DIAMONDS

Diabetes and Mental Illness, Improving Outcomes and Self-management: Randomised Controlled Trial

STATISTICAL ANALYSIS PLAN

Version 1

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1 Contents

2 Document scope and relevant SOPs and guidance documents

This statistical analysis plan (SAP) deals only with the statistical analysis of effectiveness, the cost-effectiveness analysis will be detailed in a separate plan. Version 1 was written prior to the completion of recruitment and according to York Trials Unit (YTU) Standard Operating Procedures (SOPs) and guidance documents.

3 Definition of terms/acronyms

AE	Adverse event
BMI	Body mass index
BPRS	Brief Psychiatric Rating Scale
CACE	Complier average causal effect
CI	Confidence interval
CONSORT	Consolidated standards of reporting trials
COS	Change Of Status
CPRD	Clinical Practice Research Datalink
CRF	Case report form
ICC	Intraclass correlation
IMB	Index of Multiple Deprivation
IPAQ	International Physical Activity Questionnaire
IQR	Interquartile range
ITT	Intention to treat
LTC	Long-term condition
MICE	Multiple Imputation by Chained Equation
MoA	Mechanisms of action
PAID	Problem Areas in Diabetes
PHQ-9	Patient Health Questionnaire-9
R&D	Research and Design
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD	Standard deviation
SDSCA	Summary of Diabetes Self-Care Activities Measure
SMI	Severe mental illness
SOP	Standard Operating Procedure
UoY	University of York
VIFs	Variance Inflation Factors
YTU	York Trials Unit

4 Design

Taken from the protocol: this study is a multi-centre, two-armed, parallel, individually randomised controlled trial with embedded process and economic evaluations. The two arms are the intervention plus standard care and standard care alone. The trial includes a 12-month internal pilot phase to assess recruitment assumptions and trial processes. The trial has a 22-month recruitment period (including the pilot). Follow up outcomes will be collected at 6 and 12-months post-randomisation.

5 Trial Objectives

The objectives of the trial are to investigate the clinical and cost-effectiveness of the DIAMONDS intervention for people with severe mental illnesses compared to usual care. The following are taken from the protocol.

1. To undertake a 12-month internal pilot to obtain estimates of recruitment and retention and to confirm trial viability.
2. To undertake a randomised parallel group comparison to determine the effects of the DIAMONDS intervention on glycated haemoglobin (HbA1c) at 12 months post-randomisation.
3. To undertake a randomised parallel group comparison to determine the effects of the DIAMONDS intervention on other outcomes related to physical health, psychological health and diabetes taken at 6 months and 12 months post-randomisation.
4. To conduct a detailed economic evaluation to assess the cost-effectiveness of the DIAMONDS intervention for both the trial period and the longer term (this will be presented elsewhere).
5. To conduct a process evaluation that will harness data form both qualitative and quantitative sources to address questions about whether the intervention was delivered as intended and how outcomes were produced. Additionally, the process evaluation will aim to identify barriers and enablers to post-trial implementation and scale-up, including whether the intervention can support self-management of other long-term conditions (LTCs) in people with severe mental illness (SMI).

6 Follow-up

Data will be collected at baseline, 6- and 12-month post-randomisation from participants.

Table 1: Schedule of data collection

		Baseline	6 months	12 months
Demographics				
Age	Self-report	X	-	-
Sex	Self-report	X	-	-
Ethnicity	Self-report	X	-	-
Index of Multiple Deprivation (IMD)	Determined by study team based on participant's postcode	X	-	-
Type of SMI	Medical records	X	-	-
Date diagnosed with SMI	Medical records	X	-	-
Date diagnosed with diabetes	Medical records	X	-	-
Physical Health				
Height	Measured by study team	X	X	X
Weight	Measured by study team	X	X	X
BMI (calculated from height and weight)	Calculated by study team	X	X	X
Waist circumference	Measured by study team	X	X	X
Blood pressure	Measured by study team	X	X	X
HbA1c	From central lab or medical records	X	X	X
Total HDL and LDL cholesterol	From central lab or medical records	X	X	X

Triglycerides	From central lab or medical records	x	x	x
Haemoglobin	From central lab or medical records	X	X	X
Psychological health				
Brief Psychiatric Rating Scale (BPRS)	Self-report	X	X	X
Patient Health Questionnaire-9 (PHQ-9)	Self-report	X	X	X
Diabetes Measures				
Diabetes distress (PAID-5)	Self-report	X	X	X
Summary of Diabetes Self-Care Activities	Self-report	X	X	X
Smoking status	Self-report	X	X	X
Physical activity (IPAQ)	Self-report	X	X	X
Diabetes microvascular and macrovascular compilations	Medical records or self-report	X	X	X
Urine albumin to creatinine ratio	Medical records or self-report	x		x
Amputation	Medical records or self-report	x		x
Health economic outcomes				
Health-related quality of life (EQ-5D-5L)	Self-report	X	X	X
Health resource use	Self-report	X	X	X
Process evaluation measures				
Mechanisms of Action*	Self-report	X	X	X

*The Mechanisms of Action questions are also completed in a monthly CRF

7 Outcomes

7.1 Primary outcome(s)

The primary outcome of the main trial is glycated haemoglobin (HbA1c) at 12 months post-randomisation. It will also be measured at 6 months post randomisation as a secondary outcome. Participants who do not want a blood test can consent to their most recent routine blood test results being used if that test was taken between 6 weeks before and 6 weeks after the follow up date. This measure is collected in the bloods case report form (CRF).

