be applied to the high-risk cohort in case of missing PHQ-9 scores. The imputation model will include the PHQ-9 scores measured at each timepoint, a variable indicating the cluster, a variable indicating the intervention and all key socio-demographic, clinical and medical baseline variables. We will start by assuming that those with a missing PHQ-9 score at follow-up visits were more likely to have a poorer outcome than those with a non-missing PHQ-9 score. We will therefore add 5 to their imputed PHQ-9 score (with a maximum score of 27). The same imputation strategy will be applied to remission – the remission outcome will be set to 'no' for high-risk participants with a missing remission outcome at 12 months in the 100 sets of imputed data. We will then analyse the 100 modified-imputed datasets and combine the results using the same strategy as for the base set of imputed data.

We plan to apply multiple imputations to the analysis of the following endpoints: behaviour score, PHQ-9 score and remission. Additional imputation and/or tipping point analyses will be considered post-hoc.

7.4 Additional analyses

7.4.1 Adjusted analyses

The analyses described for the primary and secondary outcomes (sections7.2.1 and 7.2.2) will be rerun after adding the following baseline covariates: sex, age, past stressful event (yes/no), any mental disorder, CD-RISC 10 score, and substance use (yes/no). Age and CD-RISC 10 score will be entered as continuous variables and a linear relationship with outcome will be assumed.

7.4.2 Subgroup analyses

Subgroup analyses will be conducted for both the two primary outcomes - behaviour score and remission at 12 months, according to the following subgroups:

- Site (Delhi vs. Vijaywada)
- Cluster-level characteristics – adolescent population size and proportion positive during rescreening, categorized using the median
- Participant-level characteristics:
    - Age group: 10-14 and 15-19 years

- Sex: Male vs. Female

The following subgroup analyses will be conducted for specific outcomes:

- Depression severity at baseline: high (suicide score >=2 or PHQ-9≥15) vs. low (suicide score < 2 and PHQ-9 < 15) (only high-risk cohort) for remission at 12 months only
- Risk cohort (high-risk vs. non-high-risk) for behaviour score only.

For behaviour score, analyses for each subgroup will be performed by adding the subgroup variable, its interaction with intervention and visit as well as the three-way interaction between subgroup, intervention and visit as fixed effects to the model described in sections 7.2.1.1. For remission at 12 months, analyses for each subgroup will be performed by adding the subgroup variable and its interaction with the intervention as fixed effects to the model described in section**Error! Reference source not found.** 7.2.1.2. For each subgroup, summary measures, mean difference or odds ratio and 95% confidence interval will be presented. The results will be displayed on a forest plot including the p-value for heterogeneity corresponding to the interaction term between the intervention and the subgroup variable.

7.4.3 Additional outcomes

Following additional outcomes that are produced as part of primary and secondary analyses will be reported

- Mean difference in behaviour, knowledge and attitude scores and mean difference in stigma scores in the combined cohort at 3 and 6 months.
- Mean difference in PHQ9 scores at 3 and 6 months in high-risk cohort
- CD-RISC score at 12 months in combined cohort

7.4.4 Disaggregated analyses, by sex and geography

- All analyses will be carried out separately by sex (male and female) and geography (Delhi and Vijayawada) and will be reported either as supplementary material or in a separate paper.

7.4.5 Exposure to intervention

Variables measuring exposure to the interventions – the mHealth component in the high-risk cohort and the anti-stigma campaign in the combined cohort, will be summarized to understand the extent of exposure to these components. Specifically, the following variables will be analyzed and descriptive summaries will be presented:

- Proportion that witnessed the anti-stigma campaign
- Proportion of adolescents participating in specific components of the campaign
- Proportion of adolescents participating in all components of the campaign
- Proportion of high-risk adolescents followed up by community health workers (CHWs) at least once
- Average number of times a high-risk adolescent has been followed up by CHW
- Number of times a high-risk adolescent has been seen by doctor
- Proportion of recommended follow-up visits that were actually made

7.4.6 Treatment history during intervention

Variables measuring receipt of treatment for mental health condition, capturing place and mode of delivery of treatment, adherence to prescribed medicines/counselling, and reasons behind non-receipt of treatment and non-adherence to prescribed medicines/counselling, will be examined using descriptive statistics. Frequency tables and bar graphs will be used to present distributions across the two treatment arms.

