A community-based primary prevention programme for type 2 diabetes mellitus integrating identification and lifestyle intervention for prevention: a cluster randomised controlled trial

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Scientific summary

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Scientific summary

Background

The number of people diagnosed with type 2 diabetes mellitus (T2DM) is reaching epidemic proportions. The rising number of cases and the associated health-care costs mean that diabetes mellitus prevention is one of the most significant and pressing health challenges of our time. It is well established that prior to an individual being diagnosed with T2DM there is a period of impaired glucose regulation, often referred to as prediabetes mellitus (PDM). Interventions targeted at this PDM stage have the potential to slow down progression to T2DM; however, as many individuals with PDM are asymptomatic, often individuals will not present to a health-care practitioner until T2DM has been established for some time. Therefore, one of the key elements of a successful prevention programme is the development of a screening tool that can accurately identify those individuals at highest risk of T2DM. Once identified, an effective programme needs to be employed to help individuals to address and modulate their risk. Although several initiatives to promote preventative measures have been developed over recent years, there has been a lack of empirical data when testing prevention programmes in a real-world routine care setting. In addition, evidence on the cost-effectiveness of such programmes is sparse.

Objectives

The objectives of the study were to:

- develop and validate a risk score to identify those who require diagnostic testing, to identify undiagnosed T2DM and to identify those at high risk of future T2DM and cardiovascular disease in a multiethnic population
- use this risk score to identify and engage those at highest risk of T2DM and offer them a lifestyle self-management programme with the aim of reducing the risk of progression to T2DM and reducing cardiovascular risk
- pilot and test a lifestyle self-management programme based on group care, targeting five key areas, using information currently collated from the European Union-funded Diabetes in Europe Prevention using Lifestyle, physical Activity and Nutritional intervention project
- develop a training and quality-assurance programme for community-based health trainers, who may include health-care professionals, to deliver the initial programme and provide ongoing support to those at highest risk of T2DM
- evaluate the lifestyle self-management programme and its cost-effectiveness
- explore how a two-stage screening programme and prevention intervention can be implemented in primary care.

Development of the intervention

This structured education intervention has been developed to meet the current need for an evidence-based diabetes mellitus prevention programme that meets current National Institute for Health and Care Excellence (NICE) recommendations and which can be implemented within a UK health-care setting. The intervention encourages self-management of PDM, using simple, non-technical language and visual aids. The Diabetes Education and Self-Management for Ongoing and Newly Diagnosed programme was the first national education programme for people with T2DM to meet NICE criteria and has been used as a basis for the development of the Let's Prevent programme. The development process was informed by the Medical Research Council framework. An iterative cycle (including initial development, piloting, collecting

and collating qualitative and quantitative data, reflection and modification of the intervention) was used to inform and refine the lifestyle intervention until it was considered fit for purpose for evaluation in the randomised controlled trial (RCT).

Methods

The study consisted of two phases. Phase one included the development and validation of a risk score that could be applied within a primary care practice, using routinely available data to identify individuals at high risk of T2DM. This risk score was then used to identify people at high risk of T2DM for invitation to screening.

Phase one: two-stage screening study using a risk score

The Leicester Practice Risk Score (LPRS) was developed using data from a completed population-based screening study conducted in the same location as this study. It was validated using data from a second screening study. The risk score was designed for use in primary care and, therefore, included only routinely available risk factors. The risk score included age, sex, ethnicity, body mass index (BMI), family history of diabetes mellitus and antihypertensive medication. The score was found to have high levels of discrimination and calibration. A piece of software was developed that enabled the risk score to be easily used in primary care.

For the screening study, the risk score was applied to data from 44 practices. The top 10% of patients with the highest score were invited for screening. Following an informed consent process, a number of clinical assessments and measurements were performed. All participants undertook an oral glucose tolerance test (OGTT). All participants identified as having PDM took part in the RCT, with the screening data forming the baseline assessment for the trial. PDM was defined as fasting plasma glucose > 6.1 mmol/l but < 7.0 mmol/l, or a 2-hour post-glucose reading > 7.8 mmol/l but < 11.1 mmol/l. If a participant had an OGTT result in the range for diabetes mellitus, they were recalled for a second confirmatory test. In accordance with the World Health Organization criteria, diabetes mellitus was defined as a fasting blood glucose ≥ 7.0 mmol/l and/or 2-hour plasma glucose of ≥ 11.1 mmol/l. Any participant found to have diabetes mellitus at baseline was excluded from the study and returned to their general practitioner (GP) for commencement of standard care.

Other samples collected were lipids, liver function tests, glycated haemoglobin (HbA_{1c}), biomarkers and whole genetic blood samples. A number of anthropometric data were also collected; these consisted of weight, BMI, waist circumference, hip circumference and blood pressure (using the average of three readings). The 7-day step count was assessed using a sealed piezoelectric pedometer (NL-800; New Lifestyles Inc., Lee's Summit, MO, USA). A questionnaire was also administered, which consisted of a number of validated tools to assess various aspects of diet, physical activity and psychosocial well-being. The Dietary Instrument for Nutrition Education was used to assess dietary fat and fibre intake; the Health State Descriptive System and European Quality of Life-5 Dimensions (EQ-5D) explored quality of life; the Hospital Anxiety & Depression Scale examined depression and anxiety; the Brief Illness Perception Questionnaire looked at cognitive and emotional representations of illness; and the International Physical Activity Questionnaire (short form) determined health-related physical activity.

Outcome measures

The primary outcome of the screening phase was the proportion of people detected with PDM or T2DM using the LPRS (positive predictive value). Secondary outcomes included the response rate to the invitation to screening. Those with PDM took part in phase two, that is, the diabetes mellitus prevention cluster RCT.