7.2 Secondary outcome(s)

The following have been taken from the protocol:

Physical health

Cholesterol: Measured as part of a biochemical lipid profile (blood test) taken at the same time as the blood for the HbA1c measurement. Total cholesterol, LDL, HDL cholesterol, and triglycerides (all measured in mmol/L) will be recorded. These measures are collected in the bloods CRF.

Haemoglobin: Blood test taken at the same time as blood for HbA1c measurements and lipid profile. Haemoglobin will be recorded in g/L.

Body mass index (BMI): Calculated using weight (kg) and height (metres) measurements using the following formula: $weight\ (kg)\ /\ height\ (metres)^2$. These measurements will be recorded in the investigator CRF.

Waist circumference: Measured following standard trust procedures and recorded in cm or inches. This measurement will be recorded in the investigator CRF.

Blood pressure: Systolic and diastolic blood pressure measured following standard trust procedure and recorded in mmHg. This measurement will be recorded in the investigator CRF.

Smoking status: Assessed through participant self-report: yes/no/never. This is recorded in the participant CRF.

Urinary albumin to creatinine ratio: Will be extracted from participants' medical records as a measure of diabetic nephropathy (this measure is only collected at baseline and Month 12).

Physical Activity: Physical activity will be measured using the International Physical Activity Questionnaire (IPAQ)(1). This instrument is a 7-item self-reported (short form) assessing physical activity in the last 7 days. Results will be reported in categories of activity levels (low, moderate, high).

In addition, we will provide all participants with wearable wrist accelerometers to obtain an objective measure of physical activity. Accelerometers will be given to participants at their baseline assessment and again at the six months follow-up time point, where they will be asked to wear the device continually for seven days. At the end of the seven-day period, they will be asked to return the device to the UoY team; this will be facilitated by the study team as needed. The University of York (UoY) team will carry out all data download and device set-up. The Research and Design (R&D) teams will receive instructions on how to activate the devices to start data collection.

Acceptability of wrist-worn accelerometers in this population has been confirmed in the STEPWISE study and the DIAMONDS feasibility study.

We will convert accelerometery data into activity profiles to assess time spent (a) in a sedentary state, (b) doing mild activity, or (c) doing moderate (or high) intensity activity.

Psychological health measures

Psychiatric symptoms: Assessed using the Brief Psychiatric Rating Scale (BPRS)(2). The BPRS assesses the level of 18 symptom constructs such as hostility, suspiciousness, hallucination, and grandiosity. Each symptom construct ranges from 1 (not present) to 7 (extremely severe). This measure is taken in the investigator CRF.

Depressive symptoms: Assessed using the Patient Health Questionnaire-9 (PHQ-9)(3). The questionnaire comprises nine items which are individually scored as 0 (not at all) to 3 (nearly every day) and then added to provide an overall score. The lower the overall score, the lower the severity of depression. This measure is taken in the participant CRF.

Diabetes measures

Diabetes distress: Assessed using the short form version of Problem Areas in Diabetes (PAID-5) scale (4), a validated self-report measure of diabetes distress. Each of the questionnaire's 5 items are measured on a five-point scale from 0 (not a problem) to 4 (a serious problem). Total scores on the PAID-5 can range from 0 to 20, with higher scores suggesting greater diabetes-related emotional distress This is measured in the participant CRF.

Summary of diabetes self-care activities: Assessed using the Summary of Diabetes Self-Care Activities Measure (SDSCA)(5). This tool contains 11 items, which measure the frequency of performing diabetes self-care activities over the last seven days. The respondent marks the number of days on which the indicated behaviour was performed using an eight-point Likert scale. These measures are taken in the participant CRF.

Insulin use: Assessed through participant self-report (yes/no) in the participant CRF.

Diabetes complications: Extracted from medical records or self-report.

- Microvascular: Retinopathy, Neuropathy, Nephropathy
- Macrovascular: Myocardial infarction, Peripheral vascular disease Nepthropathy, Stroke or Foot ulcers
- If amputation occurred

Quality of Life

Health-related quality of life: Assessed using the EQ-5D-5L, a validated self-report measure(6). This generic, validated, patient-reported outcome measure has five health domains (mobility; self-care; usual activities; pain/discomfort; and anxiety/depression) with five response options for each domain (no problems, slight problems, moderate problems, severe problems, and extreme problems). The scoring and more detailed analysis will be described as part of the health economic analysis plan.

Table 2: Summary of scoring methods and score interpretation for instruments used in the DIAMONDS trial

Name	Score Range	Description	Score calculation	How missing items will be handled	Interpretation of score
IPAQ	MET minutes: 0-	7-item self-report questions assessing physical activity in the past 7 days.	MET minutes is the sum of the MET minutes of each category. Each MET minutes category is calculated by taking the number of minutes doing a category of activity multiplied by that category's constant. Each category is limited to 180 minutes of activity per day. Those constants are: Walking = 3.3 Moderate activity = 4 Vigorous activity = 8	No guidance is provided. MET minutes will only be calculated if all items are present.	High: Vigorous activity for at least 3 days, achieving at least 1500 MET minutes OR 7 days of any activity achieving at least 3000 MET minutes. Moderate: 3 or more days of vigorous activity/walking for at least 30 minutes a day OR 5 or more days of moderate activity/walking for at least 30 minutes a day OR 5 or more days of any activity, achieving at least 600 MET minutes. Low: Any other amount of activity. Direction of positive effect: Increase
BPRS	18-126	Assesses the level of 18 psychiatric symptoms, each range from 1 (not present) to 7 (extremely severe)	Sum the scores.	No guidance is provided by developers; however, we will accept up to 4 items to be missing. If so an average of completed items can be imputed for the missing items	<31: Not significantly ill 31-40: Mildly ill 41-50: Moderately ill >51: Markedly ill Direction of positive effect: Decrease
PHQ-9	0-27	Comprises nine items measuring depressive symptoms, each scored as 0 (not at all)	Scoring: scores are summed for a total.	No guidance is provided by developers however, we will allow up to 2 items to be missing. If so, an average of	0 = No or minimal depression 27 = Severe depression

