A PROTOCOL FOR A RANDOMISED CONTROLLED, SINGLE BLINDED, FEASIBILITY TRIAL OF AN ADAPTED BEHAVIOURAL ACTIVATION INTERVENTION (DiaDeM) FOR PEOPLE WITH DEPRESSION AND DIABETES IN SOUTH ASIA

University of York, UK:
Professor Catherine Hewitt (workstream lead and PI)
Professor Najma Siddiqi (PI)
Dr Gerardo Zavala
Dr Hannah Jennings
Mr Simon Walker
Prof Rowena Jaccobs
Faraz Siddiqui

University College London, UK:
Professor Edward Fottrell (workstream lead and PI)

Khyber Medical University Pakistan:
Professor Zia Ul Haq (workstream lead and PI)
Dr Saima Afaq
Dr Zara Nisar
Ms Hira Shakoor

Institute of Psychiatry, Rawalpindi, Pakistan:
Prof Asad Tamizuddin Nizami
Dr Faiza Aslam
Ms Anam Naaz

University of Leeds, UK:
Dr Ian Kellar

BADAS, Bangladesh:
Professor Kishwar Azad
Dr Naveed Ahmed
Dr Abdul Kuddus
Sanjit Kumer Shaha
Mr Ashraful Alam Anas

ARK Foundation, Bangladesh:
Professor Rumana Huque
Dr Mumtahana Nabi

SUMMARY

Title	A Protocol for a Randomised Controlled, Single Blinded, Feasibility Trial of an Adapted Behavioural Activation Intervention (DiaDeM) for People with Depression and Diabetes in South Asia.
Short Title	DiaDeM feasibility trial.
Version	V 1.2.
Date	19/02/2022
ISRCTN	75501608
Ethics Approvals	Health Sciences Research Governance Committee (HSRGC), University of York (Ref: HSRGC/2020/409/B) Diabetic Association of Bangladesh (Ref: BADAS-ERC/EC/20/00300) National Bioethics Committee Pakistan (Ref: No.4-87/NBC-578/20/ 1101) Institutional Research and Ethics Forum of Rawalpindi Medical University (Ref:242/IREF/RMU/2020) Ethics Committee of Office of Research Innovation & Commercialization (ORIC) Khyber Medical University (KMU), Pakistan on 08/10/2020 (Ref:DIR/KMU/UEC/25)
Study design	Feasibility randomised controlled trial.
Study duration	13 months: March 2022 to February 2023.
Population	Adults diagnosed with type 2 diabetes and confirmed mild, moderate or severe depression.
Setting	Two diabetes clinics in Bangladesh and four in Pakistan.
Treatment(s)	*DiaDeM Behavioural Activation intervention group:* Structured individual therapy delivered by Behavioural Activation facilitators based in diabetes services, supported by a treatment manual and participant's and facilitator's booklets, with supervision by a mental health specialist. Six, 30-40 minutes sessions over a period of 6 to 12 weeks will be offered. The sessions will be delivered either face to face or remotely according to the participant's preference. The 'optimised usual care' information leaflet will also be offered. *Control group:* Participants will receive an 'optimised usual care' information leaflet, describing depression and its treatment and details of how to access help locally.

Study aim	To test the feasibility of delivering and evaluating an adapted behavioural activation intervention among people with diabetes and depression in Bangladesh and Pakistan.
Study outcome(s)	*Primary outcomes (feasibility and acceptability of recruitment and retention):* 1. Recruitment rates, assessed as the number of participants eligible, consenting and randomised, out of those screened. 2. Reasons for ineligibility/non-participation/non-consent of participants. 3. Length of time required to achieve the required sample size. 4. Retention in the study, assessed as the number of participants randomised who are successfully followed up at 3 and 6 months. *Feasibility of intervention delivery:* 5. Retention in treatment reported as the number of sessions attended out of the total number of sessions offered. 6. Intervention fidelity of delivery of the behavioural activation intervention. *Feasibility of baseline and outcomes data collection:* 7. Data completeness at baseline and at follow-up (see table 1) a. Demographic data (baseline only). b. Health risk behaviours: tobacco use, physical activity, alcohol use (using IPAQ) c. Caseness and severity of depression symptoms, using Physical Health Questionnaire (PHQ-9). d. Caseness and severity of anxiety symptoms: Generalised Anxiety Disorder (GAD-7). e. Diabetes-related outcomes: Glycaemic control (Glycosylated haemoglobin, $HbA1_C$), diabetes distress (PAID-5), diabetes self-management activities (PDSMS, SDSCA), self-efficacy (DES-SF), history of diabetes microvascular and macrovascular complications. f. Health-related quality of life (EQ5D-5L). g. Comorbidity, self-reported. h. Blood tests: Haemoglobin level (Hb), white blood cell count (WBC), renal function tests including serum urea, serum creatinine and estimated Glomerular Filtration Rate (eGFR), lipid function test including triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), thyroid function tests including serum triiodothyronine (T3), thyroxine test (T4), thyroid-stimulating hormone (TSH), random blood sugar (RBS), and liver function test only serum Alanine Transaminase (ALT); (baseline only) i. Weight, height, BMI, waist circumference, hip circumference, waist–hip ratio, and blood pressure. j. Potential mediators (derived from the intervention logic model): Knowledge about depression/symptoms and regarding the link between behaviour and depression, intention to plan and regularly do healthy activities, beliefs about consequences. k. Changes in avoidance and activation over the course of Behavioral Activation for depression.(PAAS) *Feasibility of collecting economic data:* 8. Health care resource use, out-of-pocket payments, cost of delivering the DiaDeM intervention, economic outcomes, employment status, productivity loss and the

	opportunity cost of time. and other economic data including patient self-report using an adapted Client Service Receipt Inventory and health service data.
Number of participants	128 in total, 64 in intervention and 64 control arm
Main inclusion/ exclusion criteria	*Inclusion Criteria:* ● Adults (≥18 years old) diagnosed with type 2 diabetes, confirmed by the health care staff of the diabetes centres based on their standardized diagnostic criteria that include $HbA1_C$, clinical presentation and diabetes centre's registration record. ● Persons scoring ≥3 on Patient Health Questionnaire-2 (PHQ-2) that will be administered by the health care staff at Diabetes centre as part of depression screening and mild, moderate or severe depression confirmed if scoring ≥5 on Patient Health Questionnaire-9 (PHQ-9) and through Mini-International Neuropsychiatric Interview (MINI). ● Willing to participate ● Able to attend therapy sessions in person or remotely. *Exclusion Criteria:* ● Already receiving psychotherapy for depression. ● Lacking capacity to provide informed consent. ● Unable to take part in therapy because of cognitive impairment, or severity of mental or physical illness.
Estimated period of recruitment	3 months
Total duration of follow-up per participant	6 months
Blinding	Outcomes will be assessed by researchers blinded to allocation
Statistical methodology	The number of individuals approached, randomly assigned and participants receiving the intervention, completing the study protocol and providing baseline/outcome data will be summarised (and participants withdrawing from the intervention and reasons for withdrawal) overall, by study arm and country. A CONSORT diagram will be provided to display the flow of participants through the study. Data from the clinical outcome measures will be summarised descriptively. The recruitment rate and 95% confidence interval (CI) will be estimated.
Economic evaluation	We will test the feasibility of data collection tools required for the economic analyses of the main trial.
Sponsor	University of York.

