The Bangladesh DClare Trial:

Diabetes: Community-led Action, Response & Evaluation

Statistical Analysis Plan

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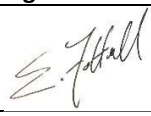
Prof. Edward Fottrell Principal Investigator		16/09/2022
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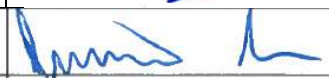
Dr David Beran Chair of Trial Steering Committee		26.09.2022

Contents

1. Overview

1.1 Background

Our DMagic Trial (ISRCTN41083256) was the first trial to show impact of a Participatory Learning and Action (PLA) community mobilisation intervention on prevalence of intermediate hyperglycaemia and diabetes and on two-year cumulative incidence of diabetes among individuals with intermediate hyperglycaemia at baseline. The current trial (DClare) seeks to evaluate the effectiveness of the PLA community mobilisation intervention when scaled up in Alfadanga Upazilla, Faridpur District, Bangladesh.

1.2 Scope of this SAP

This SAP specifies the study results to be included in the primary results publication. It does not cover the health economics or process/implementation analyses described in the overall study protocol.

1.3 Timing and approvals and of SAP

The first draft of this SAP was prepared on 8th July 2022. Intervention delivery is scheduled to be completed in August 2022. Endline data collection is scheduled to begin in late August and be completed by mid-October 2022. This SAP will be shared with the TSC and DMC before endline data collection begins and any amendments to the SAP must be made before data collection ends. A final draft of this SAP will be approved by the PI (Fottrell), Trial Statistician (Copas), Trial Steering Committee Statistical Advisor (Davey or Thompson) and Chair of the DMC (Shahidullah) before trial analysis begins.

2. Intervention

2.1 Participatory Learning & Action (PLA)

Community mobilisation through Participatory Learning and Action (PLA) is a specific approach to community interventions that has four phases: Phase 1 will focus on problem identification whereby participants themselves identify and prioritise factors that affect their health, specifically threats that increase their risk of developing or failing to manage diabetes; phase 2 involves the collective design of strategies that group participants and their communities can implement to address the problems and threats identified in phase 1; during phase 3, the participants implement these strategies; in phase 4 the participants reflect on and evaluate the success of the strategies they have implemented.

A minimum of 108 PLA groups, approximately 18 in in each of six clusters, will proceed through a series of meetings and wider community-level engagement activities following the four phase principles of PLA. 108 groups across six clusters in Alfadanga Upazilla gives a population coverage of approximately 1 group per 200 adults. A minimum of 13 meetings will be held over a total implementation period of 20 months. Though numbers will be limited to 20 participants, groups will be open to all and people with T2DM and at high-risk of T2DM will be particularly encouraged to attend. Those attending groups will be encouraged to share learnings and key messages with other members of the community who were unable to attend. Participatory groups will be led by group

facilitators, with a total of 12 facilitators (6 males, 6 female) recruited, and two facilitators in each cluster.

The target group for the PLA community mobilisation intervention is male and female residents within defined geographical areas, aged 30 years or more, as this is the group that we expect to benefit the most from the intervention. While PLA community groups will be available and accessible to any community member, including health care providers, we will particularly encourage high-risk individuals and those with T2DM to attend. For evaluation components we will restrict recruitment to non-pregnant, permanent residents of households within sampled communities.

2.2 Control clusters

Following implementation of PLA in the trial intervention clusters and on the condition that analysis of trial data indicates a positive effect of the intervention, it will be rolled out across the six control clusters over approximately 13 months.

3. The trial

3.1 Trial aim

In this trial we test the effectiveness of PLA on prevalence of diabetes and intermediate hyperglycaemia when the intervention is horizontally scaled-up to cover a population of approximately 60,000 in Alfadanga Upazilla, Faridpur District, Bangladesh and in the context of the COVID-19 pandemic. We hypothesise that horizontal scale-up pf PLA across Alfadanga Upazilla will significantly increase population-level awareness of diabetes prevention and control and will reduce the combined prevalence of intermediate hyperglycaemia and diabetes by at least 30% in intervention clusters relative to control.

3.2 Primary research question

Can the effectiveness of PLA on the prevalence of diabetes and intermediate hyperglycaemia observed in the DMagic trial be replicated when horizontally scaled-up?