7.5 References

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Appendix 1: Tools and scores

A1. KAB scale and knowledge, attitude, and behaviour scores.

Question	Response	Score
To what extent you agree or disagree with the following statements?		
Knowledge		
Mentally ill people tend to be violent.	Disagree strongly Disagree slightly Neither disagree nor agree Agree slightly Agree strongly Don't know	5 4 3 2 1 3
People with mental illness cannot live a good, rewarding life.		
People with severe mental health problems can fully recover.	Disagree strongly Disagree slightly Neither disagree nor agree Agree slightly Agree strongly Don't know	1 2 3 4 5 3
Medication can be an effective treatment for people with mental health problems.		
Attitude		
Mentally ill people shouldn't get married.	Disagree strongly Disagree slightly Neither disagree nor agree Agree slightly Agree strongly Don't know	5 4 3 2 1 3
People with mental health problems should not be given any responsibility.		
People with mental health problems are far less of a danger than most people suppose.	Disagree strongly Disagree slightly Neither disagree nor agree Agree slightly Agree strongly Don't know	1 2 3 4 5 3
We need to adopt a far more tolerant attitude toward people with mental illness in our society.		
Behaviour		

I would be willing to live with someone with a mental health problem.	Disagree strongly Disagree slightly Neither disagree nor agree Agree slightly Agree strongly Don't know	1 2 3 4 5 3
I would be willing to work with someone with a mental health problem		
I would be willing to live nearby someone with a mental health problem		
I would be willing to continue a relationship with a friend who developed a mental health problem.		

Knowledge, attitude, and behaviour scores for each respondent will be derived by adding together the response values for the questions in that category. The response 'Don't know' has been assigned a neutral value of 3 (that is, the same as 'Neither disagree nor agree') for the purposes of deriving a total score.

A2. PHQ-9 score.

Question	Response	Score
Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all Several days More than half the days Nearly every day	0 1 2 3
Little interest or pleasure in doing things		
Feeling down, depressed, or hopeless		
Trouble falling or staying asleep, or sleeping too much		
Feeling tired or having little energy		
Poor appetite or overeating		
Feeling bad about yourself, or that you are a failure or have let yourself or your family down		
Trouble concentrating on things, such as reading the newspaper or watching television		
Moving or speaking so slowly that other people could have noticed? Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual		
Thoughts that you would be better off dead or of hurting yourself in some way		

PHQ-9 score will be calculated by summing over the response values for the 9 questions.

A3. Barriers to Access to Care Evaluation-Treatment Stigma Subscale and stigma score.

Question	Response	Score
Concern that I might be seen as weak for having a mental health problem	This has stopped, delayed or discouraged me from seeking care Not at all A little Quite a lot A lot	0 1 2 3
Concern that it might harm my chances when applying for jobs Not applicable □		
Concern about what my family might think, say, do or feel		
Feeing embarrassed or ashamed		
Concern that I might be seen as 'crazy'		
Concern that I might be seen as a bad parent Not applicable □		
Concern that people I know might find out		
Concern that people might not take me seriously if they found out I was having professional care		
Not wanting a mental health problem to be on my medical records		
Concern that my children may be taken into care or that I may lose access or custody without my agreement Not applicable □		
Concern about what my friends might think, say or do		
Concern about what people at work might think, say or do Not applicable □		

The BACE-treatment stigma subscale score for a respondent will be the mean of response values for the applicable items.

Appendix 2: Proposed tables and figures

Table 1. Subject disposition.

