TRIAL PROTOCOL
Thailand

A Scalable Solution for Delivery of Diabetes Self-Management Education in Thailand

ISRCTN
NCT *(clinicaltrials.gov)*

DSME Thailand

Version 1.0 (08th October 2018)

SPONSOR: London School of Hygiene & Tropical Medicine (LSHTM)

FUNDERS: UK Medical Research Council (MRC) and the Thailand Research Fund (TRF)

STUDY COORDINATION CENTRE: London School of Hygiene and Tropical Medicine (UK)
Chiang Mai University UNLISTED (Thailand)

LSHTM Ethics Reference: 16113/RR/12850

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LIST OF ABBREVIATIONS

RCT	Randomised controlled trial
DSME	Diabetes Self-Management Education
BMI	Body Mass Index
MRC	Medical Research Council
LSHTM	London School of Hygiene and Tropical Medicine
CMU	Chiang Mai University
TMG	Trial Management Group
TSC	Trial Steering Committee
CSV	Comma Separated Value
WS	Workstream
HbA1c	Haemoglobin A1c levels
LTFUP	Lost to Follow up
IRB	Institution Review Board

STATEMENT OF COMPLIANCE

The study will be carried out in accordance with Good Clinical Practice (GCP) as required by the following:

- UK Policy Framework for Health and Social Care Research applicable to clinical trials.
- SI 2004/1031, Schedule 1, Part 2, 8.
- Medicines for Human Use (Clinical Trials) (2004) regulations .

PROTOCOL SUMMARY

TITLE A Scalable Solution for Delivery of Diabetes Self-Management Education in Thailand (DSME Thailand)

DESIGN 3 Arm Cluster randomised controlled trial

AIMS To develop a culturally-tailored DSME program for Thailand and evaluate its clinical and cost-effectiveness under two alternative modes of delivery: nurse-led and peer-led.

OUTCOME MEASURES

1. Biophysical data: HbA1C; blood glucose and lipids; BMI; Waist circumference; blood pressure.
2. Psychosocial and lifestyle data: Quality of life (WHOQOLBREF and EQ-5D); depression and stress (Hospital Anxiety and Depression scale and Perceived stress questionnaire); Diabetes knowledge and skills Brief diabetes illness perception questionnaire, Diabetes Self-Management Education and Support (DMSES), Summary of Diabetes self-care activities questionnaire (SDSCA); Diet (24 Hour Food Recall); smoking; physical activity (International Physical Activity Questionnaire).
3. Intervention related data: satisfaction with delivery of educational sessions (Modified Medical Interview Satisfaction scale); peer support (Family and Friends subscale of Chronic Illness Resources survey).

POPULATION Patients attending clinics in Chiang Mai and Lampang province in Northern Thailand

ELIGIBILITY Adults newly diagnosed type 2 diabetes and those with poor controlled type 2 diabetes within three years of diagnosis, across 21 primary care units in the Chiang Mai and Lampang province of Thailand.

INTERVENTION Educational/behavioural film-based intervention, delivered to health care professionals, health volunteers and newly diagnosed diabetes patients and those with poor control within three years of diagnosis plus family

TRIAL DURATION 36 months

STUDY SYNOPSIS

Type 2 diabetes is amongst the foremost challenges facing policy makers in Thailand, accounting for considerable death, disability and healthcare expenditure. Under Thailand's strong primary health system, medical management of diabetes is widely available. However, control of blood glucose and other cardiovascular disease risk factors, and regular screening for early detection of complications remain low due to a lack of services for education and counselling to support behavioural changes necessary for good self-management of the condition. A substantial literature documents the effectiveness of Diabetes Self-Management Education (DSME) programs for improving diabetes outcomes, although little high-quality data are available in Thailand, and traditional delivery models (health-professional led one-to-one or small-group sessions) are unlikely to be scalable in Thailand given current human resource and budgetary constraints. Thus, we propose to develop a low-cost DSME program and scalable delivery model for roll-out within the Thai primary care system.

The intervention is based on behaviour-change and social support theories. This will be delivered in monthly group meetings by lay health workers or nurses, and aided by a suite of short films to introduce key topics and stimulate discussion. We will randomise 21 primary care units to offer DSME to adults diagnosed newly diagnosed with type 2 diabetes and those with poor controlled type 2 diabetes diagnosed within the first three years. This will be delivered by lay health workers, nurses (for comparative effectiveness), or usual care. After 12 months, we will compare glycaemic control and cardiovascular risk scores between the three arms. We will conduct cost-effectiveness, process and policy evaluations to produce best-buy recommendations for the Thai Ministry of Public Health.

