A feasibility cluster randomised controlled trial of technology-assisted diabetes foot care in Pakistan- a study protocol.

Background

Diabetes is one of the most chronic diseases that affects millions of people worldwide. According to the International Diabetes Federation (IDF), the global prevalence of diabetes was 537 (10.5%) million in 2021, and it is estimated to reach 783 million (46%) by 2045. Around 75% of the diabetics live in lower-middle-income countries (1). Globally, Pakistan ranks 7th among the top ten countries with a high burden of diabetes. According to the International Diabetes Federation, approximately 19.4 million people in Pakistan have diabetes (2).

A severe chronic complication associated with diabetes is diabetic foot. Globally, the prevalence of diabetic foot is approximately 6.4%, and due to diabetes, every 30 seconds, an amputation is done, resulting in the loss of a lower limb or part of a lower limb. The pooled prevalence of diabetes foot ulcers in Pakistan is estimated to be 12.2% (3). The increase in the prevalence of diabetes and prolonged life expectancy of diabetics is leading to a further increase in the incidence of diabetic foot, with an estimated lifetime incidence of developing a foot ulcer as high as up to 25% (4-6). Of those diabetes patients who develop a foot ulcer, more than half are likely to die within five years (7). The treatment of diabetic foot ulcers is expensive and complicated, requiring long-term medication and/or hospitalization (8). Diabetic patients with foot ulcers incur five times higher health expenditure than those without ulcers. Therefore, to avoid the catastrophic health and financial implications of diabetic foot conditions, prevention and early treatment at the basic primary care level are required.

The World Health Organisation (WHO) guidelines for preventing and managing diabetic foot ulcers have emphasized the need for comprehensive foot care services, including screening, risk assessment, and patient education (9). In addition to these measures, the International Diabetes Federation (IDF) also emphasizes the training of healthcare professionals in managing and treating diabetic foot. People with diabetes should be educated about foot care, including regular foot examinations, proper footwear, and self-care techniques (10), which have proven to reduce the risk of amputation by 45-85% (11, 12). In addition, mobile applications have also been found effective in improving foot care knowledge and self-care (13).

In Pakistan's existing public health infrastructure, diabetes core care is available at the primary health centres and sub-district hospitals by the routine medical and allied staff. These publicly funded healthcare facilities provide their catchment populations free-of-cost services (i.e., clinical and diagnostic). The Directorate General Health Services and Association for Social Development, with the support of the World Diabetes Foundation, has successfully integrated a standardized diabetes-hypertension core care package in twenty districts of Pakistan. The NCD Program, considering the significant implications of the diabetic foot on the public health care system, has planned to integrate diabetic foot care in primary healthcare facilities, i.e., RHCs and hospitals. The Programme and the Association have developed products by adapting international best practice guidelines (14, 15). These guidelines and a context review informed the technical working group's development of the intervention package. These products were aimed to integrate diabetic foot care and improve patient engagement in diabetic foot care as well as behaviour or self-care practices.

Intervention Components:

1. Integrated foot care intervention design, i.e., staff roles and operational strategies to deliver integrated foot care and footwear components (given in Table 1).
2. Staff enabling package, i.e., training of doctors and allied staff
3. A flipbook (pictorial tool) for in-person patient counselling on footcare and suitable footwear
4. Mobile App for meaningful patient engagement in footcare and suitable footwear

Table 1- Integrated Foot Care Intervention Components:

Footcare tasks	**Brief description/comments**
Screening/ foot assessment: history and physical exam	A tailor-made screening tool for foot assessment
Educate/ counsel on footcare and footwear (in-person and mobile App.)	• Individual in-person counselling - using pictorial flipbook • Mobile App.: download the App. on the patient's mobile, and educate them to access/ seek knowledge on footcare and footwear (pictorial and written with voice-over)
Access to suitable footwear and silicone rubber insoles/ orthotics	Footwear: ○ access to on-shelf suitable shoes in the market (for all)