		to 3 (nearly every day).		completed items can be imputed for the missing items.	Direction of positive effect: Decrease
PAID-5	0-20	5 items measured on a scale from 0 (not a problem) to 4 (a serious problem) measuring diabetes distress.	Scoring: scores are summed to generate a score out of 20.	No guidance is provided by developers. As there are only 5 items, scores will only be calculated if all items are completed.	Direction of positive effect: Decrease
SDSCA	0-7 (except smoking status which is 0 or 1 and the number of cigarettes smoked)	11 items measuring frequency of diabetes self-care activities. Each item is measured on an eight-point Likert scale.	Scoring: Scores are calculated for five categories. General diet: mean of items 1 and 2 Specific diet: reverse the value of item 4 (0=7, 1=6, …), then take the mean of items 3 and 4 Exercise: mean of items 5 and 6 Blood-Glucose Testing: mean of items 7 and 8 Foot-Care: mean of items 9 and 10 Smoking status: item 11 and number of cigarettes per day	No guidance is provided by developers. Due to the small number of items within each category, all items within a category must be present for that category to be scored.	Direction of positive effect: Increase

Health resource use

A bespoke health resource use questionnaire that has been tested in the feasibility study and refined in line with feedback received will be used to collect participants' use of primary care, secondary care and community-based services over a six-month period. This measure is taken in the participant CRF. These measures will be used as part of the health economic evaluation, the planned analysis for which will be presented separately.

Mechanisms of Action

We will quantitatively collect information about the mechanisms of action (MoAs) used in the DIAMONDS intervention. The 'Change One Thing' app has built-in monthly reviews of MoAs that participants will work through with their DIAMONDS Coach at their 1-to-1 sessions. In addition, we will use a set of self-report process measures at baseline and follow-up. The mechanisms of action data are collected using a bespoke MoA CRF.

7.3 Other collected variables

Participant characteristics are collected at baseline. These characteristics are participant age, sex, ethnicity, index of multiple deprivation, type of SMI, date diagnosed with SMI and date diagnosed with diabetes.

Intervention use data are collected: number of coaching sessions, session duration, content of sessions and use of the Change One Thing app.

Any adverse events (AEs) or serious adverse events (SAEs) will be reported to the Chief Investigator and will be reviewed by a clinician independent to the DIAMONDS study team. The reporting period will be from study entry up to the last follow-up visit. Details about AEs/SAEs will be captured at each clinical contact point or study assessment. AEs/SAEs that might have occurred since the previous visit or assessment are elicited from the participant by open questioning and recorded. All events related to the DIAMONDS intervention will be recorded on adverse events forms. Further information may be requested for follow up of these events. Detailed records will be kept of all adverse events.

8 Data

8.1 Case Report Forms

There are multiple CRFs, the table below shows when they should be completed:

Table 3: CRF schedule

CRF	Baseline	6-Months	12-Months	When needed
Bloods	X	X	X	
Investigator	X	X	X	
Participant	X	X	X	
Mechanisms of Action (MoA)*	X	X	X	

Change of Status (CoS)				X
Adverse events & serious adverse events				X
Eligibility	X			

*There is also a monthly MoA CRF
The baseline participant CRF includes a section on demographics that is not in the follow up versions.

Trained members of the R&D team are sent paper copies of the CRFs to fill out and return by post. The CRFs will be completed in person but if needed, will be completed over the phone or by post. YTU will process the CRFs when received. CRFs can be found in: "\\hsci.york.ac.uk\hsciytu\Project -- DIAMONDS - Statistics\1 Statistics\WP4 - RCT\Documentation\CRFs".

8.2 External datasets

8.2.1 Intervention delivery

Data on the delivery of the intervention will be collected via Qualtrics and the Change One Thing app:

- Session duration;
- Number of sessions delivered;
- Mode of delivery (remote, phone, in person): frequencies/percentages;
- List of content areas with number of participants who discussed each content area;
- Duration a participant stayed with the same action plan/content area;
- Number of content areas covered during total intervention period and workbook and/or Change One Thing app.

9 Sample Size

Original sample size calculation

The sample size calculation was based on detecting a clinically meaningful difference of 5.5 mmol/mol (0.5%) in HbA1c at 12 months. This difference was selected based on data from trials of diabetes self-management in the general diabetes population and NICE guideline on type 2 diabetes management. Based on the variation observed in HbA1c in a Clinical Practice Research Datalink (CPRD) population study, we assumed a standard deviation of 15.3 mmol/mol. Based on attrition rates in previous severe mental illness trials, we expect approximately 20% attrition. In the intervention arm, a DIAMONDS Coach will deliver the intervention to multiple participants, and therefore the outcomes of participants with the same coach may be correlated. Although only a small clustering effect is expected, this provides a more conservative sample size estimate. The sample size was therefore adjusted for clustering in the intervention arm.

For approximately 90% power, at the 5% significance level, assuming an average cluster size of 10-12 participants per DIAMONDS coach with an intraclass correlation (ICC) of 0.02 in the intervention

arm, and adjusting for 20% attrition, we estimate we will need to randomise 450 participants, with 225 per treatment group.