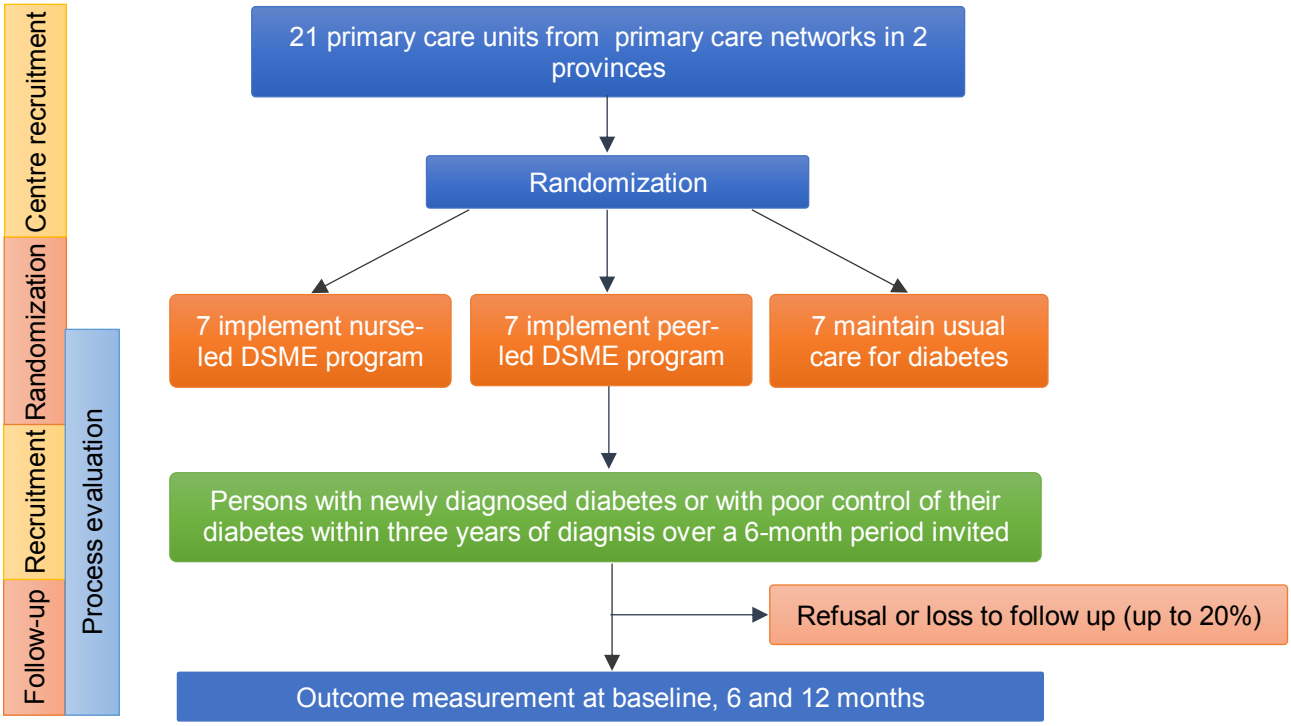
Through our 3-arm trial design, we will be able to compare effectiveness of nurse-, peer-delivered and standard care, and this along with the process evaluation will provide important lessons for the field of peer-delivery of interventions. In particular, questions remain whether peer educators can be easily trained to effectively deliver state-of-the-art behavioural counselling techniques based on a manualised intervention. The potential for peers to offer long-term support, which might better sustain behaviour change, is also untested and will be investigated through our process evaluation.

While there is much interest in theory-based behaviour change, it is relatively unquestioned whether approaches will be applicable in diverse cultural contexts, which may also have different baseline levels of health education, self-efficacy, social support, etc. Ethnographic observations and follow-up interviews with health workers and participants will explore this issue and produce findings relevant to the psychological theory-based behaviour change field. To ensure that our work reaches a range of academic beneficiaries, we plan to publish our findings in high-impact open access medical, psychological and health policy journals. We will share our study data with other researchers, advertising via our publications and web presence. In particular, we are committed to sharing our findings and data with academic audiences in Thailand and other LMICs.

SCHEMATIC OF STUDY DESIGN

Methodology and experimental design annex

Figure 1: Trial flow diagram



1. KEY ROLES

Trial Management Group

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2. INTRODUCTION: BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

2.1 BACKGROUND INFORMATION

Type 2 diabetes mellitus (hereto referred to as diabetes) is amongst the foremost health challenges facing policy makers in Thailand. The prevalence of diabetes has more than tripled over the last two decades with an estimated 4 million adults (age-adjusted prevalence 7.1%) living with diabetes in 2015.[1,2]
Diabetes is associated with several macro vascular (e.g. ischaemic heart disease) and microvascular complications (e.g. nephropathy, retinopathy, neuropathy, and foot disease). This primarily accounts for the considerable death and disability (of which diabetes is the 5th leading cause in Thailand), two-fold higher healthcare expenditure, and loss of economic productivity (of persons with diabetes and their carers) associated with this condition in Thailand.[1–4]
The complications of diabetes can be largely prevented or delayed by good control of their risk factors (blood glucose, lipids and blood pressure), through lifestyle change and medication where necessary, and regular screening for early detection and management of complications.[3,4]
Under Thailand's universal health coverage, nearly everyone diagnosed with diabetes receives timely medical care (>97%) and has access to screening. Yet, surveys suggest that only about half of the people with diabetes achieve optimal control of risk factors (e.g. HbA1C <7% in 33%, LDL cholesterol<100 mmol/L in 44%, BP<130/80 mmHg in 52%). Alternatively, they receive annual screening for microvascular complications (53-60%).[1,5] Limited data support a lack of engagement and self-management skills among those diagnosed with diabetes as the main underlying reasons for this.[6]