	○ refer to a designated source of customized shoes (if needed) ○ Insoles – provision through project facilitation
Patients are to report footcare and footwear challenges and care delivery to respond to these challenges	Through the mobile App., the patients will be enabled to report their care and social challenges, and these reported difficulties will be addressed through peer support
Periodic follow-up screening and response (at RHCs)	Patient feet are to be screened periodically for foot condition (frequency subject to foot condition). The patients get advised according to their foot condition.
Digital referral for secondary care	• Patients with foot ulcers, with(out) infection and/or necrosis, are to be referred for specialist care at DHQ hospital. • These patients (after specialist care at DHQ) will continue getting follow-up care at their respective RHCs.
Staff maintain care records, and the district monitors performance	• Diabetes footcare records are to be added to the patient card (for diabetics). • Desk monitoring (EMR-based) is also supplemented by periodic supervisory visits of the RHCs.
Trial considerations:	
Trial enrolment	The facility staff inform the patient (per prescribed protocol) and seeks their consent (to use their data in trial results). ○ If they consent – they will get enrolled in the trial. ○ If they do not consent, they will be offered care as per program guidance (without including in the trial)
Outcome measurement (trial)	Data on foot care assessment and additionally on foot care practices will be collected at the baseline and the endline of study period.

Aim

A well-designed RCT is required to test the effectiveness of this intervention package in diabetic foot care. Currently, there is insufficient data to inform the planning of a full-scale randomized controlled trial.

This feasibility trial will inform the design of a full RCT on technology-assisted diabetic foot care in primary healthcare facilities, i.e., RHCs.

Objective

To assess the feasibility of conducting a cluster randomized controlled trial comparing the effectiveness of the intervention package versus the routine care.

Methods

Study design

A pragmatic feasibility randomised controlled trial will be conducted comparing the contextualised intervention package with routine care. The study will start patient recruitment in July 2024 and complete end-line assessments in December 2024.

Eligibility

Inclusion Criteria

The study will recruit diabetes patients aged 25 or older registered for diabetes care at the primary health care facility, i.e., RHC. The age range has been kept broad to explore the outcomes across age ranges to inform a fully powered trial. As this is a pragmatic trial, participants will not be excluded based on comorbidities as the intervention would also cater to these groups when adopted on a large scale by the NCD Control Program. The patients will be included in the trial if written consent is obtained. The patients will also need access to a smartphone (i.e., personal smartphone or access to a smartphone within the household).

Exclusion Criteria:

Diabetes patients who plan to move out of the RHC catchment area during the study period will not be recruited in the trial. Those who refuse to give consent to participate will also be excluded.

Randomisation, Recruitment and Consent

Four districts will be randomized (i.e., two in each intervention and control arm). Two healthcare facilities will be randomly selected from each of the randomized districts. These RHCs will be sent a letter by the Directorate General Health Services (DGHS) to participate in the trial.

The diabetes patients at these facilities will be informed about the study objectives and the management and use of their data using an information sheet. The patients can ask questions to ensure they understand the project. A voluntary written consent will be obtained at the time of trial registration. The reasons for refusal will be noted. Patients who refuse to participate in the trial will receive the same program-recommended care, but their data will not be included in the trial. All patient records and personal information will be kept confidential to ensure privacy, and only healthcare providers and the project team will have access to these records. Recruitment of the

patients will be prospective. Each participant, once recruited, will be followed up for six months. Please see the Gantt chart at the end of the protocol for the study schedule.

Sample Size:

A formal size calculation is not required as this is a feasibility study. We have considered that collecting outcome data on approximately 320 patients (160 in each arm) would be sufficient to address our objectives. As this is a cluster-level trial, we estimate recruiting four districts (i.e., two districts per arm) with two randomly selected health facilities from each district. All health facilities are estimated to recruit 40 diabetic patients.

Intervention and Control Site Packages:

- At both intervention and control sites:

  Healthcare staff will be able to assess the diabetic foot and maintain records. This includes the provision of foot assessment-related materials (e.g., microfilament, tuning fork).
- At intervention sites, only:

  Healthcare staff will be enabled to offer enhanced foot care and footwear intervention. The enabling includes contextualized implementation products: a) desk-guide for doctors; flip book for patient education; b) materials for foot care and footwear, e.g., silicone rubber insoles; c) digital mobile App. for patient engagement.
- At control sites:

  Current footcare practices (as per individual physician discretion) will be continued, with an enhanced foot assessment and record keeping (as mentioned above). (Note: the enhanced assessment and record keeping will help ensure standardization and comparability of data between control and intervention arms).