3.3 Ancillary research questions

What is the effect of a scaled-up PLA participatory community mobilisation intervention on:

1) 18-month cumulative incidence of T2DM among individuals with intermediate hyperglycaemia, identified during the baseline surveys
2) Blood pressure
3) Overweight and obesity
4) Health behaviours (physical activity, fruit and vegetable consumption)
5) Knowledge and awareness of diabetes
6) Psychological wellbeing
7) Utilisation of diabetic services

3.4 Trial design

The trial is a parallel-arm two group cluster RCT with 1:1 allocation (12 clusters, 6 randomised to each arm). Evaluation is based on data collected at baseline (post randomisation but pre-intervention delivery) and endline (post intervention) cross-sectional surveys using two-stage simple

random sampling i.e. (largely) different people providing data at baseline and endline. In addition, individuals 30 years or older with plasma glucose cut-off intermediate hyperglycaemia at baseline are followed-up and subject to all data capture (interview survey and physical measurements) again at endline (i.e. an intermediate hyperglycaemia cohort). Therefore we describe the total endline collection as including a cross-sectional sample, and a cohort sample of those with intermediate hyperglycaemia at baseline. Some individuals with baseline intermediate hyperglycaemia may by chance be sampled in the cross-sectional survey at endline – these individuals are considered to belong to both samples. Note that the primary outcome is defined only for those in the cross-sectional sample at endline.

3.5 Population studied & eligibility criteria

The trial is being implemented in 12 clusters in Alfadanga Upazilla, Faridpur District, Bangladesh. Alfadanga has six unions, and an approximate population of 120,000 people. Using available administrative maps, each union was divided into two clusters of approximately equal geographical size and population, using 2011 census data, inflated by 10% to allow for population growth.

The cRCT is at risk of between cluster contamination whereby outcome assessment in control clusters may include participants who are exposed to the intervention in a neighbouring cluster. To minimise the risk of this we employ a 'fried-egg' design to our evaluation surveys whereby participants residing in riskier contamination zones (i.e. boarder areas) are excluded from the survey. A list of eligible, central cluster villages was developed, based on the 2011 census listing of villages, GPS point confirmation, and field supervisor visits to the study area. Eligible villages are those which do not sit on a border with a neighbouring study cluster, do not act as a major trading centre or administrative centre, and have a minimum of 50 households.

Individual eligibility criteria for survey participants are: non-pregnant female and male permanent residents aged 30 years and above. Permanent residence is defined as residence in the village for a minimum of 6 months at the time of the endline survey.

Individuals with blood glucose levels meeting definitions of intermediate hyperglycaemia during the baseline survey, will be purposefully sampled in the endline survey.

3.6 Consent for participation and enrolment in the trial

Community level consent for participation and enrolment in the trial took place at a public orientation meeting in Faridpur town attended by community leaders and district officials. Consent for participation and enrolment was obtained from Union leaders before randomisation.

3.7 Randomisation

Using simple randomisation, the 12 clusters were randomly allocated a number between 1 and 12 designating whether they will be intervention clusters (1-6) or control clusters (7-12). The name of each cluster was written on pieces of paper, which when folded were indistinguishable from each other. The 12 folded pieces of paper were placed into a container and then drawn by community leaders and representatives at a public community orientation meeting in Alfadanga attended by the project director, deputy project director and independent observers. The order in which clusters were drawn from the container determined the cluster number and hence allocation. The entire randomisation process was filmed and photographs were taken to document every stage.

3.8 Outcome measures

Primary and secondary outcome measures to be included in the main trial report and their data type are shown in Table 1.

Explanatory outcome measures assessed through quantitative analysis are shown in Appendix 1.

Table 1 Study outcomes and data type

Outcome Type	Outcome	Definition	Denominator (available cases)	Data type
Primary	combined prevalence of intermediate hyperglycaemia and T2DM	WHO categorisations for intermediate hyperglycaemia (impaired fasting glucose or impaired glucose tolerance) and T2DM based on fasting and 2-h blood glucose measures **or** self-reported diagnosis of T2DM	endline cross-sectional sample with valid endline blood glucose measurements.	binary
Secondary	awareness of diabetic status	self-reported diabetes	endline cross-sectional sample with valid endline blood glucose measurements that meet the classification of diabetes and who complete the endline questionnaire	binary
	physical activity	average time spent engaged in physical activity per week	endline cross-sectional sample with valid self-reported physical activity data	continuous
	blood pressure	diastolic and systolic blood pressure	endline cross-sectional sample with valid blood pressure measurements	continuous
	Hypertension	systolic blood pressure ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg or current treatment with antihypertensive medication	endline cross-sectional sample with valid blood pressure measurements	Binary
	Body Mass Index	body mass index (weight (KG)/height(m)^2)	endline cross-sectional sample with valid weight and height measurements	Continuous
	abdominal obesity	waist:hip ratio (WHR)	endline cross-sectional sample with valid waist and hip measurements	continuous
	dietary diversity	Dietary Diversity Score (DDS)	endline cross-sectional sample with valid DDS data	continuous
	knowledge about diabetes symptoms and complications	proportion of adults aged 30 years and above who are able to: a) name at least one cause of diabetes; b) report at least one symptom of diabetes; c) report at least one complication of diabetes; d) report at	endline cross-sectional sample of with valid knowledge data	Binary