Phase two: diabetes mellitus prevention cluster randomised controlled trial study design

Phase two was a cluster RCT providing a structured intervention for people with PDM, with randomisation at practice level to negate contamination between individual participants. The practices were randomly assigned 1 : 1 to either the standard care or the intervention arm by a researcher, who was independent of the study team, using stratification by list size (< 6000, ≥ 6000) and ethnicity (percentage South Asian $< 21\%$, $\geq 21\%$). Phase two was designed to adhere to internationally recognised criteria for developing complex interventions and for undertaking and reporting cluster RCTs.

Participants within the standard care practices were managed by national guidelines for the condition, whereby participants were given an information booklet and general lifestyle advice by their GP or practice nurse. The booklet gave information on risk factors for T2DM and discussed how dietary and lifestyle changes and increased physical activity could be used to prevent progression of the disease.

Participants in the intervention practices were given the same written information as the control group and were also invited to attend 'Let's Prevent', which was a 6-hour structured group education session. In addition, they received a telephone call every 3 months from nursing staff, trained to offer ongoing support in behaviour change and to encourage participants to achieve their individual goals. Finally, each participant within the intervention arm was invited to attend a 3-hour refresher session once per year.

The intervention

The structured group education programme was named Let's Prevent, and sessions followed a detailed written curriculum. It consisted of 1 full day (6 hours) or 2 half-days (3 hours each). For black and minority ethnic groups in which the English language was not readily spoken, four sessions of 3 hours each were delivered by educators and interpreters.

Outcome measures

The primary outcome was progression to diabetes mellitus at 3 years in people with screen-detected PDM.

The main secondary outcomes included:

- changes in participant's glucose levels: HbA_{1c}, blood glucose levels fasting and post-glucose load
- change in cardiovascular risk as calculated by the Framingham risk calculator
- 7-day step count
- presence of metabolic syndrome as defined by the National Cholesterol Education Program Adult Treatment Panel III
- cost-effectiveness of the intervention.

All outcomes recorded at the screening visit (listed above), which form the baseline data for the trial, were also collected at 6, 12, 24 and 36 months.

Inclusion criteria

- Diagnosed with PDM.
- Aged 40–75 years if English speaking, or 25–75 years if South Asian.
- Able to attend group education sessions.

Exclusion criteria

- Unable to give consent.
- Unable to attend group education sessions.
- Diagnosed with diabetes mellitus at screening.
- Required an interpreter for a language other than a South Asian one.

Sample size and statistical methods

Assuming a 3-year cumulative conversion rate to T2DM of 35% in the control group, an intraclass correlation of 0.05, an average of 17 participants per practice and a dropout rate of 20%, we calculated that we would need 374 participants per group to detect a 40% risk reduction in the intervention group (data from 44 practices, with 80% power at the 5% significance level). Analysis of the primary outcome was on an intention-to-treat basis. The event rate per 1000 person-years was calculated by intervention group. Cox proportional hazards models with the intervention group as a covariate were fitted; practices were assumed to have the same frailty. Hazard ratios (HR) along with their 95% confidence intervals (CIs) were presented. The analysis was repeated excluding those from the intervention group who did not attend the education sessions (per-protocol analysis). All other outcomes were analysed using a multilevel model taking into account the practice-level clustering.

Cost-effectiveness analysis

A within-trial cost-effectiveness analysis of the trial results was conducted, using resource use information collected as part of the study and using quality-adjusted life-years (QALYs) as our primary outcome measure. QALYs were calculated as the mean of the utility scores (from EQ-5D or health-state descriptive system) at the start and end of the year, or as the mean at the start, end and 6-month point in the case of the first year. The intervention cost (£200.34) was the total cost of providing the initial intervention, refreshers and support over the 3-year trial period. One-off costs, such as educator training and teaching materials, were also included in the intervention cost calculation. Information on health-care use was recorded via participant self-reports in an economic questionnaire administered at 12-, 24- and 36-month follow-up points. Analysis did not include inpatient costs. We calculated an incremental cost-effective ratio (ICER) by dividing the mean cost difference between intervention and standard care groups by the mean QALY difference. We report the probability that the intervention is the most cost-effective option at a threshold of £20,000 per QALY gained.

Results

A total of 17,972 individuals from 44 practices identified through the risk score as being at high risk of T2DM were invited for screening, of whom 3449 (19.2%) attended. All received a 75-g OGTT. PDM was detected in 880 (25.5%) of those screened. Those with PDM were included in the trial; 36% were female, the average age was 64 years and 16% were from an ethnic minority group. Of those included in the trial, 131 participants developed T2DM over the 3-year follow-up period. There was a 26% reduced risk of developing T2DM in the intervention arm compared with standard care, but this did not reach statistical significance (HR 0.74, 95% CI 0.48 to 1.14; $p = 0.18$). This was increased when analysing per-protocol (HR 0.65, 95% CI 0.41 to 1.03; $p = 0.07$). There were also statistically significant improvements in HbA_{1c}, low-density lipoprotein cholesterol, psychosocial well-being, sedentary time and step count. The intervention was found to result in a net gain of 0.046 QALYs over 3 years at an overall cost of £168 per patient, with an ICER of £3643 and a probability of 0.86 of being cost-effective at a willingness-to-pay threshold of £20,000.

Conclusions

We have developed and validated a risk score for detecting those at high risk of undiagnosed PDM/T2DM. We have screened > 3400 people using a two-stage screening programme. The RCT showed that a relatively low-resource pragmatic programme fit for implementation in the UK NHS may lead to a reduction in T2DM and improved biomedical and psychosocial outcomes, and is cost-effective. Future research should focus on increasing attendance to both screening and prevention programmes and offering the programme in different modalities, such as web-based modalities.

Study registration

This trial is registered as ISRCTN80605705.

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