Status	High-risk cohort	Non-high-risk cohort	Total
Screened	x	x	x
Rescreened	x/x (x.xx)		
Enrolled	N	N	N
Visit month 3	x/N (x.xx)	x/N (x.xx)	x/N (x.xx)
Visit month 6	x/N (x.xx)	x/N (x.xx)	x/N (x.xx)
Visit month 12	x/N (x.xx)	x/N (x.xx)	x/N (x.xx)
Withdrawn/lost to FU at 12 months	x/N (x.xx)	x/N (x.xx)	x/N (x.xx)

* For screened population, high-risk are screen-positives (PHQ-9 score ≥ 10 and score ≥2 to the suicide risk question on the PHQ-9 >2) and non-high-risk are screen-negatives. For rescreened population, high-risk are those found positive during rescreening. For enrolled cohort, high-risk are those among screen-positives who were found to be positive (PHQ-9 score ≥ 10 and score ≥2 to the suicide risk question on the PHQ-9 >2) during rescreening and non-high-risk are sampled from the screen-negatives.

Table 2. Baseline characteristics of study participants in high-risk, non-high-risk and combined cohort.

Characteristic	High-risk cohort		Non-high-risk cohort	
	Intervention	Control	Intervention	Control
Age				
N				
Mean (SD)				
Median (Q1,Q3)				
Min-Max				
Sex				
Male				
Female				
Marital Status				
Never married				
Currently Married				
Divorced/ Separated/Widowed				
Highest level of formal education				
No Schooling				
Primary/Upper School (5th class to 7th class)				
Secondary/ Higher Secondary School				
Under graduation and above				
Dropout student				
Present occupation				
Student				
Unemployed				
Organized sector (Government employee, private employee)				

Unorganized sector (Agriculture labourer, domestic worker, manual labourer, skilled worker, vendor/trader)				
Housewife				
Religious leaders				
Contractors				
Substance use (tobacco, alcohol or other substances)				
Ever				
Never				
Ever diagnosed with any mental disorder				
Yes				
No				
Got treatment for mental disorder (out of total having mental disorder)				
Yes				
No				
Taking medicines for mental disorder as prescribed by the doctor on a regular basis (out of the total getting treatment for mental disorder)				
Yes				
Sometimes				
No				
Family history of any mental disorder #				
Yes				
No				
Support for personal problem score (0-18)				
Mean (SD)				
Median (Q1, Q3)				
Min-Max				

Financial support score (0-18)				
Mean (SD)				
Median (Q1, Q3)				
Min-Max				
Social support score (0-36)				
Mean (SD)				
Median (Q1, Q3)				
Min-Max				
DV indicator (witnessing domestic violence)				
Mean (SD)				
Median (Q1, Q3)				
Min-Max				
IPV indicator				
Mean (SD)				
Median (Q1, Q3)				
Min-Max				
Spousal violence indicator (0-9) (out of the total number of currently married)				
Mean (SD)				
Median (Q1, Q3)				
Min-Max				
CD-RISC score (0-40)				
Mean (SD)				
Median (Q1, Q3)				
Min-Max				
Stress indicator (0-22)				

Mean (SD)				
Median (Q1, Q3)				
Min-Max				

[¥] Unorganized sector: agricultural labourer, manual labourer, farmer, skilled worker, business/trader; Organised sector: Government employee, private employee.

[€] ridiculed either by parents, teachers or friends for the way you look; difficulty in getting up early in the morning for work/school; pressure to perform in school/abiding by school rules; lack of freedom and not having enough time for leisure and fun activities after work/school hours; financial pressure; natural disaster or forced migration leading to loss of income or property; death/injury/serious illness/arrest/assault of a family member /loved ones/close friend; sad/upset/worried because a family members/close friend struggled with addiction; experience any major crime or were a victim or witness of a major crime like theft, assault/beating, murder/attempted murder or sexual violence; self/friend cheated by or separated from another close friend

[#] close relatives (mother, father, brother, sister, uncles or aunts who are related by blood) had ever suffered from any mental disorder diagnosed by a doctor?

Table 3. Characteristics of slums.