		least one way to reduce the risk of getting diabetes; and e) report at least one way to control diabetes if diagnoses.		
	utilisation of services for treatment or advice for diabetes	proportion of diabetics with known diagnosis of diabetes receiving care or advice from a medical professional	endline cross-sectional sample of known (pre-diagnosed) diabetic individuals	binary
	depression	proportion of adults aged 30 years and above with a PHQ score or 10 or more.	endline cross-sectional sample of with valid PHQ data. All those who screen PHQ-2 negative and those who screen PHQ-2 positive but PHQ-9 negative will be in the denominator (i.e. "no depression")	binary
	Anxiety	Proportion of adults aged 30 years and above with a GAD-7 score $\geq$10.	endline cross-sectional sample of with valid GAD-7 data	binary
	18 month cumulative incidence of T2DM among individuals with intermediate hyperglycaemia at baseline	proportion of adults aged 30 years or older with plasma glucose cut-off categorisations for intermediate hyperglycaemia at baseline who are categorised as T2DM at endline	cohort sample of adults aged 30 years or older with plasma glucose cut-off intermediate hyperglycaemia at baseline and followed-up to endline	binary

3.9 Sample size calculation

The sample size is calculated based on using both baseline and endline data. Assuming a baseline outcome prevalence of 40% (data from January 2020), an intra-cluster correlation of 0.02, and conservative estimated autocorrelation between baseline and endline of 0.4[1], we will have 78% power to detect a 30% reduction in the primary outcome (combined T2DM and intermediate hyperglycaemia). This is based on methods described by Copas and Hooper (2020) for cluster randomised trials with different numbers of measurements at baseline and endline and is suited to a cluster summaries approach[2]. We used an average of 116 participants per cluster in the baseline survey, and 125 participants per cluster in the endline survey. We will sample approximately 132 respondents for the endline survey, to account for non-participation. Therefore we estimate the cross-sectional samples (which are used in estimation of the intervention effect on the primary

[1] Power is reduced to 76% if we assume autocorrelation of 0.2 and increases to 83% if we assume autocorrelation of 0.6.

2 Copas AJ, Hooper R. Cluster randomised trials with different numbers of measurements at baseline and endline: Sample size and optimal allocation. Clin Trials. 2020 Feb;17(1):69-76. doi: 10.1177/1740774519873888. Epub 2019 Oct 3. PMID: 31580144; PMCID: PMC7334046.

outcome) will be around 1400 respondents at baseline and 1500 respondents at endline. Note that in addition the trial collects data from a cohort with intermediate hyperglycaemia at baseline and so the total endline sample will be approximately 1800.

4. Data procedures

4.1 Data collection

Sampled individuals will be visited at their household, informed of the study and their verbal and written consent will be obtained. All sampled individuals in a single cluster will be informed of the anthropometric, blood glucose, and blood pressure measurement requirements of the study and will be requested to attend a local centre on the morning of a specified day following an overnight fast. The centre will be established by the field team for the purposes of the study and will be at a central, convenient location in the village. Home visits will be made to those who are unable to attend the centre. Collection of questionnaire data will take place at a private outside location near the respondent's home before or after the physical measurements or at the time of physical measurement in the testing centre. Data will be linked using a study ID number.

Data are to be collected by six teams of fieldworkers comprised of one male and one female with at least higher secondary education who will be recruited locally and selected through a written assessment and interview. All fieldworkers will undergo 10 days training on survey methods and how to take physical measurements followed by one-week supervised field practice and daily debriefs in villages in Faridpur that were not included in the study. Data collectors will be supervised by two field supervisors with experience in survey methods. Each supervisor will be responsible for three data collection teams, spending half a day observing and verifying data within each team at least every two days. Within each village, teams will be aided by a volunteer, usually a young male, to assist data collectors in their duties. Questionnaire data will be gathered using Huawei Tablet 9.6 inch android systems using ODK Collect with all other functions disabled.

4.1.1 Individual Questionnaire

Detailed information on the sociodemographic characteristics of all sampled individuals will be collected by trained field workers using a structured interview survey instrument adapted from the WHO Stepwise tool[15] and the 2014 Bangladesh Demographic and Health Survey[16] and using established mental health screening tools to measure depression (PHQ-9) and anxiety (GAD-7), and psychological distress and ability to self-manage one health among individuals living with diabetes (Appraisal of Diabetes Scale).