Funder	National Institute of Health Research [Grant reference: Research & Innovation for Global Health Transformation (RIGHT) NIHR200806].
Principal Investigators	Professor Catherine Hewitt, University of York, UK Professor Edward Fottrell, University College London, UK Professor Zia Ul Haq, Khyber Medical University Pakistan Professor Najma Siddiqi, University of York, UK.

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1. INTRODUCTION

The prevalence of diabetes has been increasing across the globe, with an estimated prevalence of 10.5% (536.6 million people) in 2021, and it is projected to reach 11.3% (624.7 million) by 2030 and 12.2% (783.2 million) by 2045(1). Diabetes has strikingly affected Low and Middle Income countries (LMIC) whereby 80% of the adult population diagnosed with diabetes, lives in LMIC. (2). It is the most common non-communicable disease (NCD) in South Asia(3), with an estimated prevalence of 16.7% in Pakistan(4) and 11.4% in Bangladesh(5).

Amongst people with NCDs, there is a 2 to 3 fold increased risk of co-occurrence of depression (6,7). Depression and diabetes multimorbidity is associated with poorer health and clinical outcomes of both, negative impacts on quality of life and higher mortality rates(8–10). Depression occurring with diabetes contributes to deterioration in diabetes self-care, glycemic control, and diabetes complications(11–13).

Healthcare use and expenditure are also increased for individuals suffering from diabetes and depression compared to those presenting with diabetes alone(14). Therefore, timely diagnosis and treatment of depression are important in people with diabetes. Clinically and cost-effective screening methods and programmes should be in place to recognise depression for those with diabetes(15). For the management of depression, both pharmacological treatment as well as psychological interventions have been shown to be effective (16–18). Resource-constrained LMIC health systems require an integrated or holistic approach to the management of comorbid mental conditions with chronic illnesses especially NCDs to improve the outcomes and quality of life (19,20).

There is a dearth of certainty and evidence regarding the effectiveness and delivery of interventions in multimorbidities and there are calls for future trials globally and especially in the LMICs (21–23). Many reviews testament the effectiveness of psychological interventions for improving depression in people with diabetes (24–26). A recent update of a Cochrane review which identified 17 randomised controlled trials (RCTs) that assessed the effectiveness of interventions for people with multimorbidity, revealed small differences in clinical outcomes and health service use but showed there was an improvement in depression(27).

Behavioural activation (BA), is a simple behavioural psychotherapy approach that since its emergence in the 1970s, underwent a lot of variations over time, and has progressively secured attention and importance as an efficient treatment for depression (28–32). BA is a simple and effective psychological intervention that has been adapted for different cultures and populations(33). Its straightforward stepped activity scheduling approach is unrestrained by the complicated and stigmatizing techniques (30–32,34–36). It is less resource-intensive and can be effectively and easily administered by mental health staff or as non-mental health specialists, after brief non-intensive training (37,38).

However, there is a sparsity of trial evidence of the effectiveness of BA for treating depression in combination with chronic physical illnesses, particularly in LMICs. A recent Cochrane review assessing the efficacy and acceptability of BA for treating depression in NCDs identified two studies from the United States, one for stroke and one for breast cancer, but the results were inconclusive (39–41). However, a multicomponent intervention including BA strategies as one of its components has been shown to be effective in a recent trial in India (42). Further trial evidence of the effectiveness of BA for depression in people with diabetes is needed, particularly from LMIC.

To conduct such a trial, we first need to establish the feasibility and acceptability of BA (adapted for cultural context and for people with diabetes) and the feasibility of trial procedures.

2. STUDY AIMS

2.1. Overall aim

To test the feasibility and acceptability of an adapted behavioural activation intervention for people with diabetes and depression (which we are calling DiaDeM intervention) and the feasibility of trial procedures in Bangladesh and Pakistan.

2.2. Objectives

2.2.1. To test the feasibility and acceptability of delivering an adapted behavioural activation, DiaDeM intervention among people with diabetes and depression.
2.2.2. To test the feasibility and acceptability of carrying out a definitive full trial.

2.3.Research questions

2.3.1. Delivering the intervention

2.3.1.1. What is the feasibility and acceptability of delivering the DiaDeM intervention in people with diabetes and depression, by non-mental health specialist staff in diabetes centres?
2.3.1.2. Are adaptations needed to the DiaDeM intervention before it is evaluated in a definitive trial?
2.3.1.3. To what degree can the DiaDeM intervention be delivered as planned?

2.3.2. Recruitment and retention

2.3.2.1. What is the overall recruitment rate?
2.3.2.2. What are the retention rates i.e. the proportion of participants remaining in the study at 3 months and 6 months post-randomization?
2.3.2.3. Are proposed recruitment and randomisation procedures feasible and acceptable?

2.3.3. Identification of measures for data collection

2.3.3.1. What is the feasibility and acceptability of collecting data using the proposed tools and methods for baseline and follow-up outcome measures?
2.3.3.2. Can sites achieve >60% completion rates for PHQ-2 in routine care?

2.3.4. Testing methods of collecting service use and other economic data

What is the feasibility of collecting service use and other economic data to be used in the economic analysis of the main trial?

2.3.5. Informing the sample size of the full trial

What is the standard deviation for the primary outcome in this population (to inform the sample size for the main trial)?

3. OVERALL STUDY DESIGN

We will conduct an individually randomised controlled feasibility trial of DiaDeM with nested economic and mixed methods process evaluations.

4. FEASIBILITY TESTING

This is a parallel open-label randomised, controlled feasibility trial in which participants will be allocated 1:1 to either the DiaDeM intervention or to a control intervention.

4.1. Study groups

4.1.1. DiaDeM intervention

All participants will receive the DiaDeM intervention. Core components include:
i) A structured individual therapy, BA.

ii) Delivery by non-mental health specialist staff based in diabetes services, referred to as BA facilitators, hereafter.
iii) Supported by a treatment manual and materials, and
iv) Supervision by a mental health specialist, referred to as BA supervisors, hereafter.

BA therapy will comprise 4-6 individual sessions, over a period of 6-12 weeks. The duration of each session may vary from person to person but usually would be 30 to 40 minutes per session.

The DiaDeM intervention is designed for face-to-face delivery or to be delivered remotely (telephone or online e.g. Whatsapp, Skype, Messenger, Zoom), or in combination. It will be delivered by facilitators, using a range of materials in lay language.

BA facilitators will be selected and then trained, from non-mental health specialist staff working in diabetes services at study sites, and BA supervisors will be mental health specialists available to supervise the intervention as part of their routine work.

In addition, the 'optimised usual care' leaflet, describing depression, its treatment with details of how to access help, will also be offered to the intervention group.

4.1.2. Controls

Participants randomised to the control arm will receive optimized routine care. They will continue to receive diabetes care from the same facility and will receive verbal and written advice on accessing treatment for depression. If they are already receiving treatment, they will be advised to continue treatment or advised to seek assessment and management as per the optimized care pathway. The referral and advice to the control group will be provided by non-mental health specialist staff working at each facility. Participants in this trial arm will not have any further contact from the non-mental health specialist (for study purposes) and will continue their routine management at the diabetes centre. Control participants will also receive an 'optimised usual care' leaflet, describing depression and its treatment with details of how to access help.