Successful management of diabetes involves a considerable degree of self-management.
People with diabetes need to adhere to multiple behaviours, including healthy lifestyles, regular monitoring and medication, problem solving and healthy coping. In this, they are greatly supported by diabetes self-management education (DSME), defined as 'a collaborative and ongoing process intended to facilitate the development of knowledge, skills, and abilities that are required for successful self-management of diabetes'.[7]
Evidence from over 100 studies, including many randomised controlled trials, conducted predominantly in high-income countries, suggests that DSME programs are associated with improvements in a range of behavioural (knowledge, behaviours, self-efficacy, psychosocial) and clinical (physiological risk factors, screening for complications, quality of life) outcomes, [8,9] and are also cost-effective;[10] therefore, they are recommended by most clinical guidelines.[7]

Despite this, there is considerable heterogeneity in the effectiveness of DSME programs.[8,9]
Programs that are more effective usually offer more than 10 hours contact, incorporate behavioural approaches, and provide longer-term support mechanisms. Providing intensive and sustained support however has cost implications, resulting in ongoing efforts to identify more cost-efficient ways to deliver DSME, notably through digital technology (with variable effectiveness) and peers.
Peers can support sustained changes in complex health behaviours by providing assistance in daily management, social and emotional support, linkage to clinical care, and ongoing availability of support.[11,12] Unlike the educational/psychological framework of professional support, peer support operates on a social support framework. Although traditionally restricted to those with experience of disease, the definition of peers has been expanded to include other non-professionals with close relations to the community (e.g. community health workers).[13] However, despite widespread interest, empirical data on effectiveness of peers in supporting behaviour change in chronic diseases, including diabetes, is limited and inconsistent. [11,12] In an earlier review, the World Health Organisation did not find sufficient evidence to recommend peer support programs as a policy option for diabetes management in LMICs.[14] Data on cost-effectiveness, acceptability and potential adverse consequences of peer support programs from diverse settings, as well as optimal strategies for mobilising and integrating peers in diabetes care pathways, are lacking.[12]

Since the 1960s, community health workers (called village health volunteers) have been a regular part of the Thai healthcare system, linking communities with healthcare providers and providing a range of assistance and

outreach services. The presence of a nationwide network of community health workers (1 million) offers a unique opportunity to develop a scalable model of DSME provision, while building local capacity, and generating critical data on role of peer support programs in LMICs. Taking a similar approach, a multi-country demonstration project in 2010, successfully trained village health volunteers in Thailand for DSME delivery.[15] The study authors reported a substantial engagement and acceptance of the program; however, clinical outcomes could not be robustly evaluated due to fieldwork challenges (before-after data were available for 53 participants only).

In Thai healthcare system, structured DSME is not routinely available (other than brief didactic educational sessions in some centres). While several small-scale studies from Thailand have demonstrated, that DSME can strengthen self-management of diabetes, negative perceptions of educational programs (potentially sustained in the absence of high-quality local data on effectiveness). These concerns about the burden on existing staff time and costs, have so far prevented the introduction of DSME.[1,16] However, recent policy developments in Thailand are supportive of DSME introduction, if a scalable model can be found. The Thailand Healthy Lifestyles Strategic plan (2011-20) lists reduction of diabetes incidence, complications, disability, mortality, and expense as one of its five main development goals. The current primary healthcare reform of 2017 integrates clinicians, public health staff, and community health workers into primary care clusters to provide community-based and multidisciplinary care; a particular focus is on care of non-communicable diseases and people with disability through improvements in health literacy and self-efficacy.

2.2 RATIONALE

The health and economic consequences of Type 2 diabetes mellitus are largely attributable to its complications, which may be prevented or delayed through good disease control. This can be achieved through medical care and self-management. Diabetes Self-Management Education (DSME) programs are effective and cost-effective, and part of standard care in high-income countries, but are unavailable in Thai healthcare system, despite universal coverage of medical aspects of diabetes care. Negative perceptions of educational programs, sustained by a lack of high-quality local data, and concerns about burden on existing staff time and costs are thought to be responsible.

