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A community based primary prevention programme for type 2 diabetes integrating identification and lifestyle intervention for prevention: the Let's Prevent Diabetes cluster randomised controlled trial☆

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ABSTRACT

Objectives. Prevention of type 2 diabetes (T2DM) is a priority in healthcare, but there is a lack of evidence investigating how to effectively translate prevention research into a UK primary care setting. We assessed whether a structured education programme targeting lifestyle and behaviour change was effective at preventing progression to T2DM in people with pre-diabetes.

Materials and methods. Forty-four general practices were randomised to receive either standard care or a 6 hour group structured education programme with an annual refresher course, and regular phone contact. Participants were followed up for 3 years. The primary outcome was progression to T2DM.

Results. Eight hundred and eighty participants were included (36% female, mean age 64 years, 16% ethnic minority group); 131 participants developed T2DM. There was a non-significant 26% reduced risk of developing T2DM in the intervention arm compared to standard care (HR 0.74, 95% CI 0.48, 1.14, $p = 0.18$). The reduction in T2DM risk when excluding those who did not attend the initial education session was also non-significant (HR 0.65, 0.41, 1.03, $p = 0.07$). There were statistically significant improvements in HbA1c (−0.06, −0.11, −0.01), LDL cholesterol (−0.08, −0.15, −0.01), sedentary time (−26.29, −45.26, −7.32) and step count (498.15, 162.10, 834.20) when data were analysed across all time points.

Conclusions. This study suggests that a relatively low resource, pragmatic diabetes prevention programme resulted in modest benefits to biomedical, lifestyle and psychosocial outcomes, however the reduction to the risk of T2DM did not reach significance. The findings have important implications for future research and primary care.

Introduction

Type 2 diabetes mellitus (T2DM) is associated with reduced quality of life and serious complications. The life expectancy of individuals with T2DM may be shortened by as much as 10 years, with most dying of cardiovascular diseases (CVD) (Roper et al., 2001). The management of T2DM consumes around 10% of health care expenditure (Hex et al., 2012). Consequently, the prevention of T2DM is a priority and has been highlighted by the NHS, UK, as one of four priority areas (NHS, 2014).

Pre-diabetes (PDM) is a high-risk state where glucose levels are elevated but do not reach the threshold for diagnosis of T2DM. Trials have unequivocally demonstrated that lifestyle interventions, which promote moderate to vigorous-intensity physical activity, a healthy diet and weight regulation, reduce the risk of progressing to T2DM by 30%–60% in those with PDM (Gillies et al., 2007). For example, the

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Finnish Diabetes Prevention Study (DPS) found that the risk of T2DM was reduced by 58% in those referred to an intensive lifestyle intervention compared to usual care over a three-year period (Tuomilehto et al., 2001). Consistent findings have been reported from the USA Diabetes Prevention Program (DPP) (Knowler et al., 2002).

Despite the strong evidence for lifestyle interventions in the prevention of T2DM, there has been a translational gap between trial evidence and implementation into routine care. This is predominantly due to the resource-intensive nature of lifestyle interventions tested. For example, in the first year of the DPP programme, participants received 16 1 h one-to-one counselling sessions followed by an average of eight additional contacts and two telephone consultations. The participants were also offered supervised exercise classes (Knowler et al., 2002). This intensity of care is incompatible with routine care pathways. Therefore, the emphasis needs to be shifted to examining the effectiveness of approaches designed for implementation within routine primary care. As healthcare services have differences in funding, organisation and infrastructure, programmes cannot be assumed to be generalisable across contexts. To date there has been a dearth of evidence concerning T2DM prevention in the UK, with small-scale projects showing mixed results (Yates et al., 2009; Dyson et al., 1997; Oldroyd et al., 2006; Bhopal et al., 2014).

This study assesses whether the Let's Prevent T2DM programme is effective at preventing progression to T2DM in people with PDM identified through a systematic screening pathway within primary care. Let's Prevent is a pragmatic, relatively low resource, group-based structured-education programme targeting lifestyle behaviour change specifically designed for implementation within a community setting.

Methods

The study had two phases. The first was a screening phase which identified people at risk of PDM/T2DM through the use of a screening tool that had been developed and validated for use within primary care (Gray et al., 2012a; Gray et al., 2012b). In the second phase, the participants who had been screened and found to have PDM progressed to the cluster RCT. The cluster RCT design has been described in detail elsewhere (Gray et al., 2012c). The trial randomised practices to avoid the risk of contamination. Ethical approval was sought and the study involved practice level and individual level informed consent. The recruitment took place between May 2009 and June 2011, with follow-up data collected up to July 2014.