Characteristic[€]	Intervention (n=30)	Control (n=30)
Slum adolescent population size		
Mean (SD)		
Median (Q1,Q3)		
Min-Max		
Proportion of high-risk adolescents found positive during rescreening		
Mean (SD)		
Median (Q1,Q3)		
Min-Max		
Proportion of high-risk adolescents who were in remission during rescreening		
Mean (SD)		
Median (Q1,Q3)		
Min-Max		
Slum adversity index[¶]		
Mean (SD)		
Median (Q1,Q3)		
Min-Max		

[¶] Slum adversity index is defined as sum of responses to few variables - conflicts with any neighbours, threatened with eviction, home demolished, home burned down or faced anxiety due to fire, home flooded with water, difficulty in obtaining water and time spent in getting water negatively impacting studies/work.

Table 4. Summary of PHQ-9, KAB and BACE stigma scores at baseline, 3, 6 and 12months, by treatment arm.

Score	Baseline		3 months		6 months		12 months	
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
Combined cohort								
Behaviour score								
N								
Mean (SD)								
Median (Q1, Q3)								
Min-Max								
Knowledge score								
N								
Mean (SD)								
Median (Q1, Q3)								
Min-Max								
Attitude score								
N								
Mean (SD)								
Median (Q1, Q3)								
Min-Max								
BACE stigma score								
N								
Mean (SD)								
Median (Q1, Q3)								
Min-Max								
High-risk cohort								
PHQ-9 (high-risk cohort)								
N								
Mean (SD)								
Median (Q1, Q3)								
Min-Max								
Suicide risk score ≥ 2								

Table 5. : Intervention fidelity – anti-stigma campaign components.

Characteristic of slum cluster (Median (IQI))	Non-high-risk cohort	High-risk cohort
% participating in all components (except rally)		
% participating in/receiving		
Brochure		
Game (snake & ladder, cricket, hopscotch)		
Animation video		
Lived experience		
Audio drama		
Street play		
Magic show		
Rally*		

- not compulsory

Table 6. : Intervention fidelity – digital health care model for the high-risk cohort.

Characteristic of slum cluster	Median (IQI)
% followed up by CHWs at least once	
% seen by doctor at least once	
% followed up by CHWs at least 6 times and seen by doctor	
Mean visits by CHW	

Table 7. Missing data pattern – reasons for loss to follow-up.

Reason	High-risk cohort		Non-high-risk cohort	
	Intervention	Control	Intervention	Control
Died				
Temporary shift				
Permanent shift				
Lock-up				
Refused				

Table 8. Analysis of outcomes (at 12 months).

	Mean (SE) or % at 12 months		Mean difference (continuous outcomes) or Odds ratio (OR)/Risk difference (binary outcomes) (95%CI)	p-value
	Intervention	Control		
High-risk cohort				
Primary outcome				
% achieving remission				
% achieving remission (adjusted for PHQ-9 at baseline)				
Secondary outcomes				
PHQ-9 score				
Combined cohort				
Primary outcome				
Behaviour score				
Secondary outcomes				
Attitude score				
Knowledge score				
Stigma score				

Table 9. Analysis of additional outcomes.

	Mean (SE) or %		Mean difference (continuous outcomes) or Odds ratio (OR) (binary outcomes) (95%CI)	p-value
	Intervention	Control		
High-risk cohort				
PHQ-9 score at 3 months				
PHQ-9 score at 6 months				
Remission component: PHQ-9 score <5 at 12 months				
Remission component: PHQ-9 score <5 at 12 months (adjusted for PHQ-9 at baseline)				
Remission component: suicide score <2 at 12 months				
Remission component: suicide score <2 at 12 months (adjusted for PHQ-9 at baseline)				
Combined cohort				
Behaviour score at 3 months				
Behaviour score at 6 months				
Attitude score at 3 months				
Attitude score at 6 months				
Knowledge score at 3 months				
Knowledge score at 6 months				
Stigma score at 3 months				
Stigma score at 6 months				
CD-RISC score at 12 months				