4.1.2 Physical measurements

Teams of fieldworkers at the testing centres will be trained to measure blood pressure, blood glucose concentration, body weight, height, and waist and hip girth using standard methods. Two systolic and diastolic blood pressure measurements will be taken at approximately 5-minute intervals and the respondent's blood pressure obtained by averaging these measurements. Measurements of height, weight, and waist and hip girth will be taken with light clothes without shoes. The weighing scales will be calibrated daily by known weight. Physical measures will be recorded onto specifically designed paper forms before being entered onto ODK forms on the tablets and linked to the survey data using unique personal identification numbers.

Blood glucose will be measured using the One Touch Varioflex Glucometer (Lifescan, Inc., Milpitas, CA 95035) in whole blood obtained by finger prick from capillaries in the middle or ring finger after an overnight fast. The One Touch Varioflex Glucometer automatically converts whole blood glucose readings to the equivalent plasma value so no additional conversion will be required. All individuals will then be asked to drink a 75g glucose load dissolved in 250 ml of water and will have a repeat capillary blood 120 minutes (+/- 5 mins) post ingestion to determine glucose tolerance status and differentiate between individuals with intermediate hyperglycaemia and those with diabetes according to WHO criteria (Table 2). Individuals who report a prior diagnosis of T2DM will not be asked to fast or be given a glucose tolerance test, but will instead be asked to provide a random (non-fasting) blood glucose sample, which will be used to understand diabetes control (a secondary outcome).

4.1.3 Baseline survey

A baseline survey using a random sample of the population took place between January and March 2021 prior to any intervention implementation. This survey had an 88% response rate and constitutes the baseline survey in the trial analysis.

Note that we also conducted a survey between January 2020 and March 2020, but this was terminated early (~72% complete) due to the COVID-19 pandemic and these data will not be used in the trial analysis.

4.1.4 Endline survey

The endline (post-intervention) survey will be conducted between September and October 2022.

Table 2: Glycaemic definitions and diagnostic criteria to be used in the DClare trial, adapted from WHO 2006

Definition		Diagnostic Criteria
Normoglycaemia		Fasting plasma glucose ≤6.0mmol/l
Intermediate Hyperglycaemia	Impaired Fasting Glucose	Fasting plasma glucose ≥6.1mmol/l to <7.0mmol/l **AND** two-hour post ingestion of 75g glucose load plasma glucose <7.8mmol/l
	Impaired Glucose Tolerance	Fasting plasma glucose <7.0mmol/l **AND** two-hour post ingestion of 75g glucose load plasma glucose ≥7.8mmol/l to <11.1mmol/l
Type 2 Diabetes Mellitus		Fasting plasma glucose ≥7.0 mmol/l **OR*** two-hour post ingestion of 75g glucose load plasma glucose ≥11.1mmol/l **OR** Self-reported prior diagnosis of diabetes^

*Diabetes cannot be excluded without 2-h post oral glucose load test

^See section 6.7 for details on sensitivity analyses with regards to self-reported diagnoses.

Adapted from: http://apps.who.int/iris/bitstream/10665/43588/1/9241594934_eng.pdf

4.2 Data storage and management

Data will be transferred from each data collectors' tablet onto a laptop in the field every three days, by one of the field supervisors. The laptop is backed up every day. Field supervisors keep track of

completed surveys each day and only supervisors are able to edit the content of the tablets (i.e. data collectors cannot delete any data from the phone). Gathered data are transferred from the laptop to the data manager in Dhaka once per week.

Data quality control is ensured through a) careful preparation of the ODK data collection tools, including range and logic checks, b) frequent supervisor observation of data collection and some repeat measurements by the supervisor at the point of data collection, c) data checking in Dhaka, with reports of errors and requests for verification sent back to the field team in Faridpur. In addition, all data collectors keep daily records and note any difficulties in gathering data or any unusual cases, which are then followed-up by the supervisor.

After data checking, the data manager in Dhaka uploads the data onto a cloud server held by Karolinska Institute, Sweden, where project data leads (King/Beard) run Stata scripts for further data verification providing feedback to Dhaka and Faridpur as necessary. The raw data are stored on password-protected, encrypted, secure computers in lockable rooms at the Diabetic Association of Bangladesh offices at BIRDEM hospital.

The data leads will also run Stata scripts to prepare data for analysis, performing pseudonymisation, labelling and recoding. For the primary outcome analysis, the study arm will be unlabelled. Data will be stored primarily on the Karolinska Institute cloud server, with working copies on password-protected and encrypted laptops as necessary.

4.3 Data coding

4.3.1 Derivation and coding of primary and secondary outcomes

Our primary outcome is the combined prevalence of intermediate hyperglycaemia (i.e. impaired fasting glucose or impaired glucose tolerance) and T2DM among adults aged 30 years or older defined using WHO definitions and blood glucose cut-offs for normoglycaemia, impaired fasting glucose, impaired glucose tolerance and T2DM, or self-reported prior diagnosis of diabetes, as summarised in Table 2.