4.2. Study sites and settings

The DiaDeM feasibility trial will be conducted in the following tertiary care level facility sites in Bangladesh and Pakistan:

1. BIRDEM General Hospital (Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders), Dhaka, Bangladesh.
2. Sylhet Diabetic Hospital, Sylhet, Bangladesh.
3. Sugar Hospital, Phase IV, Hayatabad, Peshawar, KPK, Pakistan.
4. District Headquarters Hospital, Kohat, KPK, Pakistan.
5. Sughra Diabetic Centre, Benazir Bhutto Hospital, Rawalpindi, Punjab, Pakistan.
6. District Headquarters hospital, Rawalpindi, Punjab, Pakistan.

4.3. Study population

The study population will comprise adults diagnosed with type 2 diabetes with confirmed mild, moderate or severe depression presenting in the outpatient departments of the study sites.

4.4. Eligibility

4.4.1. Inclusion criteria

- Adults (≥18 years old) diagnosed with type 2 diabetes confirmed by the health care staff of the diabetes centres, based on standardized diagnostic criteria including glycaemic levels measured using $HbA1_C$, clinical presentation and diabetes centres' registration record.

- Persons scoring ≥3 on the PHQ-2 scale (43), routinely administered by the healthcare staff at diabetes centres (as part of routine depression screening).
- With mild, moderate or severe depression confirmed by clinically trained researchers administering the PHQ-9 (44,45) using a cut-off score of ≥ 5, and confirmed using the depression schedule of the MINI(46).
- Willing to participate.
- Able to attend therapy sessions in person or remotely.

4.4.2. Exclusion criteria

- Already receiving psychotherapy for depression.
- Lacking capacity to provide informed consent and/or to take part in therapy because of cognitive impairment, or severity of mental or physical illness.

4.5. Sample size

In each country, we will recruit 64 participants who will be randomised to intervention or control treatments on a 1:1 basis. This will allow estimation of recruitment (50%) and follow-up rates (80%) to within a 9% and 10% margin of error. We will ensure that sufficient numbers of participants will be recruited across severity groups (mild and moderate/severe).

4.6. Eligibility assessment and recruitment

At the study sites in both Bangladesh and Pakistan, persons diagnosed with type 2 diabetes will be recruited after a two-stepped screening process. PHQ-2 will be administered during routine clinical practice. For all those persons screening positive (PHQ-2≥3), the staff at the diabetes centre will provide brief study information leaflets. Those indicating they are interested in participating will be approached by a researcher, who will take consent to be assessed further for eligibility using the PHQ-9 and MINI for those scoring above the threshold and will be provided with detailed information.

Diagnosis of depression will be confirmed by trained researchers using the PHQ-9 and by the relevant module/schedule of depression from the MINI version 6.0 (46). The MINI is a short diagnostic structured interview to explore mental disorders. It is designed to allow administration by non-specialist interviewers (47). It is available in Bengali as well as in Urdu languages. These versions are available from the developers of the MINI and have undergone a linguistic validation process including forward and backward translation. The research assistants (RAs) at each site will be trained in administering the MINI.

If a potential participant is observed to be indecisive to give consent, RAs will request contact details of the person, to contact again and re-invite.

A unique screening number will be given to every person screened and included on each screening form. Only those persons eligible to participate will be invited to the trial by providing the information sheet. Recruitments will be either face-to-face, telephone or video-call depending on the availability of the facility and convenience of the participants.

4.7. Informed written consent

As above for PHQ-9 consent, eligible participants will receive a detailed information sheet written in local languages and complying with local ethics committee requirements. The information sheet will introduce the research, its methods and assessment procedures and also the potential benefits and risks of participation. Eligible participants will be provided an opportunity to read the information sheet; for those with literacy problems, the RAs will read it aloud. Consent will then be sought. Those willing to participate will be provided with written consent forms. Participants can complete them immediately or take them home to discuss with family. They will be asked to contact/call the research team within the next 48 hours if they wish to participate. Otherwise, a research assistant will call them on the third day to inquire about their decision. Signatures of the participants will be taken, while for illiterate persons thumb impressions

will be taken. Those unable to provide a signature will be requested to indicate their consent with a thumbprint.

The process of obtaining informed consent will be changed from face to face mode to remote mode in case of any restrictions due to Covid 19 pandemic and remote recruitments. The verbal consent provided through telephone or video call will be recorded contemporaneously and a note added to the consent form. Where possible, a PDF will be sent to participants.

Once informed written consent is acquired, the research assistant will assign a unique patient identifier (ID) to the participant. The patient's consent status and contact information will be written into a participant log and also entered into an electronic database. This database will be different from the outcome measurements tools.

Participants will be informed that they can withdraw consent and leave the trial at any point in time, without giving a reason and by informing any of the research team or the staff at the Diabetes centre. If the withdrawing participant will be willing to give contact details for any future research purposes, their contact details will be saved. The withdrawing participant will be assured that no further data will be collected after withdrawal. The data collected up until the day of withdrawal will be maintained and used in the analysis unless otherwise instructed.

4.8. Reimbursement

The amount of reimbursement will be in concordance with the specifications by the local/National Ethics Review Boards. The participants will be paid an amount for reimbursement of the actual travel cost and the time spent for each intervention session as well as for every follow-up visit. Those who will be interviewed for the process evaluation (PE) will also be paid the actual travel cost and the time spent for each interview. The participants of the feasibility trial will receive PKR 500 in Pakistan and BDT 600 in Bangladesh for each follow-up visit/intervention session, whether face to face or remotely delivered, whereas those who will be interviewed for the process evaluation will be paid PKR 1000 in Pakistan and BDT 600 in Bangladesh.

4.9. Randomisation procedure

Eligible participants who consent will be allocated a unique study ID and randomly assigned to one of the trial arms using a computer-generated blocked stratified (by country) randomisation sequence created using Stata version 15 (or later), with an allocation ratio of 1:1. A statistician based at the University of York, who is not involved in the recruitment of trial participants, will generate the randomisation sequence and online randomization will be done at each trial site to randomly allocate participants to the trial arms, after a participant has provided written informed consent and completed a baseline assessment. Allocation will be recorded on the participant record.

4.11. Blinding

Outcomes will be assessed by researchers blinded to allocation. The trial manager will set up a log of the participants recruited and the RAs who recruited that participant and the RAs who will do the follow-up assessments. It will be strictly ensured that the RAs who will recruit, randomise and allocate a participant to the trial will only complete the baseline assessment for that patient. They will not complete the 3 months and 6 months follow-up CRFs of the study participants which will be undertaken by another RA at the same site.

4.12. Study outcomes

The study will focus on the following primary (feasibility and acceptability) and secondary outcomes:

4.12.1. Primary Outcomes (feasibility and acceptability of recruitment and retention)

4.12.1.1. Recruitment rates, assessed as the number of participants eligible, consenting and randomised, out of those screened.