Revised sample size calculation

In February 2024 following discussion with the TSC, an amendment was made to the original sample size calculation described above due to slower than anticipated recruitment. We amended the sample size by including an adjustment for the correlation between baseline and 12-month HbA1c (0.3) to reflect the repeated measures analysis model planned for the primary analysis. This led to a minimum sample size of 380 participants needed; keeping all other assumptions the same would achieve 88% power. However, we will continue recruiting beyond this minimum target until the end of the agreed recruitment window.

10 Randomisation and blinding

As stated in the protocol:

Consenting participants will be randomised on a 1:1 allocation ratio to either the DIAMONDS intervention or the usual care group using computer generated permuted blocks of random sizes. Randomisation will be carried out by York Trials Unit (YTU) independently of the R&D team using a secure, online randomisation service to ensure allocation concealment.

The DIAMONDS Programme Manager and Trial Coordinators will be unblinded to allocation in order to facilitate contact between randomised participants and their designated DIAMONDS Coach, if required. Following randomisation, the participating site will contact DIAMONDS Coaches to advise them to approach participants randomised to the intervention group to arrange the first intervention session.

Statisticians will not remain blind during the study but will not see any unblinded primary outcome data until a version 1 of the statistical analysis plan has been signed off.

11 Analysis of internal pilot trial/phase

As stated in the protocol:

Recruitment rate and the 95% confidence interval will be estimated from the pilot data collected. A CONSORT diagram will produced with the following outcomes: number of eligible participants; proportion of eligible participants approached for consent; proportion of eligible participants not approached and reasons why; proportion of participants approached who provide consent; proportion of participants approached who do not provide consent; proportion of participants providing consent who are randomised; proportion of participants randomised who do not receive the randomly allocated treatment; proportion of participants dropping out between randomisation and follow-up.

Reasons why eligible participants were not approached; reasons for participants declining to participate in the study; reasons why randomised participants did not receive their allocated treatment and reasons for dropout will be summarised if available.

Results will be compared against the recruitment assumptions and progression targets, and continuation of the trial and any appropriate adaptations to the trial will be decided by the Steering Committee and the funding body.

Progression from the pilot phase to the main trial will depend on satisfying the following pre-specified targets at 12 months from the start of the trial:

	Green	Amber	Red
a) Average number of participants per site per month	2 participant per month	1.3 to <2 participants per month	<1.3 participants per month
b) Recruitment of sites	15 sites	10 to 14 sites	<10 sites
c) Completeness of outcome (HbA1c) data at 6-months	80% of participants with complete outcome	65% to <80% of participants with complete outcome	<65% of participants with complete outcome

The following actions will be taken based on the targets achieved above:

- Green: continue the trial without any adaptations.
- Amber: review procedures to identify underlying problems, and put in place strategies to address these, review after an interval and terminate the trial if recruitment trajectory does not indicate that full recruitment will occur within scheduled recruitment period.
- Red: terminate the trial unless we can confidently identify successful strategies or rapidly resolve the problem.

The internal pilot had been completed at the time of writing the statistical analysis plan.

12 Final analysis

12.1 Analysis software

All analyses will be conducted in the most recent version of Stata (7) or R(8).

12.2 Analysis principles and populations

Analysis of primary and secondary outcomes will be intention-to-treat (ITT) (unless otherwise stated) and tests will be two sided at 5% significance level.

12.3 Screening, eligibility, recruitment and follow-up data

A CONSORT flow diagram will be presented (Ref: Figure 1). Tables will be presented with reasons for participant ineligibility and withdrawal. Recruitment numbers will be reported by site and allocation arm. CRF return rates will also be reported.

12.4 Baseline data

Baseline characteristics will be reported descriptively by randomised group (Ref: Tables 2-3). Continuous data will be summarised as means, standard deviations (SD), medians and interquartile ranges (IQR), and categorical data will be summarised as frequencies and percentages. No formal statistical comparisons of baseline data will be undertaken. Data will be reviewed, and any imbalance reported.

Participant demographic information (e.g. age, gender, ethnicity, etc), other key characteristics (type of SMI diagnosis, whether single or multiple SMI diagnoses, whether SMI or diabetes was diagnosed first, smoking status, insulin use etc) and baseline measures will be summarised by randomised group.

12.5 Intervention delivery

Participants randomised to the DIAMONDS Intervention will be offered individual sessions over a six-month period with a DIAMONDS Coach. Within the six-month period, the Coach and participant will have the flexibility to meet as often as they both would like. Summaries of the intervention delivery will be presented in tables and graphically (Ref: Table 6, Fig 2) and will include:

- Number of sessions received (mean, SD, median, IQR);
- Number of participants who attended at least 1 session;
- Session duration (mean, SD, median, IQR);
- Number and percentage of the mode of delivery of sessions (remote, phone, in person);
- Number and percentage of participants who discussed each content area;
- Average duration a participant stayed with the same action plan/content area;
- Average number of content areas covered during total intervention period and workbook and/or Change One Thing app.

12.6 Primary analysis

The primary outcome (HbA1c at 12-month post-randomisation) will be analysed using a partially-nested mixed effects regression model, with HbA1c scores at 6- and 12-months follow-up as the dependent variable, adjusting for baseline HbA1c scores and outcome source (central lab or medical records), randomised treatment group, time and a treatment group-by-time interaction will be included as fixed effects and participant and DIAMONDS coach as a random effect nested within treatment arm (9). Different covariance patterns for the repeated measurements will be explored and the most appropriate pattern will be used for the final model. Diagnostics including Akaike's information criterion will be compared for each model (smaller values are preferred). The model assumptions (normality of residuals, homoskedasticity and multicollinearity) will be evaluated using residual plots and calculating variance inflation factors (VIFs).