Secondary and exploratory outcomes are generally derived using standard procedures (e.g. calculating BMI) or through simple derivation either a count or a binary indicator that one or more items have been reported (e.g. knowledge about diabetes outcomes).

4.3.2 Derivation and coding of exposure and adjustment factors

The primary exposure, i.e. allocation to intervention, is a direct part of the randomisation. For each outcome the baseline value of the outcome at the cluster level will also be adjusted for. Additionally, we will adjust for age and gender as detailed in Table 3. To control for a possible screening effect of being part of the baseline survey will adjust for participation in the baseline cross-sectional survey if the total proportion of individuals who participate in both the baseline and endline cross-sectional surveys is 10% or higher, or if it is at least 5% in both arms and differs by more than 4%. These minimum thresholds are set to avoid analytical problems caused by small cell sizes.

Table 3. Derivation of exposure and adjustment factors.

Confounders/covariates to adjust for in analysis:	How derived for analysis:
Gender (male/female)	Binary indicator derived from interview survey
Age (years)	Continuous measure derived from interview survey
Participation in baseline survey (yes/no) (if ≥10%, participation in baseline survey sample **or** ≥5% in each arm and a difference of ≥4% between arms)	Variable indicating if individual participated in baseline and endline cross-sectional surveys

5. General Analytical Principles

5.1 Interim analysis

No interim effectiveness analysis will be conducted. Analysis of baseline data (e.g. for epidemiological exploration of NCD risk in the study sample and comparison of pre- and post-first COVID wave measures) ignores trial arms.

5.2 Intention-to-treat

The primary analysis for each outcome will be undertaken on an intention-to-treat (ITT) basis, i.e. with individuals analysed according to the trial arm to which their village of permanent residence was randomised. We will not conduct a per protocol analysis – intervention protocol is to implement PLA community groups, which has been done successfully in all intervention areas. Subsequent process evaluation, including analysis by group activity and engagement is not part of this primary trial analysis and will take place at a later stage.

Participation in and exposure to (knowing someone who attends) the PLA intervention will be summarised by trial arm (see Dummy Table 2 in appendix).

5.3 Blinding and analysis checking

For the primary outcome the primary analysis will be conducted independently by the trial PI and trial statistician. Although both are blind to cluster allocation, in case of arm identification based on total number of participants etc. and to provide greater reassurance, the analysis will first be conducted using a 'dummy' trial indicator. Specifically, the data manager (Beard/King) will produce a blinded dataset using a new numeric cluster identifier and without the real trial arm or information on exposures that reveal trial arm. The clusters will be randomly allocated a dummy trial arm which will be used to develop analysis programs. After the two analysts have derived the required variables and conducted the primary analysis of the primary outcome then they will share results and discrepancies will be resolved. The PI will complete the analysis of secondary outcomes using the dummy trial arm, and the code preserved. Only then will the real trial arm for the clusters be provided. Analysis will be completed unblinded, and if necessary effect measures will be 'reversed' so as to present the effect of the intervention relative to control.

5.4 Levels of Confidence and p-values

Statistical tests and confidence intervals will be two-sided. Estimates of the intervention effects will be presented with 95% confidence intervals. The statistical significance level will be set at 5%. The significance level for secondary outcomes will not be adjusted for multiple testing.

5.5. Adjustment for design and contextual factors

For each outcome, unless otherwise specified, we will conduct an 'unadjusted' and 'adjusted' analysis. All analyses will include baseline data alongside the endline data so as to gain precision and

account for any baseline imbalance. The 'unadjusted' analysis will include adjustment only for the baseline prevalence of the outcome at the cluster level. 'Adjusted' analysis includes further adjustment for age, gender, and baseline hyperglycaemia, irrespective of the degree of balance in these factors between trial arms because these factors are considered *a priori* linked to intermediate hyperglycaemia and diabetes. There are no design factors as simple randomisation was used. We consider the adjusted analysis primary for all outcomes.

We plan to adjust for sex and baseline hyperglycaemia (cluster level) as binary factors, and to include age as linear and quadratic terms. Final decisions as to how exactly baseline information will be used as covariates in regression models for the outcomes (i.e. as linear and quadratic or not) will be taken after data collection is complete, using the dataset with dummy trial arm to avoid any possibility of introducing bias. A baseline factor may not be adjusted for at all in the event of sparse data, e.g., if fewer than 20 participants in one category of a binary baseline factor, or if within a category of a baseline factor the outcome takes only one value (i.e. all are intermediate hyperglycaemic or diabetes cases or not).