4.12.1.2. Reasons for ineligibility/non-participation/non-consent of participants.
4.12.1.3. Length of time required to achieve the required sample size.
4.12.1.4. Retention in the study, assessed as the number of participants randomised who are successfully followed up at 3 and 6 months.

4.12.2. Primary outcomes (feasibility of intervention delivery)

4.12.2.1. Retention in treatment reported as the number of sessions attended out of the total number of sessions offered.
4.12.2.2. Intervention fidelity of delivery of the behavioural activation intervention.

4.12.3. Secondary outcomes (feasibility of baseline and outcomes data collection)

4.12.3.1.Data completeness at baseline and at follow-up

4.13. Baseline and follow-up data collection

We will collect proposed baseline and follow-up measures to test feasibility and burden (time, resources, missing data).

At the baseline, in addition to demographics and socioeconomic status, we plan to record weight, height, Body Mass Index (BMI), waist circumference, hip circumference, waist–hip ratio, smoking status, blood pressure, comorbidities, depression caseness and severity (44), anxiety (48), diabetes distress (49,50), self-efficacy (51,52), diabetes self-management activities (53,54), physical activity (55) diabetes microvascular and macrovascular complications, medication and health-related quality of life (56). We will also investigate blood tests (glycosylated haemoglobin ($HbA1_c$), haemoglobin level (Hb) and white blood cell count (WBC), renal function tests including serum urea, serum creatinine and estimated Glomerular Filtration Rate (eGFR), lipid function test including triglycerides, total cholesterol, high-Density Lipoprotein cholesterol (HDL), low-Density Lipoprotein cholesterol (LDL), Thyroid function tests including serum triiodothyronine (T3), Thyroxine test (T4), Thyroid-stimulating hormone (TSH), Random blood sugar (RBS), and Liver function test including only serum Alanine Transaminase (ALT).

Following randomisation and baseline data collection, participants in each arm will be followed up at three months. Only severity of depression, anxiety, health-related quality of life and HbA1c will be assessed.

At six months post-randomisation, reassessment of depression caseness and severity, anxiety, self-efficacy, diabetes self-management activities (53,54), physical activity (55), diabetes microvascular and macrovascular complications, medication, health-related quality of life (56), and glycosylated haemoglobin ($HbA1_c$) will be recorded. Potential mediators (derived from the intervention logic model): Knowledge about depression/symptoms and regarding the link between behaviour and depression, intention to plan and regularly do healthy activities, beliefs about consequences; will also be collected.

Data will be measured and collected from participants and carers face-to-face (or remotely in case of Covid-19 restrictions) at baseline, three and six months as displayed in table 1. The baseline and follow-up Case Report Form's (CRF) data and anthropometric measurements will be entered directly into an online survey tool (Qualtrics) using tablets at each site. However, for the blood test reports the data will be first entered into a paper format or blood reports log since the reports will include identifiable information (name, age and gender of the participant). From the log, the RAs will shift the information to the qualtrics data sheet mentioning only the study ID and the results.

4.13.1. Demographic data

The demographic profile of recruited participants will be assessed only at the baseline and will be adapted from the WHO STEPwise approach to Surveillance (STEPs) instrument, Version 3.2(57) to collect information about participants' age, sex, education and marital status. STEPs is a standardized tool that

facilitates comparisons within the country or across countries and has already been translated, used and validated in the general population in Bangladesh (58) and Pakistan(59).

4.13.2. Caseness and severity of depression

PHQ-9 (44) will be used to measure depressive symptoms and their severity at baseline, 3 months and 6 months follow-up. This nine-item questionnaire is scored from 0 to 27, and a higher score indicates more severe depressive symptoms.

4.13.4. Anxiety

The generalized anxiety disorder 7 item scale (GAD-7)(48,60) will be administered at baseline, 3 months and 6 months follow-up, to measure the severity of generalised anxiety disorder. It comprises seven questions and each question has been assigned the score of 0, 1, 2, and 3, concordant with the respective responses of 'not at all', 'several days', 'more than half the days', and 'nearly every day'. The total sum of the scores represents the final score (maximum attainable score is 21) with the cut off points of 5 for mild anxiety, 10 for moderate and 15 for severe anxiety.

4.13.5. Diabetes-related distress

The tool, Problem Areas in Diabetes Scale-5 (PAID-5), will be administered that consist of 5 items that measure Diabetes-related emotional distress with a focus on various common problems and feelings associated with living with diabetes(50). It determines the effect on the patients, on a scale of 0 (not a problem) to 4 (serious problem). The scores when summed up and standardized indicate levels of diabetes-related distress whereby scores ≥8 indicate diabetes-related distress.

4.13.6. Diabetes-related self-efficacy and self-management

An eight-item version of the Diabetes Empowerment Scale-Short form (DES-SF)(51) will be used to measure overall diabetes-related psychosocial self-efficacy. However, for the assessment of self-care, the Perceived Diabetes Self Management Scale (PDSMS)(52) will be administered. PDSMS comprises 8 items for which the responses may range from 1 (Strongly Disagree) to 5(Strongly Agree) where 4 items are reverse scored. The total PDSMS score may range from 8 to a maximum attainable score of 40, where higher scores indicate higher confidence in self-management.

Diabetes-related self-management activities will also be specifically determined through the Summary of self-care diabetes activities scale (SDSCA) that includes 11 items that determine different diabetes self-management activities pertinent to general diet, specific diet, exercise, blood-glucose testing, foot care and smoking (53).

4.13.7. Diabetes-related microvascular and macrovascular complications

The complications of diabetes will be assessed based on the self-reporting (i.e. history based on being informed by a health care provider) of the participants at baseline as well as 6-month follow-up. For confirmation of any previous episode or existent macrovascular complications (coronary artery disease, peripheral arterial disease, and stroke) as well as microvascular complications (diabetic nephropathy, neuropathy and retinopathy) of diabetes, related questions will be inquired as part of CRF, at baseline and at 6-month follow-up.

4.13.8. Physical activity

The International Physical Activity Questionnaires (IPAQ) short version (9 items), will be applied to determine the physical activity of the participants at baseline(55). The tool acquires information related to activities at four intensity levels for the last 7 days, i.e. 1) vigorous-intensity activity such as aerobics, 2) moderate-intensity activity e.g. leisure cycling, 3) walking, and 4) sitting.

4.13.9. Quality of life

Euroqol's instrument EQ-5D-5L will be administered to measure health-related quality of life (HRQoL). EQ-5D is a standardized measure of health status developed by the EuroQol Group. It provides a simple, generic measure of health for clinical and economic appraisal, where health is characterised on five dimensions; mobility, self-care, ability to undertake usual activities, pain/discomfort, anxiety/ depression(61). Patients' subjective evaluation of their health state based on a visual analogue scale (EQ-5D-VAS) is also included in the scale, ranging from "0 (representing worst imaginable health state) to the maximum attainable value of 100 (indicating best imaginable health state).

4.13.11. Physical body measurements

Physical body measurements will be measured by RAs, according to the WHO STEPS surveillance manual(57), at baseline and at 6-month follow-up, including the following:

1. Weight

The weight of the participant will be measured, in the unit "kilograms" using a portable digital weighing scale placed on a firm flat surface. Two consecutive readings to two decimal places will be recorded into CRF. Participants will be advised to get the weight recorded by mounting on a scale with light clothing and without footwear and socks.