The estimated treatment group difference at 12 months will be reported as the primary endpoint with the associated 95% confidence interval and p-value (Ref: Table 7). Analysis of the primary outcome will be checked by a second statistician. The analysis model does not match exactly the method used in the sample size calculation which simply compares one follow up point (12 months) with an adjustment for baseline correlation. This is a more conservative approach so we should still have adequate power for the primary analysis.

HbA1c is being collected from different sources:

Central laboratory- participant must consent to bloods being taken at their visit. The sample is then sent to a central laboratory in Manchester. Blood results are returned to YTU and recorded on a Bloods CRF by YTU staff.

Medical records- if lab results are unavailable (e.g. participant refuses to have blood samples taken), the investigator may use medical records to look up a recent blood test result and corresponding date which will be recorded on that CRF (baseline, Month 6 or Month 12).

The primary analysis will include all HbA1c values from both sources providing they are within +/-6 weeks from the date of the specified timepoint (baseline, 6- and 12-months post randomisation). Values outside of this window will be counted as missing. We will conduct analyses with all observed data. Mixed effects regression models use all available data and assume missing outcome data are missing at random. To explore this assumption, we will summarise the baseline characteristics of participants with and without missing outcome data and further sensitivity analyses are outlined in section 12.7.

12.7 Sensitivity analyses

12.7.1 Central laboratory data only

As the primary outcome data may include data from medical records, we will replicate the primary analysis (section 12.6) but only include values that came from central laboratory.

12.7.2 Missing data

The amount of missing data will be reported for each randomised arm, and we will also compare the baseline characteristics of participants who are included in the primary analysis to ensure that any attrition has not produced any imbalance in the groups in important covariates. We will explore the extent and pattern of missing data and, if appropriate, will undertake multiple imputation to assess the impact of missing data on treatment effect estimates.
Multiple Imputation by Chained Equation (MICE) will be used as the method for imputation (10)(11). The imputation model that will be used to impute Hba1c at baseline, 6 months and 12 months. We will present results from the following models:
Baseline imputed only- the imputation model will include HbA1c at baseline and 6 months, age, sex, ethnicity, IMD decile and treatment arm. Thirty multiply imputed data sets will be used. Missing 12-month HbA1c values will be imputed but removed again before analysis (12)

Baseline and 12 months- the same model described above will be used and the imputed 12-month HbA1c values will remain.
Treatment effects and their 95% CIs will be presented in a forest plot alongside those produced using the primary analysis methods and other sensitivity analyses (Ref: Table 7).

12.7.3 CACE analysis

Complier Average Causal Effect (CACE) analyses will be performed for the primary outcome to assess the impact of compliance on treatment estimates. This will be conducted at the participant level, considering compliance as a dichotomous variable (complied or not). Compliance to the intervention is difficult to pre-define as there are several components to the intervention (one-to-one sessions, workbook, app use) and is intended to be flexible. An intervention participant will be defined as non-compliant if they do not attend any coaching sessions. An instrumental variable approach will be used, with random group allocation as the instrumental variable (13).

12.8 Subgroup analyses

Subgroup analyses will be performed to explore the potential effect of the following subgroups:

- Participants with good and those with suboptimal diabetes control at baseline as defined as High control (HbA1c values <= 58 mmol/mol) and Low control (HbA1c values >58 mmol/mol)
- Ethnicity (White, Asian or Asian British, Black, Black British, Caribbean or African, Mixed or multiple ethnic groups or Other Ethnic background)
- Insulin use status (Prescribed insulin Yes or No)
- Urdu speakers (Yes or No)

As we are unable to predetermine the numbers in each subgroup, the completion of each subgroup analysis will be subject to there being sufficient numbers in the group.
The primary analysis model will be refitted with an interaction term between the randomisation group and the specified subgroup variable. Treatment effect for these subgroups will be reported as adjusted mean differences with their associated 95% CI and p-values (Ref: Table 8).
As recommended by the literature, the subgroup analysis will be restricted to the primary analysis and subgroups will be defined by baseline data i.e. data that is not dependent on the intervention(14). Subgroup analysis will be performed regardless of the results of the primary analysis.

12.9 Analysis of secondary outcomes

BMI, smoked at any point in the last 7 days (yes or no), BPRS scores, PHQ-9 scores and PAID-5 scale scores will be analysed using mixed effects regression analysis for continuous outcomes, and logistic mixed models for binary outcomes. Baseline scores, randomised treatment group, time and a treatment group-by-time interaction, sex and age will be included as fixed effects and participant and DIAMONDS coach as random effects (to reflect the primary analysis model). Models will include assessments at all available time-points and will provide an overall treatment effect over 12 months, as well as estimates at individual time-points (6 and 12 months), reported as estimates and 95% confidence intervals. Different covariance patterns for the repeated measurements will be explored, and the most appropriate pattern will be used for the final model.

Other secondary outcomes (total cholesterol, HDL cholesterol, triglycerides, LDL cholesterol, haemoglobin, systolic BP, diastolic BP, waist circumference, urinary albumin: creatinine ratio, insulin use, diabetes complications, EQ5D-5L scores, IPAQ levels and SDSCA category scores) will be presented descriptively by treatment arm.