Supplementary Tables

Table A1. Adolescent stress factors

Question	High-risk cohort		Non-high-risk cohort	
	Intervention	Control	Intervention	Control
Were you ridiculed either by parents, teachers or friends for the way you look, in the last one year?				
Yes				
No				
Do you have difficulty in getting up early in the morning to go to school/compulsorily going to school/attending online classes in the last one year?				
Yes				
No				

Table A2. Social Capital: Social Network and Social Support

	High-risk cohort		Non-high-risk cohort	
Characteristic	**Baseline**	**12 months**	**Baseline**	**12 months**
In the last one year, how many family members and relatives (who do not live with you) did you usually keep in touch with by telephone, email, WhatsApp, Facebook, Instagram or visiting?				

0				
1-5				
6-10				
11-20				

Table A3. Analyses of outcomes – adjusted for key covariates.

	Mean (SE) or % at 12 months		Mean difference (continuous outcomes) or Odds ratio (OR) (binary outcomes) (95%CI)	P-value
	Intervention	Control		
High-risk cohort				
Primary outcome				
% achieving remission				
Secondary outcomes				
PHQ-9 score				
Combined cohort				
Primary outcome				
Behaviour score				

Secondary outcomes				
Attitude score				
Knowledge score				
Stigma score				

Table A4. Primary outcomes – controlled multiple imputation analyses.

	Unadjusted		Adjusted¶	
Outcome	**Mean difference (continuous outcomes) or Odds ratio (OR) (binary outcomes) (95%CI)**	**p-value**	**Mean difference (continuous outcomes) or Odds ratio (OR) (binary outcomes) (95%CI)**	**p-value**
Behaviour score at 12 months				
Achieved remission within 12 months				

¶ adjusted for age, sex, any stressful event in last one year, and substance use (tobacco, alcohol or other substances), …….

Table A5. ICC for different outcomes.

	Baseline	12 months	
		Intervention	**Control**
High-risk cohort			
% achieving remission			
PHQ-9 score			
Combined cohort			
Behaviour score			
Attitude score			
Knowledge score			
Stigma score			

Table A6. Treatment received by adolescents.

	Intervention	Control
Child visited a doctor at least once		
# times child visited doctor		

Table A7. Experiencing domestic violence

Table A8. Slum-level adversity factors

Table A9. Past history of mental disorder or mental health service use, at baseline and 12 months, by arm.

	Baseline		12 months	
	Intervention	Control	Intervention	Control
Ever diagnosed with any mental disorder				
Yes				
No				
Got treatment for mental disorder (out of total having mental disorder)				
Yes				
No				

Type of treatment (out of the total getting treatment for mental disorder)				
Given counselling				
Given medicines				
Both				
Place of treatment				
Urban Primary healthcare centre or by primary health care workers like ASHA/ANM/public health nurses				
General hospital, but treated by a general physician				
General hospital treated by a mental health professional like psychiatrist/psychologist/psychiatric nurse				
Psychiatrist/clinical psychologist/counsellors/social workers in private hospitals				
Mental hospital				
Traditional medicine practitioners/faith healers/Registered Medical Practitioners (RMP)/witch doctors				
Taking medicines for mental disorder as prescribed by the doctor on a regular basis (out of the total getting treatment for mental disorder)				
Yes				
Sometimes				
No				

Table A10. Intervention effect – risk difference along with 95% CI, for remission in high-risk cohort.

	Risk difference (95%CI)	
	Conditional estimate (mixed effects model)	Marginal estimate (generalized estimating equation)
% achieving remission		
% achieving remission (adjusted for PHQ-9 at baseline)		

Fig S1: Distribution of responses to questions in Connor-Davidson Resilience Scale-10 (bar graph showing responses to each question, by arm and cohort)

Fig S2: Distribution of Connor-Davidson Resilience Scale-10 scores at baseline and 12 months (density plots, by arm and cohort).