5.6 Missing data

We consider data as missing where the sampled individual is unavailable, has moved away, or does not agree to provide data. Baseline data suggest approximately 88% response rate to the interview and physical measurement components of the survey and very little item non-response. We are not planning imputation of the primary or any other outcome since key parameters we might use for imputation (e.g. age, sex, baseline hyperglycaemia) are already included in model adjustments and we expect almost all of those missing primary outcome data will also be missing all other data. We will report the loss to follow-up rate in the intermediate hyperglycaemia cohort by allocation group and selected key baseline characteristics and outcomes, with reasons for missing data documented wherever possible.

5.7 Regression models & effect measures

We propose a two-stage cluster summary approach for all outcomes because of the modest number of clusters. This has a slightly different form for an unadjusted and adjusted analysis.

In the first stage of the unadjusted analysis a cluster summary of the outcome is calculated for each cluster at baseline and endline. This will be the proportion for a binary outcome, for continuous outcomes this will be the mean, after transformation if the outcome is skewed [final decisions can be made based on the dataset with dummy trial indicator]. In the second stage the endline cluster summary values are analysed using linear regression including predictors trial arm and baseline cluster summary value. The coefficient for trial arm represents an intervention effect on the difference scale.

In the first stage of the adjusted analysis we calculate adjusted cluster summary values at baseline and endline. This is done by, separately for baseline and endline, fitting a model to predict the outcome including as predictors age, gender and (for endline model only) baseline survey participation, but excluding trial arm and ignoring the clustering in the data. Then the outcome is predicted for all participants (as a probability for binary outcomes), and then the cluster mean of the predicted values is calculated for all clusters. Next a residual term is calculated for each cluster, the observed cluster mean minus the mean predicted value. In the second stage the residuals at endline

residuals are modelled using linear regression including as predictors trial arm and baseline residual. The coefficient for trial arm represents the adjusted intervention effect on the difference scale.

5.8 Participant and analysis populations

The main analysis of the primary outcome will include all individuals who provided blood glucose measures at endline from the cross-sectional survey. This includes fasting and 2-hour blood glucose measures or, for people with self-reported diagnosis of diabetes, a random blood glucose measure.

For the cumulative incidence secondary outcome, analysis includes all individuals in the cohort for whom a baseline blood glucose measurement of intermediate hyperglycaemia was taken and for whom an endline blood glucose measurement is taken. This includes fasting and 2-hour blood glucose measures or, for people with self-reported diagnosis of diabetes, a random blood glucose measure.

For outcome measures relating to a diagnosis of diabetes, the analysis population will be restricted to those with a prior diagnosis of diabetes from a medical professional and self-reported awareness of their diabetic status (see Table 1).

For all other secondary outcomes, the analysis population will be all individuals with complete data on the outcome measure in the cross-sectional endline survey.

5.9 Multiple testing

There is only one primary outcome but multiple secondary outcomes. No formal adjustment, such as to the significance level or p-values, will be made for multiple tests undertaken. Interpretation of the practical importance of any statistically significant differences between intervention and control clusters in a secondary outcome will acknowledge the range of secondary outcomes tested.

6. Proposed analyses

6.1. Recruitment, intervention uptake and follow-up

We will report the number of clusters recruited and randomised and, by trial arm, the numbers of individuals sampled and completing the baseline and endline surveys, as well as the identification of individuals with intermediate hyperglycaemia at baseline and follow-up at endline.

A CONSORT style flow chart will be produced, reporting cluster and participant numbers and reasons for non-response/loss to follow-up. Potential age and gender response and loss-to-follow-up bias by study arm will be assessed.

6.2. Analysis software

Analyses will be conducted using Stata V15 or newer.

6.3 Presentation of baseline data

Baseline data, collected post-randomisation but prior to any intervention implementation, will be cross-tabulated according to the randomised group to check for appropriate balance and to provide an overview of the study population. This will include a comparison of sociodemographic and outcome variables (see Dummy Table 1 in appendix). Baseline characteristics of each group will be summarised as the mean, standard deviation and range for continuous, approximately symmetric variables; medians, interquartile range and range for continuous, skewed variables; frequencies and

percentages of individuals in each category for categorical variables. The formal statistical comparison at baseline of randomised groups is not good practice and thus will not be undertaken – only descriptive data, as described above, will be presented.

6.4 Descriptive summaries

Descriptive summaries of outcomes at endline will also be provided (planned dummy tables are included at the end of this SAP), with effect measures and summary statistics. Endline sample sociodemographic variables will be presented by trial arm.