Accelerometer data will be collected at baseline and 6-months post-randomisation. Data will be analysed using the R-package GGIR, which performs signal processing of the raw data, including auto-calibration, detection of abnormal values, detection of non-wear, and calculation of the average magnitude of dynamic acceleration (Euclidean norm minus one g [ENMO]). Files will then be exported to Stata or similar statistical software for further analysis. Descriptive statistics will be reported by treatment group at each time point (baseline and 6 months) and differences between treatment groups will be reported, adjusted for baseline.
Based in findings from the feasibility study, analysis will be restricted to participants who had at least 4 valid days of accelerometer monitoring (out of a planned 7 days). The following summaries will be presented by treatment arm for all days and split by weekdays and weekend days:

- Number of valid days the participants wore the accelerometer (n (%), mean (SD);
- Valid wear time in hours (mean and SD);
- Number and percentage of participants with the required number of valid days;
- Time spent engaging in light activity (minutes per day) (mean and SD);
- Time spent engaging in moderate activity (minutes per day) (mean and SD);
- Time spent engaging in vigorous activity (minutes per day) (mean and SD);
- Time spent engaging in sedentary activity (minutes per day) (mean and SD).

12.10 Adverse events

The summary of AEs and SAEs experienced by participant will be reported by randomisation group (Ref: *Tables 12-13*).
All adverse events will also be assessed for seriousness and will be recorded as a serious adverse event, if it:

- Results in death;
- Presents a life-threatening risk (refers to an event in which the participant was at risk of death at the time of the event);
- Requires unplanned hospitalisation, or prolongation of existing hospitalisation (i.e. A&E attendance);
  NOTE: Hospitalisations for treatment planned prior to randomisation and hospitalisation for elective treatment of a pre-existing condition will not be considered as an SAE.
  Complications occurring during such hospitalisation will be AEs.
- Results in persistent or significant disability or incapacity;
- Is otherwise considered medically significant by clinical members of the study team.

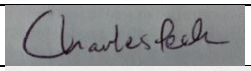
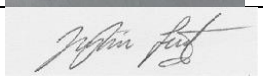
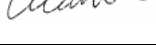
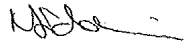
Adverse events that are deemed possibly, probably, or definitely related to participation in this study and all SAEs will be evaluated for seriousness, causality, severity and expectedness by the chief investigator and reviewed by an independent clinician/mental health specialist. All AEs/SAEs will be reviewed in terms of suspected causal relationship (e.g. unrelated, unlikely, possibly, probably, definitely) to the study intervention.

13 SAP amendment log

Amendment/addition to SAP and reason for change	New version number, name and date

14 Signatures of approval

Sign-off of the final approved version of the Statistical Analysis Plan by the principal investigator and trial statistician(s) (can also include Trial Manager/Co-ordinator)

Name	**Trial Role**	**Signature**	**Date**
Laura Mandefield	Trial Statistician		20/09/2024
Charlie Peck	Trial Statistician		23/09/2024
Justin Fenty	Senior Statistician		24/09/2024
Professor Catherine Hewitt	Statistical Oversight		24/09/2024
Jennifer Brown	Programme Manager		24/09/2024
Prof Najma Siddiqi	Chief Investigator		25/09/2024

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16 Appendices

Include detailed templates of the trial CONSORT diagram, and of tables and figures.