Note: To keep the trial evidence relevant to the real-life program implementation processes, any special measure for enhanced staff adherence to the intervention protocol would be avoided.

Blinding

Blinding diabetic patients and healthcare providers will not be feasible, given the nature of the intervention. However, the data analysts will be kept blind to arm allocation.

Outcomes

The primary and secondary outcomes will be defined using the criteria of Thabane et al. (2010) for conducting feasibility studies (16) (outlined in Table 2).

Primary outcome:

The feasibility of clinical outcomes will be taken as the primary outcome.

Secondary outcomes:

The feasibility of operational and economic outcomes will be the secondary outcomes.

Table 2- Feasibility Outcome Indicators:

Indicators type	**Quantitative Measures**
Clinical	• Uptake of recommended foot care behaviour (through Nottingham Assessment of Functional Footcare (NAFF)) • Quality of Life (through European Quality of Life 5 Dimensions 5 Level Version (EQ-5D-5L)) • Uptake of follow-up footcare visits (outputs) • Uptake of suitable footwear/adherence to footwear (outputs) • Uptake of mobile-App-assisted patient engagement • Uptake of referral care at DHQ hospital • Deterioration in foot condition/stage at the endline (in comparison with baseline) • Complications during footcare (necrosis, amputation, hospitalization)
Operational	• Patient enrolment – OPD load; diabetes patient load; refusal to participate in footcare intervention • Patient adherence to footcare follow-up (till endline) • Staff – skill/ time/ support for the footcare tasks • Availability of tools/ equipment for footcare tasks • Availability of setting and arrangements for delivering footcare tasks • Completeness of footcare data • Validity of footcare data (matching from ≥2 sources)
Economic	Providers' cost of: • RHC enabling • footcare per patient • desired outcome (of footcare) • Additional emergency/catastrophic costs

Data Collection

The health care staff will collect data on diabetic foot condition at baseline at the RHCs on the NCD patient record cards. The research team will conduct the surveys for patient foot care practices using the Nottingham Assessment of Functional Footcare and European Quality of Life 5 Dimensions 5 Level Version tools.

Statistical Methods

A descriptive analysis will be conducted based on the recommendations about good practices in the analysis of feasibility studies. These will be presented as means and SDs or 95% CIs, medians and IQR, or percentages. The trial will examine the effects of intervention during the analysis and use the data to inform estimates of a fully powered RCT.

Ethics

Ethical approval for this study has been obtained from the Research Ethics Board of the Association for Social Development (Ref- no: ASD-EAG-23-001). This study has been approved from The University of Oxford Research Ethics Committee (OxTREC Reference: 560-24).

There is no anticipated risk to trial patients during this study. A possible ethical concern could be that the control group will not receive the foot care intervention during the trial. However, this concern has been addressed by rolling out the intervention in the control clusters at the end of the study. Participants assigned to the control group will be placed on a waitlist. Upon completion of the study, the intervention components will be introduced to the control group, and the application will also be made available for download within the control clusters.

The patient data will be stored in accordance with the Data Protection Act 1998. The hard copy of patients' record will be kept in a lock, and all the patient's data will be pseudo-anonymised using a unique patient ID number for each participant. This pseudo-anonymised data will be saved on a secure, password-protected computer drive, which will only be accessible to the research team.

Strengths and Limitations

The trial will be conducted under routine programme circumstances with no additional resources required. The study will address an area which has minimal available evidence. However, blinding healthcare professionals and participants will not be possible due to the nature of the intervention.

Dissemination plan

The results of this study will be published in peer-reviewed journals. The protocol and project updates will also be available on the Open Science Framework. The study findings will be presented in as many research conferences at national and international level as possible. These findings will be disseminated in a workshop to all policymakers, i.e., Directorate General Health Services and Provincial NCD Disease Control Programmes. In addition, social media will be used to ensure the coverage of our findings.

Gantt Chart

Tasks	2024			2025							
	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	June	July	Aug
Recruitment in trial (including baseline assessment & screening)											
Follow-up											
Endpoint assessment											
Data cleaning and analysis											

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