6.5 Presentation of comparative analyses

For each of the continuous outcomes (Table 1), the mean and standard deviation for each allocated group will be presented together with the mean between-group difference, 95% confidence interval for the difference and p-value. If data are skewed, transformation (e.g. log transformation) will be performed and the ratio of the e.g. geometric means will be used to estimate relative effect size. For binary outcomes (Table 1), the percentage and frequency of individuals in the outcome of interest will be presented for each allocated group, along with the prevalence difference (the intervention effect), 95% confidence interval for that difference and p-value. For all outcomes number of clusters included in each analysis will be presented. The intervention effects reported, 95% CIs and p-values will all be calculated using the two-stage method described in section 5.7, and both unadjusted and adjusted effects will be reported.

6.6 Subgroup analyses of primary and secondary outcomes

Exploratory analyses of the following possible interactions will be undertaken to assess whether the effect of the interventions on primary and secondary outcomes is modified by (1) gender, (2) household wealth, (3) age, (4) village size (smaller vs. larger villages), and (5) inclusion in baseline survey. Age and wealth will be included as continuous interaction terms while gender, village size and inclusion in the baseline survey will be binary. The cluster summary approach described in Section 5.7 is the most appropriate analytical approach for our primary trial analysis but becomes complex for sub-group analyses. Therefore, despite the modest number of clusters, to avoid complexity, we propose an individual level analysis of endline data. Specifically, we will use independence estimating equations with robust standard errors through the use of the complex survey 'svy' functions in Stata. These subgroup analyses will be performed by adding the interaction term between allocated group and subgroup variable into a logistic regression (odds) model. A test of interaction will be performed to assess whether there is evidence that the effect of the intervention differs across the sub-groups. As the study is not powered for these interaction analyses the results will be treated with caution and the emphasis will be on the interpretation of the corresponding confidence intervals for the subgroups. This sub-group analysis using the individual level approach will not replicate the primary cluster-summary results without interaction and we will not report the main trial effect from this analysis, but rather will focus on interactions.

Note that in addition to these subgroup analyses, the trial process evaluation will explore further sub-groups, including levels of intervention exposure.

6.7 Secondary (sensitivity) analyses of primary outcome

To assess effects of possible misclassification in the primary outcome based on self-reported diagnoses, we will conduct sensitivity analysis of intervention effect on the primary outcome whereby a) all cases of self-reported diabetes are dropped from the analysis and b) all cases are

defined based on blood glucose measures only (i.e. disregarding self-reported diagnoses) where self-reported diabetic individuals with random blood glucose values of ≥11.1mmol/l are classified as diabetic and those with values <11.1mmol/l are classified as non-diabetic.

To assess effects of possible blood glucose measurement bias we will assess intervention impact on continuous blood glucose measurements and by separately applying different arbitrary fasting blood glucose cut-offs of 5·5 mmol/L, 6·3 mmol/L, and 7·8 mmol/L and 2-h blood glucose cut-offs of 6·8 mmol/L and 10·4 mmol/L for classifications of intermediate hyperglycaemia or diabetes.

7. Tables and figures for primary publication

Example dummy results tables to be included in the trial paper are given below.

8. Appendix

8.1 Explanatory outcomes

Outcome	Definition	Denominator (available cases)	Data type
Diabetes Control*	Individuals with self-reported prior diagnosis of diabetes whose blood glucose reading is <11.1 mmol/l at endline	Endline cross-sectional sample of known (pre-diagnosed) diabetic individuals who provided endline blood glucose measurements	Binary
Diabetes complications*	Individuals with self-reported prior diagnosis of diabetes who report a diagnosed health condition said to be associated with their diabetes	Endline cross-sectional sample of known (pre-diagnosed) diabetic individuals who completed the interview survey	Binary
At least monthly blood glucose testing*	Individuals with self-reported prior diagnosis of diabetes who report blood glucose testing on a monthly or more frequent basis	Endline cross-sectional sample of known (pre-diagnosed) diabetic individuals who completed the interview survey	Binary
Stigma*	Individuals with self-reported prior diagnosis of diabetes who report agreeing with statements that they: a) cannot fulfil their responsibilities b) are seen as a lesser person c) are embarrassed in social situations d) are ashamed of having diabetes (Note a-d are separate outcomes)	Total endline sample of known (pre-diagnosed) diabetic individuals who completed the interview survey	Binary
Family support/abuse related to T2DM diagnosis*	Individuals with self-reported prior diagnosis of diabetes who report: a) feeling supported by their family in managing their diabetes b) report experiencing any physical, mental or social abuse because of their diabetes (Note a & b are separate outcomes)	Total endline sample of known (pre-diagnosed) diabetic individuals who completed the interview survey	Binary
Social norms	Individuals reporting negative feelings or family or social reactions to in relation to hypothetical/real behaviours: a) going for a morning walk alone (women only) b) going for a morning walk with a female relative (women only) c) eating less than usual or refusing oily or sugary foods and drinks at a social gathering?	Total endline sample who completed the interview survey. (Females only for (a) and (b)).	Binary