Figure 1: CONSORT Flow diagram

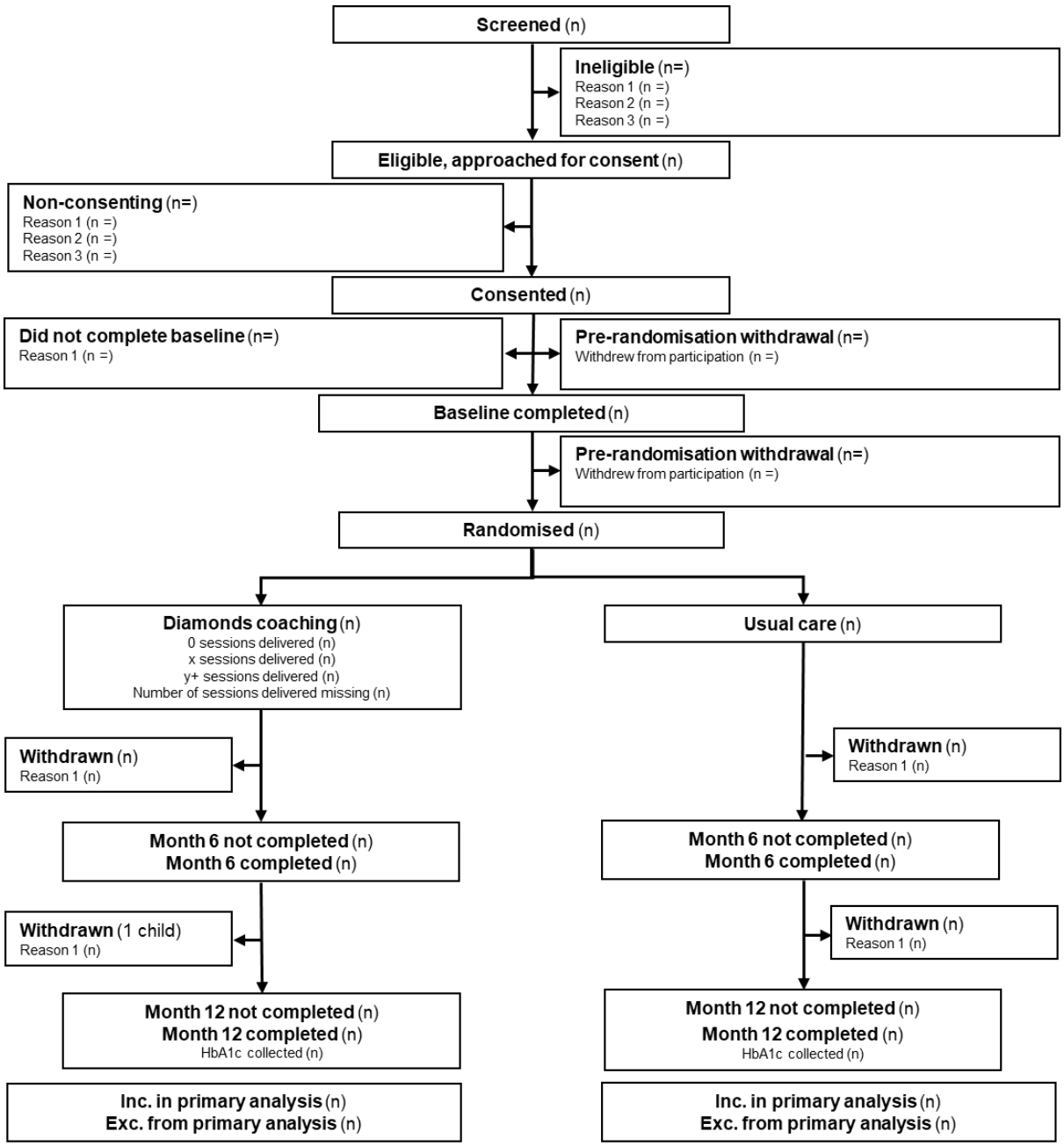

Table 1: Number of participants who met and did not meet inclusion and exclusion criteria

Inclusion Criteria	**Number of patients who met criteria*, n (%)**
Patient has a confirmed severe mental illness diagnosis of at least three-month duration.	
Is the person aged 18 years or over?	
Does the person have a diagnosis of type 2 diabetes of at least three months duration?	
Does the person have a cognitive impairment?	
Does the person have a diagnosis of any of the following: -Type 1 diabetes -Gestational diabetes -Diabetes caused by genetic defect -Diabetes secondary to pancreatitis -Diabetes secondary to a different endocrine condition	
Does the person lack capacity under the 2005 Mental Capacity Act?	
Is the person currently an inpatient?	

***potential participants may tick more than one criterion**

Table 2: Recruited participant demographics

	Intervention	**Control**	**Total**
Age			
N			
Mean (SD)			
Median (IQR)			
Not reported			
Gender, n(%)			
Male			

	Intervention	Control	Total
Female			
Non-binary			
Not reported			
Ethnicity, n (%)			
Asian Pakistani			
Black African			
Black Other			
White and Asian			
White and Black African			
White and Black Caribbean			
White British			
White Irish			
White Other			
Prefer not to say			
Not Reported			
Index of Multiple Deprivation (decile)			
1			
2			
…			
Not reported			
Type of SMI			
Time since date of SMI diagnosis			
N			
Mean (SD)			
Median (IQR)			
Not reported			
Time since date of diabetes diagnosis (years)			
N			
Mean (SD)			
Median (IQR)			
Not reported			

Table 3: Baseline outcome measures

Physical Health			Total
Height (cm)			
N			
Mean (SD)			
Median (IQR)			
Not reported			

Physical Health			Total
Weight (kg)			
N			
Mean (SD)			
Median (IQR)			
Not reported			
BMI			
N			
Mean (SD)			
Median (IQR)			
Not reported			
Waist circumference (cm)			
N			
Mean (SD)			
Median (IQR)			
Not reported			
Systolic Blood pressure			
N			
Mean (SD)			
Median (IQR)			
Not reported			
Diastolic Blood pressure			
N			
Mean (SD)			
Median (IQR)			
Not reported			
Hb1Ac			
N			
Mean (SD)			
Median (IQR)			
Not reported			
Total cholesterol			
N			
Mean (SD)			
Median (IQR)			
Not reported			
LDL cholesterol			
N			
Mean (SD)			
Median (IQR)			
Not reported			
HDL cholesterol			
N			
Mean (SD)			
Median (IQR)			
Not reported			
Haemoglobin			
N			
Mean (SD)			

Physical Health			Total
Median (IQR)			
Not reported			

	Intervention	Control	Total
IPAQ			
Low physical activity (mins/week)* n (%) Mean (SD) Median (IQR) Min, Max			
Not reported			
Moderate physical activity (mins/week) n (%) Mean (SD) Median (IQR) Min, Max			
Not reported			
Vigorous physical activity (mins/week) n (%) Mean (SD) Median (IQR) Min, Max			
Not reported			
Total physical activity (MET-mins/week)* n (%) Mean (SD) Median (IQR) Min, Max			
Not reported			
IPAQ score categories, n (%)* *Number with data* Low Moderate High			
Not reported			
Sedentary activity (mins/weekday) n (%) Mean (SD) Median (IQR) Min, Max			
Not reported			
BPRS			
BPRS total score (range 18-126)			

	Intervention	Control	Total
n (%) Mean (SD)			
Not reported			
BPRS total score Group, n (%) *Number with data* No symptoms (≤ 24) Mildly ill (25-32) Moderately ill (33-49) Markedly ill (50-69) Severely ill (70-89) Extremely ill (≥90)			
Not reported			
PHQ-9			
PHQ-9 score (range 0-27) n (%) Mean (SD)			
Not reported			
PHQ-9 Score Group, n (%) *Number with data* No Depression (≤4) Mild Depression (5-9) Moderate Depression (10-14) Moderately Severe Depression (15-19) Severe Depression (20-27)			
Not reported			
PAID-5			
PAID-5 score (range 0-20) n (%) Mean (SD)			
Not reported			
Participants in high distress, n (%) *Number with data* Not in high distress (PAID score <8) High distress (PAID score ≥8)			
Not reported			
SDSCA (scores represent number of days 0-7)			
General Diet Score (days) n (%) Mean (SD) Median (IQR)			
Not reported			
Specific Diet Score (days) n (%)			