Given the focus on community-based education for chronic diseases in recent primary healthcare reforms, it is timely to scale-up DSME in Thailand, if an affordable model of delivery for a locally-tailored intervention can be found. Taking this opportunity, we propose to work in close collaboration with the Thai Ministry of Public Health to develop, pilot and evaluate a peer-based DSME program and delivery model, finally producing a list of policy recommendations for optimal integration into the Thai healthcare system. Participants will be free to drop into any number of meetings (full or partial) and encouraged to contact their nurse or village health volunteer for advice as necessary. While there is a theoretical risk that this could increase the cost of the program, it is anticipated that it will be regulated by the unwillingness of the participants to attend the program beyond its usefulness; identifying this potential unintended consequence will form part of our process evaluation.

The proposal is to develop a culturally tailored DSME program for Thailand and evaluate its clinical and cost-effectiveness under two alternative modes of delivery: nurse-led and peer-led.
While the exact structure of the intervention will be determined by the formative research carried out under this proposal, a low-impact and sustained delivery model is most likely to achieve our twin objectives of long-term behaviour change and scalability.[17]

3. STUDY OBJECTIVES

The aim is to identify a scalable model for delivery of DSME across Thailand.
Specific project objectives:
1. To design a prototype of the DSME intervention
2. To refine the intervention prototype and trial design
3. To evaluate the effectiveness and cost effectiveness of intervention under two alternative modes of delivery (nurse-led and peer-led)

4. To identify the most scalable model for DSME delivery in the Thai healthcare system

The primary hypothesis is that either model of DSME delivery will be effective and cost-effective; however, the peer-led model will be a more scalable option for the Thai healthcare system.

4. STUDY DESIGN

4.1 DESCRIPTION OF THE STUDY DESIGN

This is a four Workstream (WS) programme design based in Thailand aimed at improving cardiovascular risk and control of blood glucose among people with diabetes.
WS1 and WS2: Intervention development (content and delivery model) for DSME.
WS3 and WS4: A 3-arm cluster randomised trial in primary care units with an inbuilt process and economic evaluation. Twenty-one primary care units will be randomized (seven each) to provide nurse-led DSME, peer-led DSME, or standard care. People with diabetes are the units of analysis. The trial will be unblinded.

4.1.1 STUDY OUTCOME MEASURES

The study outcomes are:

i. A difference in trial arms at one-year follow-up in HbA1c (co-primary outcome 1)
ii. A difference in trial aims at one-year follow-up in total cardiovascular risk (co-primary outcome 2)

4.1.2 SETTING

Primary care networks in Chiang Mai and Lampang Province in Northern Thailand, which include 21 primary care units.

5. RANDOMISATION

Twenty-one primary care units will be randomized (7 each) to provide nurse-led DSME, peer-led DSME, or standard care (1:1:1). Randomisation will be minimised by primary care networks to account for any variation in practice, although this is expected to be small because it is determined by the tertiary care hospital, which is same for both. The nurses and village health volunteers in intervention arms will be trained to deliver the intervention (at the community hospital or neighbourhoods as appropriate) using training films. No changes will be made to standard care, which currently involves a brief didactic educational session at the time of diagnosis of diabetes. While diabetes is diagnosed at tertiary hospitals, it is managed at, which are served by a full-time nurse (doctor visits weekly), and 10-15 village health volunteers linking patients in the community.

6. SELECTION AND WITHDRAWAL OF PARTICIPANTS

All new referrals for diabetes management and those having difficulties managing their diabetes the first three years of diagnosis at the 21 primary units over a 6-month period (N=693) will be recruited to the trial, and offered intervention determined by the trial arm. Prospective participants will be made aware of the study through posters and information sheets. All new referrals will be invited to take part. Local fieldworkers will visit the hospitals and obtain informed consent for study participation. Once consent has been provided, participants will be asked to complete a short questionnaire and to give contact details.

6.1 INCLUSION CRITERIA

1. People aged over 18 years with a new referral for type 2 diabetes management at the 21 hospitals

2. People aged over 18 years with difficulties managing diabetes within the first three years of diagnosis at the 21 hospitals.
2. Willingness to attend educational group meetings
3. Available for six and 12-month follow-up

6.2 EXCLUSION CRITERIA

1. Advanced diabetes complications such as receiving dialysis, registered blind, above ankle amputations.
2. Co-morbid learning difficulties, dementia or current active severe mental illness
3. Lacking the capacity to consent

6.3 CONSENT

Written informed consent will be obtained from all study participants in a language they understand before any study procedures are undertaken (enrolment and follow up interviews, blood draws). Local fieldworkers will explain the study and patients through the patient information sheet. The right of the participant to refuse to participate without giving reasons will be respected.

6.4 RISKS AND BENEFITS

No major ethical issues are expected since only interventions recommended in established recent guidance issued will be offered. By participating in the study, participants will not be denied any form of care that is currently available to them, subject to local provision of services. Participants may find minor discomfort from the taking blood samples. Trained phlebotomists will take the blood sample. Results of Interim blood test, that is not part of routine care, such as HbA1c will be fed back by the study team to health care professionals only if there is a need for additional clinical treatment/management. The information sheet will stress the independence of the research team and that all data will be anonymised

The Patient Information Sheet will provide potential participants with information about the possible benefits and anticipated risks of taking part in the study either as a participant in the main intervention or in the qualitative study. Participants will be given the opportunity to discuss any issues with their healthcare provider or researcher prior to consenting to participate. The researcher will inform the participant if new information comes to light that may affect the participant's willingness to participate in the study.