2. Height

A portable height measuring board without footwear and headgear will be used to measure the height of the participants, in the unit "centimetres". Duplicate readings, to a precision of 0.1 cm will be recorded into the CRFs.

3. Body Mass Index

Body Mass Index (BMI) measurement is reflective of the nutritional status in adults. It is defined as a person's weight in kilograms divided by the square of the person's height in metres (kg/m2). The RAs will enter the height and weight in the BMI calculator in their tablets that will be computed for the participants that will be recorded in the CRFs.

4. Waist circumferences:

Waist circumference will be measured, using a flexible anthropometric tape, in the unit "centimetres". It will be measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest (hip bone), with the arms relaxed at the sides when the participant will exhale fully at the end of expiration. Two consecutive readings will be taken to a precision of 0.1 cm.

5. Hip circumference:

Hip circumference will be measured, using a flexible anthropometric tape, in the unit "centimetres". It will be measured by wrapping the tape around the widest portion of the buttocks, with the tape parallel to the floor. Two consecutive readings will be taken to a precision of 0.1 cm.

6. Waist-hip ratio: The waist-hip ratio is an indicator or measure of health, the risk of developing serious health conditions and obesity. The waist-hip ratio is calculated as waist measurement divided by hip measurement. The RAs will enter the height and weight in the hip-waist ratio calculator in their tablets that will be computed for the participants that will be recorded in the CRFs.

7. Blood pressure

Blood pressure (BP) and Heart/pulse rate will be measured using an automated blood pressure measuring instrument (OMRON®). Three consecutive readings (each with 3 minutes gap) from the same wrist/elbow will be taken using the same device and recorded in CRFs. Before taking the measurements, the

participant must be comfortable and seated. The study participant will be informed about the readings only after the whole process is completed. The measurements will be taken from the left wrist/arm but in case there will be a stroke of that side/limb then it will be measured from the right side

4.13.12. Tobacco & alcohol Use

Health risk behaviour questions adapted from the STEPs tobacco and smokeless tobacco modules (core module and a few questions from expanded module)(57) will be used to identify current tobacco users of smoked or used smokeless tobacco in the past 30 days. Moreover, questions related to alcohol use will also be used to assess the alcohol consumption status over the last 12 months.

4.13.13. Measures of potential mediators

Measures of potential mediators including; knowledge, intention and beliefs about consequences, derived from the intervention logic model will also be collected. Specific questions developed will be asked to track changes in behaviour and patient activation using the PREMIUM Abbreviated Activation Scale (PAAS) (62), a 5-item scale, adapted from the Behavioural Activation for Depression Scale (BADS-SF) (63). PAAS includes five indicators of behavioural activation assessed on a scale of 0 ('not at all) to 5 ('yes, completely') for a total continuous score of 25.

4.13.14. Comorbidities and medications

The self-report by the participants, adapted by the STEPs module for NCDs (64) will be used for confirmation of any medically-diagnosed history of raised blood pressure, heart disease, hypercholesterolemia, stroke, lung diseases and treatment advised by a health worker for these diseases will be collected. Self-report of any medically-diagnosed history of communicable/infectious diseases e.g. hepatitis B, C, Dengue, COVID-19, Tuberculosis, Malaria, Chikungunya and HIV will be recorded.

4.13.15. Blood tests

For all the consenting participants a blood sample (5-6 ml) will be drawn at the study site after recruitment at baseline for the biochemical assessment, following a standardized protocol for each study site for the tests including Hb, WBC, renal function tests including serum urea, serum creatinine and eGFR, lipid function test including triglycerides, total cholesterol, HDL, LDL, Thyroid function tests including T3, T4, TSH, RBS and Liver function test including only serum ALT. However, at the 3rd month as well as on 6th-month follow-up (only 2 ml blood) will be drawn from the consenting participants for the Glycated haemoglobin (HbA1c) test. All the tests will be performed from standardized laboratories for each site.

Table 1. Outcomes with scales and measurement schedule

OUTCOMES	Scales	Baseline	Month 3	Month 6
Demographics	Adapted from WHO STEPwise approach to Surveillance (STEPs) instrument, Version 3.2	X		
Physical body measurements (Weight, height, Body Mass Index, waist circumference, hip circumference, waist–	WHO STEPS surveillance manual for measurements	X		X

OUTCOMES	Scales	Baseline	Month 3	Month 6
hip ratio, and blood pressure)				
Blood tests: Haemoglobin level (Hb), white blood cell count (WBC), renal function tests including serum urea, serum creatinine and estimated Glomerular Filtration Rate (eGFR), lipid function test including triglycerides, total cholesterol, high-Density Lipoprotein cholesterol (HDL), low-Density Lipoprotein cholesterol (LDL), Thyroid function tests including (serum triiodothyronine (T3), Thyroxine test (T4), Thyroid-stimulating hormone (TSH), Random blood sugar (RBS), and Liver function test including only serum Alanine Transaminase.		X		
Blood test: Glycosylated haemoglobin (HbA1c)		X	X	X
Comorbidities	Adapted from the STEPs module for non-communicable diseases and communicable/infectious diseases	X		X
Caseness and severity of depression	Physical health questionnaire (PHQ-9)	X	X	X
Anxiety	Generalized Depression and Anxiety (GAD-7)	X		X

OUTCOMES	Scales	Baseline	Month 3	Month 6
Diabetes distress	Problem Areas in Diabetes Scale - 5 (PAID-5)	X		X
Self-efficacy	Diabetes Empowerment Scale-Short form (DES-SF)	X		X
Diabetes self-management and self-care	Perceived Diabetes Self-Management Scale (PDSMS) Summary of self-care diabetes activities scale (SDSCA)	X		X
Health risk behaviour: Physical activity	International Physical Activity Questionnaires (IPAQ, (short version)	X		X
Health risk behaviour: Tobacco use	An adapted version of The STEPs tobacco and smokeless tobacco modules.	X		X
Health risk behaviour: Alcohol use	Adapted questions of the STEPs alcohol module.	X		X
Diabetes complications	A set of questions in DiaDeM CRF on Diabetes-related microvascular and macrovascular complications.	X		X
Health-related quality of life (HRQoL)	EQ5D-5L including visual analogue scale (EQ-5d-VAS)	X	X	X
Mediators	A set of questions in DiaDeM-CRF for potential mediators including; Knowledge about depression/symptoms and regarding the link between behaviour and depression, intention to plan and regularly do healthy activities, beliefs about consequences, derived from the intervention logic model	X	X	X

OUTCOMES	Scales	Baseline	Month 3	Month 6
Changes in avoidance and activation over the course of Behavioral Activation for depression	PREMIUM Abbreviated Activation Scale (PAAS)	X	X	X
Economic outcomes: 1. Employment Status 2. Household status 3. Productivity Loss (income and days (hours) of work lost) 4. Out-Of-Pocket Payments (OOP) 5. Opportunity Cost of Time (average wage and time) 6. Borrowing / Selling Assets 7. Household earnings and Expenditure 8. Catastrophic Health Spending (OOP as % of household expenditure)	Set of questions related to economics outcomes in DiaDeM CRF adapted from Asset index questionnaire	X		X
Health care resource use	Modified client service receipt Inventory (CSRI)	X		X
Medication	Modified client service receipt Inventory (CSRI)	X		X