	Intervention	Control	Total
Mean (SD) Median (IQR)			
Not reported			
Exercise Score (days) n (%) Mean (SD) Median (IQR)			
Not reported			
Blood-Glucose Testing Score (days) n (%) Mean (SD) Median (IQR)			
Not reported			
Foot Care Score (days) n (%) Mean (SD) Median (IQR)			
Not reported			
Smoked in the last 7 days, n (%) *Number with data* Yes No			
Not reported			
Number of cigarettes smoked on an average day n (% of smokers) Mean (SD)			
Not reported			
EQ5D-5L score			
n (%) Mean (SD) Median (IQR) Min, Max			

Table 4: Participant Withdrawals

Site	Allocation	Full Withdrawal	Withdrawal from intervention	Withdrawal from follow-up	Died

Table 5: Data completeness by time-points

Outcome measure	Baseline		6 Weeks		6 months	
	Control N (%)	Intervention N (%)	Control N (%)	Intervention N (%)	Control N (%)	Intervention N (%)

Table 6: Summary of intervention delivery

Intervention delivery	Total
Session duration	
N	
Mean (SD)	
Median (IQR)	
Number of sessions per participant	
N	
Mean (SD)	
Median (IQR)	
Mode of delivery, N (%)	
Remote	
Phone	
In person	
Content areas covered, N (%)	
Duration of action plans	
N	
Mean (SD)	
Median (IQR)	
Content areas covered during total intervention	
N	
Mean (SD)	
Median (IQR)	

Table 7: Primary analysis including sensitivity analyses

	Mean (SD)		Adjusted Mean Difference (95% CI, p-value)
	Intervention	**Control**	
HbA1c			
Number of participants			
12 Months			
Sensitivity analysis			
Central laboratory data only			
Missing data			
Baseline only			
Baseline and 12 months			
CACE analysis			

Table 8: Subgroup analysis

		n (%)	Adjusted Mean Difference (95% CI, p-value)
Diabetes control	High (<=58mmol/mol)		
	Low (<=58mmol/mol)		
Prescribed insulin	Yes		
	No		
Speaks Urdu	Yes		
	No		
Ethnicity	Group 1		
	….		
	Group #		

Table 9: Secondary analysis

			Adjusted Mean Difference (95% CI, p-value)
	Intervention	**Control**	
Hba1c	*Mean (SD)*	*Mean (SD)*	
Number of participants			
6 Months			
BMI			
n			
6 Months			

			Adjusted Mean Difference (95% CI, p-value)
	Intervention	**Control**	
n			
12 Months			
PHQ-9 score			
n			
6 Months			
12 Months			
BPRS score			
n			
6 Months			
n			
12 Months			
PAID-5 score			
n			
6 Months			
n			
12 Months			
	n (%)	***n (%)***	***Odds ratio (95% CI)***
Smoked within last 7 days (Y/N)			
n			
6 Months			
n			
12 Months			

Table 10: Summary of secondary outcomes

	Intervention	Control	Total
Waist circumference (cm)			
N			
Mean (SD)			
Median (IQR)			
Not reported			
Systolic Blood pressure			
N			
Mean (SD)			
Median (IQR)			
Not reported			
Diastolic Blood pressure			
N			
Mean (SD)			

Median (IQR)			
Not reported			
Total cholesterol			
N			
Mean (SD)			
Median (IQR)			
Not reported			
LDL cholesterol			
N			
Mean (SD)			
Median (IQR)			
Not reported			
HDL cholesterol			
N			
Mean (SD)			
Median (IQR)			
Not reported			
Haemoglobin			
N			
Mean (SD)			
Median (IQR)			
Not reported			

Completed for 6 and 12 month outcomes

Table 11: Accelerometer data by treatment arm

	Intervention			**Control**		
	All days (n=)	**All days (n=)**	**Weekdays (n=)**	**Weekend (n=)**	**Weekdays (n=)**	**Weekend (n=)**
Number of valid days participants wore the accelerometer n (%) Mean (SD)						
Valid wear-time (hrs) n (%) Mean (SD)						
Number of participants with the required number of valid days[a], n (%) Meets requirement						

	Intervention			Control		
	All days (n=)	**All days (n=)**	**Weekdays (n=)**	**Weekend (n=)**	**Weekdays (n=)**	**Weekend (n=)**
Does not meet requirement						
Time spent engaging in <u>light</u> activity (mins/day) n (%) Mean (SD)						
Time spent engaging in <u>moderate</u> activity (mins/day) n (%) Mean (SD)						
Time spent engaging in <u>vigorous</u> activity (mins/day) n (%) Mean (SD)						
Time spent engaging in <u>sedentary</u> activity[b] (mins/day) n (%) Mean (SD)						

Table 12: Summary of AEs by intervention arm

Event	**Intervention (n=xx)**	**Control (n=xx)**
All AEs		
Participants with at least 1 AE		
Related to the intervention?		
Definite		
Probable		
Possible		
Unlikely		
Unrelated		
Not assessable		

Table 13: Summary of SAEs by intervention arm

Event	Intervention (n=)	Control (n=)
All SAEs		
Participants with at least 1 SAE		
Related to the intervention?		
Definite		
Probable		
Possible		
Unlikely		
Unrelated		
Not assessable		