Practices and participants

Practices in Leicestershire, UK, were recruited and randomised using a computer-generated list 1:1 to either the standard-care or intervention arm by an independent researcher, using stratification by list size (<6000, ≥6000), and ethnicity (percentage South Asian <21%, ≥21% — taken from ADDITION-Leicester study; Webb et al., 2010) with a block size of four. Practices and participants were informed of their allocation in the result letters after the screening/baseline measurements were complete. Eligible participants were identified from recruited practices via a two-stage screening process. The Leicester Diabetes Practice Risk Score was used in each practice to identify people at high-risk of PDM/T2DM for invitation to screening (Gray et al., 2012a). The top 10% of patients with the highest score fulfilling the inclusion criteria were invited. The inclusion criteria for screening were ages 40 to 75 if White European, or 25–75 years if South Asian. Participants were excluded if they were unable to give informed consent, pregnant or lactating, had established diabetes or a terminal illness, or if they required an interpreter for a language other than one of the locally used South Asian languages accommodated within this study. All those agreeing to take part received an oral glucose tolerance test (OGTT). Only participants who were identified as having PDM (IFG and/or IGT WHO 1999 criteria; World Health Organization, 1999) during screening took part in the RCT. In one small practice (list size = 1650) no participants were identified with PDM and this practice was excluded.

The screening–visit data formed the baseline assessment for the RCT; the participants were followed up at 6, 12, 24 and 36 months.

Interventions

All participants received an information booklet which included information on risk factors for T2DM, and how dietary and lifestyle changes and increased physical activity can prevent progression to T2DM.

The participants in the intervention practices were invited to attend the Let's Prevent programme (Gray et al., 2012c), which tailors the widely delivered DESMOND structured-education programme into a prevention context (Davies et al., 2008; Gillett et al., 2010).

Let's Prevent was delivered to groups of ten over 6 h, either over a full-day or two half-days, by two trained educators. The programme was underpinned by a theoretical basis with a philosophy centred on patient empowerment. The aim was to increase knowledge and promote realistic perceptions of PDM, and to promote healthy behaviour, with the aims of reducing body weight by 5%, limiting total and saturated fat intake to 30% and 10% of total energy intake respectively, increasing fibre intake and promoting physical activity. The physical activity section incorporated the successful PREPARE structured-education programme (Yates et al., 2009), based on providing participants with a pedometer and enabling the formation of personalised step-per-day goals. The content and educational resources used within the programme were further tailored to the need of local South Asian populations, including delivery through interpreters where required. The educators were trained using an accredited pathway, and received ongoing support and quality development to ensure consistent delivery.

The participants were invited to 3 h refresher sessions at 12 and 24 months to reinforce key messages, review risk factors and update action plans. In addition, the participants received a 15-minute telephone call every 3 months from healthcare professionals trained to offer ongoing support in behaviour change. Those who did not attend the initial session were not invited to the refresher sessions, but continued to be followed up.

Outcome measures

All outcomes were measured at the participant level. The primary outcome was progression to T2DM during 3 years. T2DM diagnosis was defined according to WHO 1999 criteria/guidelines (World Health Organization, 1999). Participants without symptoms of diabetes in whom the initial OGTT showed T2DM were recalled for a second test to confirm the diagnosis. Participants found to have T2DM at baseline were excluded. Following the update of the WHO diagnostic criteria to include HbA1c (World Health Organization, 2011) we obtained a protocol amendment in January 2013 allowing HbA1c ≥ 6.5% to become part of the diagnostic criteria for T2DM within this study. Therefore T2DM was diagnosed using OGTT prior to January 2013, and with either an OGTT or HbA1c post January 2013. The participants and their GP were informed of the results. The diagnosis of T2DM within primary care was also captured by self-report followed by confirmation through GP records. Participants diagnosed with T2DM after baseline remained in the study to complete the questionnaires and other biomedical data, but did not undertake further OGTTs.

A full list of the secondary outcomes assessed at each time point is described elsewhere (Gray et al., 2012c), these included: lipid levels, HbA1c, medical and medication history, blood pressure, weight, waist and body mass index (BMI). The participants also completed a questionnaire containing a number of validated questionnaires which assessed total self-reported physical activity, subsequently reported as metabolic equivalent minutes per week (METS.mins/week) (Craig et al., 2003), diet reported as a unitless fibre, total fat and unsaturated fat score (Roe et al., 1994), illness beliefs (Broadbent et al., 2006), anxiety and depression (Zigmond and Snaith, 2006), quality of life (Sintonen and Pekurinen, 1993) and sleep pattern; resource usage data and EQ-5D responses were also collected for the cost-effectiveness analysis (Gusi et al., 2010). The participants also wore a sealed pedometer (NL-800, New Lifestyles, Inc., Lees Summit, MO, USA) with a seven-day memory during waking hours to provide habitual ambulatory activity (average daily step count derived by summing total accumulated steps and dividing by days worn). For the purposes of this study, at least three valid days of data were required; a valid day constituted at least 10 h of wear time (Tudor-Locke and Bassett, 2004).

Other secondary outcomes included change in cardiovascular risk as calculated by the Framingham risk calculator, and presence of metabolic syndrome as defined by NCEP ATP III.

Sample size

The sample size takes into account the clustering by GP practice. Assuming a three-year cumulative conversion rate to T2DM of 35% in the standard-care group (equivalent to 117 events per 1000 follow-up years), an intraclass correlation of 0.05, and 17 participants per practice (equal clusters assumed), we needed 280 per group to detect a 40% risk reduction in the intervention group. Allowing for a 25% drop-out rate, a total of 748 participants needed to be recruited.