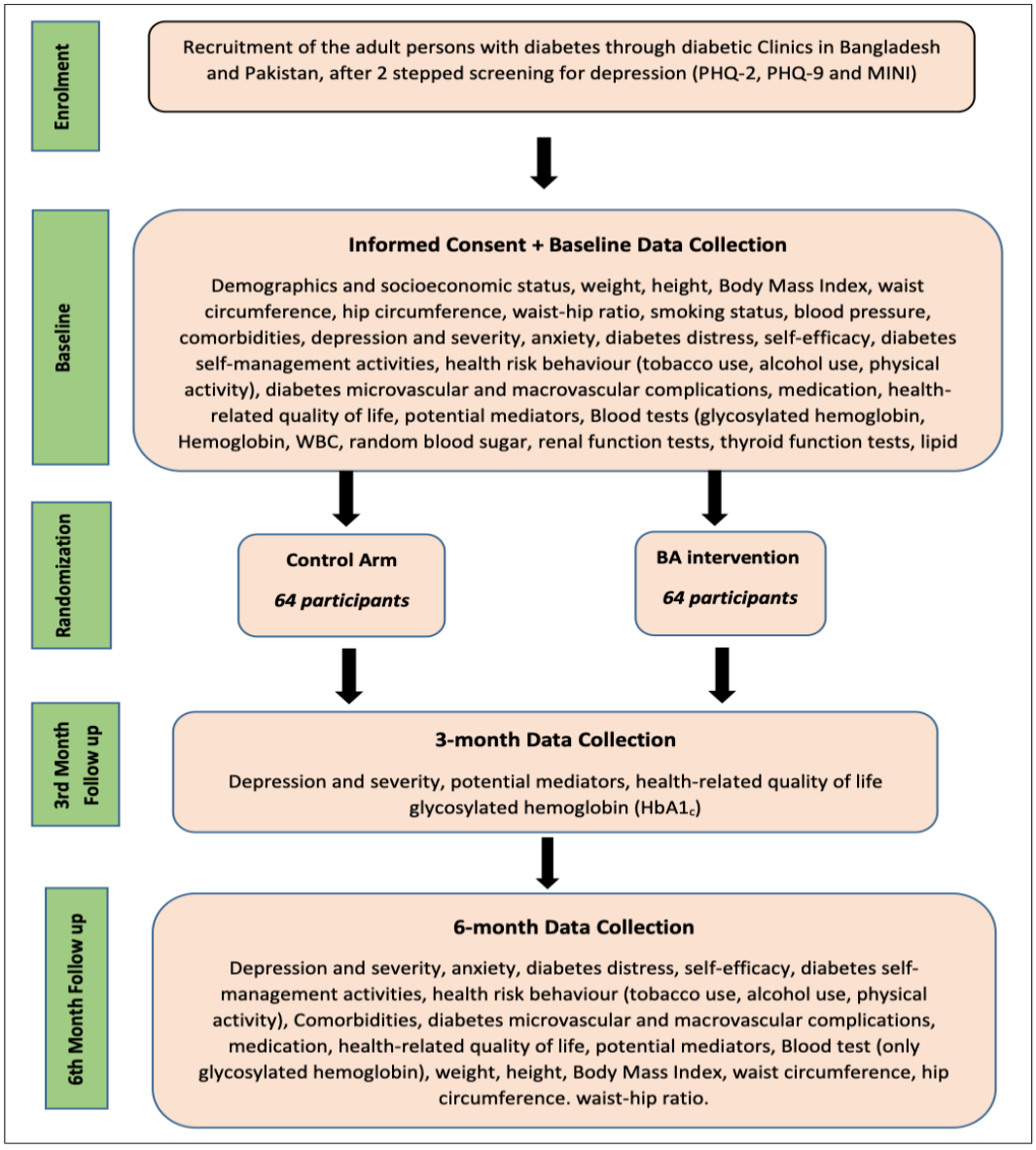
4.14. Data collection and entry

RAs recruited for the DiaDeM programme at six study sites in Bangladesh and Pakistan will screen, recruit and randomise participants, and collect baseline information. The RAs who will collect information for three months and six months follow-ups for an individual participant shall be different from those who will recruit, randomize and collect baseline information to ensure blinding. Apart from being good clinical practice (GCP) certified, the RAs will receive one week's training on trial procedures including taking informed consent, administering and completing the questionnaires/scales, recording and reporting the data, in hard copies as well as electronically in tablets, qualtrics and in all study logs. They will also be trained on ethical issues such as autonomy of individual participants on making decisions about participation, freedom to withdraw from the trial without giving any reason or consequence, privacy, confidentiality, anonymity etc. The staff involved in the trial will be trained on data protection processes. The staff will be strictly monitored to ensure compliance with privacy standards.

Data will be entered in paper format for the screening and blood test reports whereas the CRFs will be entered directly into an online survey tool (Qualtrics), a secure and password-protected resource available at the University of York. Collected data will be stored on a central database server.

The trial scheme diagram is given below:

Figure 1. Trial Flow Diagram



4.15.Statistical analysis

The following outcomes will be calculated: number of eligible patients; the proportion of eligible patients approached for consent; the proportion of eligible patients not approached and reasons why; the proportion of patients approached who provide consent; the proportion of patients approached who do not provide consent; the proportion of patients providing consent who are randomised; the proportion

of patients randomised who do not receive the randomly allocated treatment; the proportion of patients dropping out between randomisation and follow-up. A CONSORT diagram will be provided to display the flow of participants through the study. Data from the clinical outcome measures will be summarized descriptively by study arm and by severity (mild and moderate/severe): continuous data using mean, standard deviation, median and 25th and 75th percentiles; categorical data using a number of events and percentages. The recruitment rate and 95% confidence interval (CI) will be estimated. Completion rates of all the outcome measures will be reported by the study arm and by severity (mild and moderate/severe). The number of sessions attended and completed will also be reported.

5. PROCESS EVALUATION

A mixed-methods process evaluation will be embedded within the feasibility trial, focusing on what was delivered, how the delivery was achieved and how context might affect the delivery of the intervention in order to inform plans for the full trial and future scale-up. The process evaluation will follow the Medical Research Council guidance for process evaluation. (65)

Quantitative data on attendance, drop-out and delivery will be gathered as part of the feasibility trial and will be important in assessing the dose, reach and delivery of the intervention. Questions about the mediators identified in the logic model (Knowledge about depression/symptoms and regarding the link between behaviour and depression, intention to plan and regularly do healthy activities, beliefs about consequences, derived from the intervention logic model) will be collected at baseline and follow-up (table 1). Quantitative data on delivery and receipt of intervention components will be collected(65–68) checking against adherence criteria, using a pre-designed proforma or checklist which will check the extent to which components of the intervention have been delivered and patient responsiveness. Random sessions will be recorded with consent and researchers will be able to complete the proforma accordingly, this will provide information on the fidelity of the intervention and patient receptiveness.