6.5 WITHDRAWAL CRITERIA

Participants have the right to withdraw from the study at any time for any reason. It is understood by all concerned that an excessive rate of withdrawals can render the study uninterpretable; therefore, unnecessary withdrawal of patients should be avoided. Should a patient decide to withdraw from the study, all efforts will be made to report the reason for withdrawal as thoroughly as possible. Should a patient withdraw from study intervention only, efforts to continue to obtain follow-up data will be made, with the permission of the patients. Patients will be asked if they are willing to be contacted by a researcher at 6 and 12 months and if not whether the study is able to collect ongoing data from their medical records.

7. INTERVENTION

7.1 INTERVENTION DESCRIPTION AND DELIVERY

The intervention will consist of four Work packages (WPs):

WP 1: Professional development of nurses and village health volunteer (VHVs) to educate diabetes patients on self-management.

a. Mapping of the knowledge from a desktop reviews and focus groups from nurses and VHVs to develop a paper prototype of the intervention, including its hypothesised pathways of action (e.g. common-sense model of illness, empowerment, discovery learning, social learning, and social support) and a training manual for nurses and health volunteers.

b. Development of 6 brief films (5-6 minutes long) to trigger discussions on key topic areas during structured periods of the intervention meetings, and a longer film to be used a training resource for nurses and village health volunteers. There is an increasing recognition that films are a highly efficient medium for communicating large amounts of information with a better recall, particularly in low literacy settings.[20] Short films can be used to challenge existing beliefs to support behaviour change and create a connection within viewer groups to catalyse support. Films will be developed using an established theory-based process, which uses participatory approaches to ensure that films meet the cultural, psychological, and contextual constructs of the audience. Films will be in local language and use local actors.

WP 2: Piloting trial protocol and intervention of the structured diabetes self-management education programme for people with newly diagnosed and those with poor control of their diabetes within three years of diagnosis plus carers

We will pilot the intervention at four community hospitals. The pilot will not be a smaller version of the trial; instead, several independent studies will be carried out, mainly to refine the intervention. We will also collect some preliminary data to check our assumptions and processes for the trial. The intervention modules will be tested with two nurses and village health volunteers each, who will be trained to deliver them to groups of 10-20 persons with diabetes and their carers. Several modules will be tested in parallel, as they will be designed to be standalone. Data on 'what works, doesn't work, and what more needs to be added' for each session will be collected using a) ethnographic methods, involving direct observations of the sessions, which will be video recorded, and unstructured and semi-structured interviews (24 in total, purposively sampled), and b) focus group discussions, with the nurses, village health volunteers, and group participants (8 in total). The intervention modules will be refined using participatory research methodology, and following an iterative process, including piloting, feedback, analysis, reflection, and modification, until the sessions are fit for purpose. We will collect quantitative data on at least 100 consecutive persons with diabetes attending the four community hospitals (i.e. 25 at each site), and semi-structured interviews on a subsample of ~20 people, to document the current care processes, collect data on distribution of outcome measures to confirm our sample size calculations, and pilot the trial organization and study instruments, as not all have been previously used in Thai populations.

WP 3: Main trial evaluation on structured DSME for people with newly diagnosed with type 2 diabetes and those with poor control of their type 2 diabetes within three years of diagnosis and their carers.
The intervention will be evaluated in primary care networks in Chiang Mai and Lampang province in northern Thailand. While diabetes is diagnosed at tertiary hospitals, it is managed at community hospitals and health centres, which are served by a full-time nurse (doctor visits weekly), and 10-15 village health volunteers linking patients in the community. A 3-arm cluster randomized trial with inbuilt process and economic evaluation will be carried out (see Annexe for trial flow diagram). The 21 primary care units will be randomized (seven each) to provide nurse-led DSME, peer-led DSME, or standard care. Randomisation will be minimised by primary care networks to account for any variation in practice, although this is expected to be small because it is determined by the tertiary care hospital, which is same for both. The nurses and village health volunteers in intervention arms will be trained to deliver the intervention (at the community hospital or neighbourhoods as appropriate) using training films. No changes will be made to standard care, which currently involves a brief didactic educational session at the time of diagnosis of diabetes. Process evaluation will aim to assess intervention delivery (fidelity, dose and reach), clarify causal mechanisms (those hypothesised by theory of change developed within the project or identify unexpected ones), and identify contextual factors (barriers, facilitators) associated with variation in outcomes.[24] Data for economic evaluation (resource usage and quality of life using EQ-5D) will be obtained prospectively alongside the trial.