	d) providing healthy snacks to guests? (Note a-d are separate outcomes)		
Self-rated health score	Self-rated health on a scale of 0 (poor health) to 100 (perfect health)	Endline cross-sectional sample who completed the interview survey	Continuous
Smoking & tobacco use	Current daily use of tobacco products	Endline cross-sectional sample who completed the interview survey	Binary
Betel nut use	Current daily use of Betel nut products	Endline cross-sectional sample who completed the interview survey	Binary
Sedentary time	Time spent sitting/reclining (NOT sleeping) on previous day	Endline cross-sectional sample who completed the interview survey	Continuous
Average time engaged in brisk walking activity	Time spent doing brisk walking in the previous week	Endline cross-sectional sample who completed the interview survey	Continuous
Diabetes affect*	psychological distress and ability to self-manage among diabetics assessed using an adapted Appraisal of Diabetes Scale (ADS) tool	endline cross-sectional sample of known (pre-diagnosed) diabetic individuals	continuous

* Outcome relates only to individuals with a known, prior diagnosis of T2DM.

8.2 Dummy tables

Table 1: Study baseline & endline sociodemographic characteristics and blood glucose classification by trial arm

		Baseline		Endline	
Sociodemographic parameter		**Control**	**PLA**	**Control**	**PLA**
Villages (Clusters)					
Average village population aged ≥30 years (sd)					
Average number of households (sd)					
Age	**30-39 years** **40-49 years** **50-59 years** **60-69 years** **70-100 years**				
Sex	**Male** **Female**				
Education	**None** **Primary** **Secondary** **Tertiary**				
Illiterate	**Literate** **Illiterate**				
Marital status	**Married** **Not married**				
Religion	**Muslim** **Other**				
Occupation	**Not working** **Manual labour** **Non-manual labour**				
Wealth quintile	**Most poor** **Very poor** **Poor** **Less poor** **Least poor**				
Total (survey)					
Diabetes outcomes	**Normal** **Impaired Fasting Glucose** **Impaired Glucose Tolerance** **Diabetes**				
Total					

Table 2: Intervention coverage process indicators by trial arm

OUTCOMES		Allocation	
		PLA	Control
Intervention exposure	Ever participated in PLA community group (%)		
	Knows someone who attended community group (%)		

Table 3 Endline frequency, proportions, absolute (coefficient) effects and 95% confidence interval comparing prevalence of intermediate and hyperglycaemia by trial arm and when applying conditions of secondary (sensitivity) analyses

OUTCOME			Crude Difference (95% CI)	Adjusted Difference (95%CI)
	Control	Community PLA	PLA vs Control	PLA vs Control
Combined prevalence of intermediate hyperglycemia and diabetes				
Sensitivity analysis 1: All cases of self-reported diabetes excluded				
Sensitivity analysis 2: All cases defined based on blood glucose measures only (disregarding self-reported diabetes)				
Sensitivity analysis 3: Varied cut-off definitions of intermediate hyperglycemia and diabetes.				

Table 4: Secondary outcome measures between trial arms at baseline & endline

OUTCOMES		Baseline		Endline		Crude Difference (95%CI)	Adjusted Difference (95%CI)
		Control	Community PLA	Control	Community PLA		
Blood pressure	Systolic blood pressure (mmHg), mean (sd)						
	Diastolic blood pressure (mmHg), mean (sd)						
	Hypertension, n(%)						
Overweight & obesity	Body Mass Index (BMI), mean (sd)						
	Overweight or obese, n (%)						
	Waist:Hip ratio, mean (sd)						
	Abdominal obesity, n (%)						
Dietary diversity score, mean(SD)							
Time spent engaged in physical activity per week, mean (sd)							
Diabetes knowledge	Ability to report one or more valid *causes* of diabetes (%)						
	Ability to report one or more valid *symptoms* of diabetes (%)						
	Ability to report one or more valid *complications* of diabetes (%)						
	Ability to report one or more valid ways to *prevent* diabetes (%)						
	Ability to report one or more valid ways to *control* diabetes (%)						
Depression, n(%)							
Anxiety, n(%)							
Self-awareness of diabetic status among individuals identified with diabetes by blood glucose measures, n (%)							
	Diabetes control (%)						

Among individuals with prior diagnosis of diabetes	**Utilisation of services for treatment or advice for diabetes**						
	Diabetes affect (ADS) score, mean (sd)						
Two-year diabetes incidence among individuals with intermediate hyperglycaemia at baseline, n(%)							

Figure 1 CONSORT flow diagram