Semi-structured interviews and possibly focus groups will be conducted in each site with patients, facilitators, supervisors and managers (approximately N=12 patients; N=12 facilitators; N=8 managers/supervisors) immediately following the intervention. The interviews may include storytelling techniques and/or photovoice to facilitate discussion. The qualitative data will explore experiences of intervention delivery and acceptability, identify any barriers and drivers to delivery including contextual factors such as the health facility environment or any other factors that may affect delivery and implementation. Unintended consequences of the intervention, mechanisms of change, perceptions on task shifting and staff training needs will also be explored during the different interviews. The process evaluation will help us understand how the intervention is implemented in context, how the intervention is received (acceptability), components of the intervention that work well and those that do not. This information will help us to adapt the intervention further for the full trial.

To support the quality of reporting and assessment of intervention fidelity, a description of the core components of an intervention is required, (65) Informed by adherence criteria (68) developed during BA development and adaptation phase and the feasibility study, we will develop a framework to measure adherence, exposure, delivery and participant responsiveness for use in the definitive trial.

6. ECONOMIC EVALUATION

We will test methods of collecting service use and other economic data for the economic analysis of the trial (WS4). Methods to be considered include patient self-report using an adapted Client Service Receipt Inventory (66) and health services data. We will check the appropriateness and the completeness of the questions. DiaDeM Resource use questionnaire (Modified client service receipt inventory CSRI) will be used for health care resource use and medications for the last six months period. Control variables

(household and housing information, asset index, education, ethnicity, marital status, rural/urban setting and clinical information (complications and comorbidities) will be used for the economic modelling

7. DATA MANAGEMENT

Data during the feasibility trial and its nested mixed process evaluation will be collected through researcher-administered interviews, focus groups, face-to-face assessments and observations. For process evaluation and fidelity assessment of intervention delivery, some intervention sessions will be audio-recorded, with consent. The focus group discussions (FDGs) will also be audio-recorded. The written notes taken during the FGDs by the note taker will also be in hard copies. The screening forms, consent forms and blood reports will also be captured as hard copies. All baseline and outcome data in the form of the CRFs will be captured electronically via tablets.

Qualitative interviews will be transcribed in the language of the interview and anonymized but linked with the trial ID before translation for analysis. Digital recordings of the interviews will be stored in a secure, password-protected folder. Once the analysis of the interviews will be completed all the recorded versions will be erased from the digital recorders.

The researchers will ensure the anonymity and confidentiality of the participants, restricting any kind of access to non-authorized persons. Participants will be assigned unique study IDs which will be used for all tools and records so that no identifiable information is accessible to non-authorized persons. Every identifiable information of the participants will be stored at each study site securely; electronic records will be kept under password protection and hard copies will be stored in locked filing cabinets.

Encrypted data transfer between the study sites and the University of York will be via secure Drop-off services available through the University of York. All files transported in this manner should be encrypted as zip files using a strong password consisting of at least 8 characters with numbers, a mix of letters in lower and upper case, and punctuation or other symbols. Data received through this method should only be accessed on desktop computers or laptops which are connected to an encrypted server.

For non-sensitive or non-confidential data, researchers should share the data through the DiaDeM team drive on the Google Drive cloud-based storage platform, or through the University of York drop off service (https://dropoff.york.ac.uk/).

In accordance with the University of York Research Data Management Policy, all anonymised research data, which underpin published results or have a long-term value will be retained for 10 years after the completion of activities. Upon completion of the DiaDeM activities, all non-anonymised data will be destroyed.

8. DATA MONITORING

Data will be monitored for quality and completeness by a delegated trial manager at the study sites, followed by a second check by the study data lead at the University of York using verification, validation and checking processes. The data management policy of DiaDeM formulated under the guidance of the University of York Trials Unit's guidance regarding processes for data monitoring will be followed by all the research team.

Data will be reported to the Independent Trial Steering Committee (ITSC) and Data Monitoring and Ethics Committee (DMEC) as required.

9. ETHICAL CONSIDERATIONS

Formal ethical approvals have been acquired from the Health Sciences Research Governance Committee (HSRGC), University of York (Ref: HSRGC/2020/409/B), Diabetic Association of Bangladesh (Ref: BADAS-ERC/EC/20/00300), National Bioethics Committee Pakistan (Ref: No.4-87/NBC-578/20/ 1101), Institutional Research and Ethics Forum of Rawalpindi Medical University (Ref:242/IREF/RMU/2020) and Ethics Committee of Office of Research Innovation & Commercialization (ORIC), Khyber Medical University (KMU), Pakistan on 08/10/2020. (Ref: DIR/KMU/UEC/25).

The local Principal Investigator from each study site will be responsible for ensuring that all ethical principles are strictly followed and also ensuring that the study procedures and protocols are being stringently adhered to. They will be responsible for the correspondence with the local ethics bodies and to submit applications for the approval of extensions and amendments in the protocol. The study will follow international standards for the ethical conduct of research and comply with the governance regulations and requirements in force at each site and country.

The study will adhere to the fundamental principles of human rights and dignity laid down in the Declaration of Helsinki. Study procedures will comply with legislation and guidance for good practise governing the participation in research of people lacking capacity as set out in the Mental Health Act (UK) 2005.

Written informed consent, the anonymity of participants and the right of withdrawal will be followed by the research teams. The reports of the biochemical blood tests and findings of the physical measurements will be shared with the participants. For the participants, who screen positive on tests for depression or anxiety, routine usual care pathways and referral systems will be followed. In case of any comorbidity detected during the study based on the biochemical assessment or any other screening tests/scales, they will be referred to the relevant medical department, as indicated. If the answer to question 9 of the PHQ-9 scale indicates a risk of self-harm, the suicide risk pathway developed for each study site will be followed.

10. ADVERSE EVENTS

All the specific procedures and guidelines regarding the adverse event assessment, reporting and notifications as given below will be followed:

10.1. Description of potential adverse events

There is no pharmacological intervention involved and the behavioral activation also poses no risk since it will consist of only motivational support. Therefore, it is improbable that any adverse events (AEs) would be related to the context or delivery of the intervention. There are very low risks related to the study procedures like drawing of the blood samples, taking physical measurements and administration of scales, inquiring about the lifestyles, risk, mental and physical health or their management, etc.

However, any diabetes emergencies like hypoglycemia, diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) deterioration of renal function leading to chronic kidney diseases (CKD) in known renal disease patients, serious diabetes complications like angina, myocardial infarction, stroke, transient Ischemic attacks, diabetic foot, gangrene, limb, foot or toe amputations will be included in the list of potential AEs.

10.2. Adverse events exemptions

AEs will not include the following:

- Medical or surgical procedures, other than reported in the potential AEs.

- A pre-existing disease or a condition present before inclusion in the study (i.e. a disorder present and reported at the baseline that does not worsen
- Hospitalisations where no untoward or unintended response has occurred, e.g., elective cosmetic surgery, social admissions.
- Adverse events or signs and symptoms of any medication.