WP 4: Health systems analysis to identify best policy options
Using ideas from existing literature on the subject as a basis, we will undertake targeted interviews with Thai policy makers to jointly define a scalability construct of relevance to them and create a framework for operationalising it.[25] Relevant data from policy documents and available databases will be collected to undertake health system analyses. Key criteria for assessment of scalability are likely to include, among others: a) cost-effectiveness and affordability (i.e. the total cost to government of scaling up the intervention, and this cost in relation to total health budget, as these metrics may be of more interest to policy makers); b) acceptability of the intervention to users and providers, with a particular focus on integration of the new activity in the existing workload and health information systems; and c) compatibility of the new intervention with existing policy frameworks, although this will also be taken into consideration while developing the intervention. Our preliminary conversations with Thai policy makers suggest a strong interest in using DSME to improve skills of frontline workers in behavioural interventions, which could then be transported to other chronic disease interventions, suggesting that capacity building benefits may be an important consideration in policy makers' decision.

8. ASSESSMENT AND FOLLOW-UP

Each participant will be involved in the study for a minimum of 12 months after taking consent and baseline data. However, there may be a delay in contacting and scheduling participants for follow ups therefore, this may be slightly longer. The study is expected to start October 2018 and finish September 2021.

a. Questionnaire data will be collected by field workers via in-person interview for the full sample at baseline, 6 and 12 months at the community hospital where they were recruited (Table 1). A custom-designed form linked to Microsoft Access will be used to collect, validate, verify, and store respondents' data where possible or else data will be collected via paper forms and double-entered into the databases. All data files and databases will be password protected.

b. Biological samples. Blood samples will be collected from participants at baseline, 6 and 12 months, to measure Blood glucose, HbA1c and lipids, coordinating where possible with the annual routine tests offered to patients to reduce duplication. Blood will be drawn by a trained phlebotomist when participants come for interview and sent to laboratory for analysis. Data will be linked to the participant information using a unique respondent ID, which will be assigned to all study participants.

c. Interviews. During intervention development and qualitative evaluation, a subset of participants will be followed up using in-depth interviews and focus group discussions. These will be recorded on digital Dictaphones, with recordings initially stored on a personal computer or laptop in an encrypted folder with password protection. Recordings will be transcribed by professional transcribers conditional on signing of confidentiality and nondisclosure agreements.

Table 1: Questionnaire-based outcome measures

Target domain	Questionnaire	Adapted for Thailand	Validated in Thailand
Quality of life	WHOQOL	Yes	Yes[25]
	EQ-5D	Yes	Yes[26]
Depression	Hospital Anxiety and Depression Scale (HADS)	Yes	Yes[27]
	Perceived stress questionnaire	Yes	Yes[28]
Physical activity	International Physical Activity Questionnaire	Yes	Yes[29]
Diabetes knowledge and skills	Brief diabetes illness perception questionnaire	Yes	Yes[30]
	Diabetes Self-Management Education and Support (DMSES)	Yes[31]	No
	Summary of Diabetes self-care activities questionnaire (SDSCA)	Yes	Yes[32]
Satisfaction with intervention	Chronic Illness Resources survey	Yes	Yes[33]

8.1 LOSS TO FOLLOW UP

The field team shall hold weekly briefs preferably on Friday mornings with the Study Co-ordinators to generate a list of priority areas and lost to follow up (LTFUP) participant lists. Arrangements to follow up participants who have not turned up for their appointment will be made. Participants will be sent text message reminders prior to their appointment. If they fail to show, then they will be contacted by phone or by home visit if phoning is not possible to understand the reasons and reschedule another appointment within a week. They will be declared lost to follow-up if they do not show for a month and are untraceable.

9. STATISTICS AND DATA ANALYSIS

The total number of participants estimated to be involved in the study is 693.
Approximately 60 semi-structured interviews will be conducted throughout the course of the project (including intervention development, piloting and process evaluation), as well as 15-20 focus group discussions and 20 ethnographic observations.

9.1. SAMPLE SIZE CALCULATION

This study was powered to detect a clinically important difference of 0.6 units HbA1c (SD 1.5 units) between the control and intervention arms. We required 693 participants from 21 hospitals (7 per arm) to achieve 80% power at 2.5% significance level (to account for multiple testing), assuming an ICC between hospitals of 0.02 and loss to follow-up rate of 20%.[22,23]

9.2. FORMAT AND SCALE OF THE DATA

Data will be collected from approximately 693 individuals newly diagnosed with diabetes, across 21 primary care units in the Chiang Mai and Lampang province of Thailand.

The following data will be collected at baseline, 6 months and 12 months:
a. Questionnaire and body measurement data will be collected in person and entered where possible directly into a password-protected Microsoft Access database (via a form) on laptops, or else using double-entered paper forms.
b. Blood samples will be labelled and sent for analysis at the local hospital lab, and once analysed the results will be merged back into the main database. Once fully entered and validated, data will be transferred to comma separated value (csv) files for more efficient long-term storage and sharing
c. Qualitative data will be collected via interview and direct observation, and initially stored as voice and video recordings, later transcribed and data extracted using NVivo software.