10.3. Adverse event monitoring

AEs will be assessed not only by the non-mental health specialists but also by the consulting clinical staff of the diabetes centre, at each contact/visit/session with the study participant, irrespective of the trial arm, in accordance with the adverse AE review checklist. They will immediately inform the RAs about any observed AEs and or those reported by the study participant, who will record them and their potential association with study interventions or procedures will also be determined. Serious adverse events will be defined according to International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use-Good Clinical Practice (ICH GCP) and will be reported to the respective country coordinating centres according to the agreed timelines.

10.4. Adverse event reporting and notifications

Expected AE/SAEs: Not Reportable

1. Poor control of blood glucose levels
2. Hypoglycemia which is self-treated and not severe
3. Rising serum creatinine levels/worsening kidney function
4. Raised liver enzyme ALT levels.
5. Development of less serious/non-debilitating diabetes complications- retinopathy, neuropathy, diabetic foot.

Expected AEs/SAEs: Standard Reporting

1. Diabetes emergencies such as repeated hypoglycemia, hypoglycemia leading to hospitalization/unconsciousness, diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS)
2. Deterioration of renal function leading to chronic kidney diseases (CKD) or worsening of stages of CKD in patients who initially had a diagnosis of renal disease at recruitment.
3. More serious complications of diabetes leading to heart disease (angina, MI), stroke, TIAs, diabetic foot leading to gangrene/ limb amputations.

Unexpected and Related SAEs

These events will require Expedited Reporting. All unexpected SAEs judged to be related to the trial, occurring from the date of the consent up to study end must be recorded on the Related/Unexpected Serious Adverse Event Form and sent to the Programme Manager. The original form should also be posted/emailed to the University of York Trials Unit in real-time and a copy retained on site. For each Related/Unexpected SAE the following information will be collected:

- Date of SAE
- Full details in medical terms with a diagnosis, if possible
- Duration (start and end dates; times, if applicable)
- Action taken
- Outcome

Any follow-up information should be sent to the University of York Trials unit as soon as it is available. Events will be followed up until the event has been resolved or a final outcome has been reached.

All Unexpected/Related SAEs will be reviewed by the Chief Investigator and subject to expedited reporting to the Sponsor and the main REC by the Programme Manager on behalf of the Chief Investigator within 15 days.

Participants with SAEs must be followed up until clinical recovery is complete (including laboratory results returning to normal or baseline if relevant), or until the event has stabilised with proper information entered in the 'Follow-up report'

In all the reports the personal profile of the participant must not be revealed and only study ID, age and initials will be mentioned. Each study site staff will follow their institution's procedure for local notification and as per the guidelines of their local Research Ethics Committees Boards.

11. GUIDANCE FOR STOPPING THE TRIAL

The study will be stopped, as guided by the International Trial Steering Committee (ITSC) and Data Monitoring and Ethics Committee (DMEC), if:

- Any new literature indicates substantial evidence applicable to this research question in terms of benefit, futility or side effects.
- The occurrence of frequent AEs indicates that a review of the study protocol is required.
- There is any risk to the study participants and the research staff associated with the COVID-19 pandemic.

12. STUDY MANAGEMENT STRUCTURE

12.1. Study management group

The Study Management Group (SMG) includes the principal investigators, site investigators, co-investigators, trial managers, statisticians and PMG members and will supervise the planning and delivery of the project. They will monitor the methods, processes and their implementation by overseeing the trial managers, Research Fellows and researcher fellows. The SMG and other local research team members of the sites will also contribute to the write-up and dissemination of findings. The SMG will comprise of the following investigators from various collaborating organizations:

University of York, UK:
Professor Catherine Hewitt (workstream lead and PI)
Professor Najma Siddiqi (PI)
Dr Gerardo Zavala
Dr Hannah Jennings (York)
Mr Simon Walker
Prof Rowena Jaccobs
Faraz Siddiqui

University College London, UK:
Dr Edward Fottrell (workstream lead and PI)

Khyber Medical University Pakistan:
Professor Zia Ul Haq (workstream lead and PI)
Dr Saima Afaq
Zara Nisar

Institute of Psychiatry, Rawalpindi, Pakistan:
Prof Asad Tamizuddin Nizami

Dr Faiza Aslam
Ms Anam Naaz

University of Leeds, UK:
Dr Ian Kellar

BADAS, Bangladesh:
Professor Kishwar Azad
Dr Naveed Ahmed
Dr Abdul Kuddus
Sanjit Kumer Shaha
Mr Ashraful Alam Anas

ARK Foundation, Bangladesh :
Professor Rumana Huque
Sushama Kannan
Akber Kabir

12.2. Independent Trial Steering Committee (ITSC)

The Independent Trial Steering Committee (ITSC) for the feasibility trial will include an independent chair, independent statistician and at least two other independent members. Members of the DiaDeM programme steering committee will act as the ITSC members. The ITSC will meet at least twice during the feasibility trial, but the frequency may vary as per the committee's decision. The committee will provide independent oversight and supervision of the trial to ensure that the protocol of the feasibility trial is strictly adhered to according to the protocol and ethical guidelines. If required, members may be contacted for any urgent advice through email or phone.

12.3. Independent Data Monitoring and Ethics Committee (DMEC)

An Independent Data Monitoring and Ethics Committee (DMEC) for the feasibility trial will comprise 3-5 members who will safeguard the scientific integrity, ensuring estimation of the risk-benefit ratio. The DMEC will decide the frequency of their meetings before and during the feasibility trial to review the progress of the feasibility trial and the data. They will conduct an interim appraisal of recruitment status, quality and completeness of data, evidence of AEs and main endpoints apart from ensuring an independent assessment to assure that the study participants are not exposed to unnecessary risks as a consequence of their trial participation.

12.4. Community Advisory Panels (CAP)

Four Community Advisory panels (CAP) have been convened in Rawalpindi, Peshawar, Dhaka and Sylhet that meet every 6-months CAPs will ensure the programme remains focused on addressing the prioritised needs of the community and planned activities are ethically sound, culturally appropriate, feasible and have community support. Specifically, they will review plans and study materials for recruitment and data collection, advise on, and contribute to the dissemination of findings. Their involvement will improve research quality, help engender a sense of ownership of outputs by the community, helping to accelerate uptake and maximise the reach and impact of our programme.

13. PROGRESSION CRITERIA

The following criteria (Table 2) will be used by the Programme Steering Committee to determine whether and how the progression to the full trial will take place at 18 months.

Table 2. Progression criteria

	Proceed as planned	**Proceed with amendments**	**Major review of trial procedures and outcomes**
Recruitment	At least 32 (50%) recruited over 2 months	At least 32 (50%) recruited during the feasibility phase	Fewer than 32 (50%) recruited during the feasibility phase
Primary outcome available	At least 80%	50%-79%	<50%
DiaDeM fidelity	At least one session delivered to 80% of participants randomised to the intervention	At least one session delivered to 50% of participants randomised to the intervention	More than 50% of participants randomised to the intervention did not attend any sessions

14. STUDY TIMELINE

Gantt chart (Annex 1;link:(https://docs.google.com/spreadsheets/d/1lCuMD-6UCsVLeM0FvYaf_NmCcJVYf1K1/edit?usp=sharing&ouid=115695424213269068061&rtpof=true&sd=true)) displays the study timelines for the feasibility study, actual recruitment starting from March 2022 I.e. the 19th month of the DiaDeM programme.

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