10. DATA QUALITY AND STANDARDS

A data collection protocol will be developed, and the project coordinator in Thailand will provide training to fieldworkers before data collection commences. Validation will be performed on a Data Management on a random sample of questionnaire data by cross-checking with clinic records. Any discrepancies will be followed-up and addressed by field workers, re-contacting participants to clarify as necessary. Quantitative data will be entered directly via a form with built in data checks to minimise transcription errors (or where necessary collected on paper and later double-entered into the electronic form). Post entry checks will be conducted using statistical software. Blood samples will be collected by trained phlebotomists in NaF vacutainers for blood glucose estimation; stored in ice slurry and centrifuged and separated after 30 minutes of collection to prevent glycolysis, and the plasma will be dispensed to the lab for analysis. All hospital laboratories have their own internal quality assurance protocols and are also linked to a national external quality assurance mechanism. Fieldworkers will be trained in qualitative methods and an interview schedule will be devised. Project coordinators will spot-check interview transcripts to ensure quality.

10.1. DATA MANAGEMENT

Data will be uploaded to a secure server at Chiang Mai University as soon as possible. Copies of data with numerical study identifiers replacing other identifying information will be transferred to LSHTM for analysis using a secure encrypted data transfer service (MyFiles, previously Filr). Interviews will be recorded on digital Dictaphones and immediately transferred to a secure local server at CMU on completion. Following transcription, data will be transferred to LSHTM as above. Audio recordings will be kept until transcription has been completed and verified, after which they will be deleted. LSHTM data systems are maintained in accordance with LSHTM's Information Management & Security Policy, backed-up and virus scanned on a daily basis. All staff involved in research will be trained in the study procedures and data management before the study commences.

10.2. DATA ANALYSIS

10.2.1 QUANTITATIVE ANALYSIS

Available outcome data will be analysed on an intention to treat basis. Potential clustering of outcomes at the level of community hospitals will be accounted for using mixed-effects models. Adjustment for baseline imbalances in outcomes or relevant covariates will be considered as appropriate. Effects of variations in intervention uptake and other relevant effect modifiers will be explored.

10.2.2 QUALITATIVE ANALYSIS

Qualitative data will be transcribed and analysed in NVivo, using both descriptive (e.g. understanding their experiences) and interpretive (e.g. interpreting them in cultural context) phenomenology approaches. Comparative analysis will also be carried out; this method allows data from different participants to be compared and contrasted. Deviant cases will be actively sought throughout the analysis and emerging ideas and themes modified in response.

10.3. DATA STORAGE

Data and all appropriate documentation will be stored for a minimum of 10 years after the completion of the study, including the follow-up period.

10.4. MONITORING

Both UK and Thai PIs are jointly responsible for data produced in this study and assurance of its quality. The LSHTM-based research fellow and Thailand-based research assistant will conduct data collection, management, curation, security and sharing during the lifetime of the grant.

The Chief Investigator will inform the sponsor should they have concerns, which have arisen from monitoring activities, and/or if there are problems with oversight/monitoring procedures.

11. REGULATORY ISSUES

11.1 ETHICS APPROVAL

This study is to be conducted according to the international standards of Good Clinical Practice (GCP) (International Conference on Harmonization guidelines), Declaration of Helsinki, and International Ethical Guidelines for Biomedical Research Involving Human Subjects, applicable national government regulations, and Institutional research policies and procedures. All investigators will receive GCP training to the onset of the study. Ethical approvals will be sought prior to commencement of the project from Thailand's Central Research

Ethics Committee and the London School of Hygiene & Tropical Medicine. The study protocol, informed consent form, participant's information sheet and other relevant information has been submitted to and approved by Chiang Mai University and local Ethics Committee. Any future amendments of the protocol shall be submitted to and approved by the Intuition Review Board (IRB) before implementation

11.2 CONSENT

As this is a cluster-randomised study, consent to randomisation is obtained at the cluster (hospital) level. Informed consent will be obtained for procedures that are specifically for the purposes of the study, i.e. data collection and blood tests for adults newly diagnosed with diabetes and for those with poor control within three years after diagnosis. Consent to enter the study must be sought from each participant only after a full explanation has been given, an information leaflet offered, and time allowed for consideration. The PI is responsible for ensuring that all vulnerable participants are protected and participate voluntarily in an environment free from coercion or undue influence. All information sheets and consent forms will be available in English and Thai and will be verified for accuracy through back-translation. Consent discussions will be conducted in the appropriate language and a translator will be used if necessary.

11.3 CONFIDENTIALITY

Any participants' identifiable data collected by the Study Coordination Centre will be stored securely and their confidentiality protected in accordance with the Data Protection Act 1998.
To protect against the possibility that personally identifiable information will be accessed and used by unauthorised individuals, several security measures will be applied. Data collection devices (laptops/tablets) will be password protected. Access to electronic data on servers located at CMU and LSHTM will be protected using access controls including password protection; access will only be available to research personnel through the authorization of the PIs. An audit trail will record activity on the main Access databases. All staff will be trained in handling of personally identifiable data. Qualitative and quantitative data will be anonymised at the earliest opportunity. Qualitative data will be used to inform intervention development and the process evaluation only; generic identifiers (e.g. participant 1) will be used from the transcription stage onwards. The key linking participants' names with study IDs will be stored separately from other data in a double-locked file at the secure project office, with access restricted to appropriate study personnel. Paper consent forms will be stored similarly. Study reports, such as aggregated data in progress reports, will not contain identifying information. Project office computers will be safeguarded from theft and damage (e.g. using locks, encryption, and antivirus software). Fully anonymised data may be transferred for analysis to co-investigators at LSHTM and other academic and commercial partners. A secure encrypted data transfer service will be used. Upon request, participant records will be made available to the study sponsor.

11.4 INDEMNITY

London School of Hygiene & Tropical Medicine holds Public Liability ("negligent harm") and Clinical Trial ("non-negligent harm") insurance policies, which apply to this trial.

11.5 SPONSER

London School of Hygiene & Tropical Medicine will act as the main sponsor for this study. Delegated responsibilities will be assigned locally.

11.6. FUNDING

The UK Medical Research Council and The Thailand Research Fund are funding this study.

11.7. AUDITS AND INSPECTIONS

The study may be subject to audit by the London School of Hygiene & Tropical Medicine under their remit as sponsor, the Study Coordination Centre and other regulatory bodies to ensure adherence to GCP.

12. TRIAL MANAGEMENT

12.1 TRIAL MANAGEMENT GROUP

The TMG will be responsible for overseeing the progress of the trial, and will meet monthly by Skype, and once each year in person, using opportunities afforded by existing collaborations and cross-appointments. Safety and adverse events will be reviewed at TMG meetings, and any concerns will be reported to the Trial Steering Committee (TSC), and their advice followed. The TMG will also formulate key policies and working groups (e.g. communication, data management, publication).

A Trial Management Group (TMG) will be formed, consisting of the following:

- Chief investigator
- Local Principal Investigators
- Other co-investigators
- Local project managers
- Local trial administrators

12.2 TRIAL MANAGEMENT COMMITTEE

The role of the Trial Steering Committee (TSC) is to provide overall supervision of the trial. The TSC will meet bi-monthly for the first year then every six months after that. The TSC will take responsibility for the following:

- Monitoring and supervision of the trial
- Review progress towards the study milestones
- Amending the protocol if needed
- Approve any additional trial sites
- Confirm all approvals are in place before the start of recruitment
- Advise the TMG on any safety concerns
- Oversee publication of trial results

The TSC will include experts in the field of DSME, health psychology and clinical trials, and will have an independent Chair. In addition, there will be patient and carer representatives as well as policy representation. [Membership to be confirmed]

12.3 DATA MONITORING AND SAFETY OVERSIGHT

A formal Data Monitoring Safety Board will not be convened, as there are minimal risks from this educational intervention and related data collection. If any adverse events are apparent then this will reviewed and addressed through the regular TMG meetings and in consultation with local site guidelines.

12.4 LOCAL MANAGEMENT

Day-to-day management of the trial will be co-ordinated through the local Study Coordination Centre in Thailand.

Study coordinating centre	MRC and LSHTM Thailand Research Unit
Study coordinator	Kanokporn Pinyopornpanish
Local PI	Chairisi Angkurawaranon

Responsibilities of the local Principal Investigator will be detailed in an agreement in advance of starting the trial and will include:

- Ensure all necessary approvals are in place prior to starting the trial
- Delegate trial related responsibilities only to suitably trained and qualified personnel
- Agree to comply with the final trial protocol and any relevant amendments
- Ensure consent is obtained in line with local approved procedures
- Allow access to source data for monitoring, audit and inspection
- Be responsible for archiving all original trial documents including consent forms

13. PUBLICATION POLICY

A dissemination strategy will be produced at the outset by the study management group to ensure that the project and its findings are widely disseminated through a range of stakeholder meetings, the internet, and social media. Expected output and impact Research findings will be disseminated to scientific audiences at major conferences (at least two) and published in high-impact open-access scientific journals; planned publications include those on trial protocol, intervention development, primary trial results, and process evaluation, and health systems analysis, at a minimum. This study is expected to have a major policy impact due to the close involvement of a key policy maker in the project (Co-I Srivanichakorn). Towards the end of the study a dedicated workshop will be held with key governmental stakeholders to disseminate the recommended model for DSME implementation in Thailand and encourage inclusion of a large-scale scientific evaluation into any national implementation of the scheme.

14. CONFLICT OF INTEREST POLICY

Any conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the trial. The study leadership has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

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