Statistical analysis

A statistical-analysis plan was agreed before data were available. Practice and participant level characteristics were compared by group, using either means (SD) or medians (IQR) for continuous variables, and counts and percentages for nominal variables. Cluster randomisation gives balance with respect to cluster-level covariates but can lead to imbalance in participant level covariates; therefore differences were assessed using t-tests and chi-squared tests.

Progression to T2DM was analysed on an intention-to-treat basis (ITT). The event rate per 1000 person years was calculated by group. The participants were censored at the date of their last clinical appointment or at diagnosis of T2DM. Cox proportional hazard models with group as a covariate were fitted; practices were assumed to have the same frailty. Hazard ratios (HR) and 95% confidence intervals were presented. Subgroup analyses were performed by PDM status (IGT, IFG, IGT and IFG, HbA1c 6.0%–6.4%).

For all secondary outcomes, participants who developed T2DM during the study had their last value from before their diagnosis carried forward for the remainder of the study. This method was used in a previous similar study (Yates et al., 2009). All secondary outcomes were analysed using generalised estimating equation models with an exchangeable correlation structure, which adjusted for clustering. For binary outcomes we used a logit link with a binomial distribution for the outcome, and for continuous outcomes we used an identity link with a normal distribution. The analysis was repeated at each time point. The missing outcomes were not replaced and we derived an average of continuous outcomes over time. This procedure measures the cumulative effect of the intervention and has the maximum number of participants.

Subsidiary analyses were carried out for the main secondary outcomes at 12 and 36 months. The analysis was repeated: (i) excluding those from the intervention group who did not attend the initial Let's Prevent education session (per-protocol); and (ii) imputing any missing values for the secondary outcomes using multiple imputation (ITT). The imputation was carried out using the command MI in Stata. MI replaces missing values with multiple sets of simulated values to complete the data, performs standard analysis on each completed dataset, and adjusts the obtained parameter estimates for missing-data uncertainty using Rubin's rules to combine estimates.(Rubin, 2004) Adjustments were not made for multiple testing. All results from the planned analyses have been reported and p values were interpreted taking into account the overall pattern of the results. Statistical significance was set at 5%. All analyses were conducted using Stata version 13.

Results

Overall, 43 practices were included; ranging in size from 1650 to 24,000. The median number of participants with PDM recruited per practice was 23 in the standard-care arm and 17 in the intervention arm; the number recruited per practice ranged from 2 to 49. In total 880 participants were recruited (433 standard care, 447 intervention, Fig. 1). At 36 months 76% of the intervention group attended compared to 79% in the standard-care arm ($p = 0.43$). Compared to those who attended at 36 months, non-attendees were more likely to be smokers, and from more socially-deprived locations (Table A.1). Of those participants from practices randomised to the intervention, 101 (22.6%) did not attend the initial education session and were excluded in per-protocol analyses. Compared to those who attended, non-attendees were younger, more likely to be male, from more socially deprived locations, more likely to be smokers, and less physically active (see Table A.2).

At baseline higher levels of deprivation and smokers were seen in the intervention group (Table 1). Weight ($p = 0.0002$), BMI ($p = 0.003$) and waist circumference ($p = 0.0001$) were significantly higher in the standard-care group compared to the intervention group.

Development of T2DM

131 participants developed T2DM during a median follow-up of 3 years; this equates to 60.32 events per 1000 person years (95% CI 50.82, 71.58). Lower rates were seen in the intervention group: 57.60 events per 1000 person years compared to 63.16 events per 1000 person years in the standard-care group (Figure A.1). The hazard ratio (HR) showed a non-significant 26% reduced risk of developing T2DM in the intervention arm compared to standard-care ($p = 0.18$). The effect was greater (35% reduction) in the per-protocol analysis albeit still non-significant ($p = 0.07$) (Table 2). The risk of developing T2DM in the intervention group compared to standard-care was similar across all sub-groups of PDM. The ICC for the development of T2DM was 0.02 (95% CI 0, 0.05).

Secondary outcomes

In both groups improvements were seen for many secondary outcomes, see Table 3 for a summary and A.3–A.6 for the full results. A statistically significant reduction of 0.06% in HbA1c was seen in the intervention group compared to the standard-care group when analysing the mean across all time points. Significant reductions in LDL-cholesterol were seen at 12 months and overall. For all other outcomes, apart from systolic blood pressure, a greater improvement was seen in the intervention group than the standard-care group at 36 months, but none of these reached statistical significance. No differences were seen for CVD/CHD risk outcomes or the presence of metabolic syndrome.

Improvements during the study were seen in illness perceptions, quality of life and anxiety in the intervention group compared to the standard-care group. Fat intake was not significantly reduced in the intervention group compared to the standard-care group, but statistically significant increases in unsaturated fat were reported. Although no differences between the intervention and standard-care group were seen in the self-reported levels of activity, a significant reduction in sitting time of 30 min per day or more was seen in the intervention group at 12 and 24 months and overall, compared to the standard-care group. There was also an increase in objectively measured average daily step-count in the intervention group of 450–500 steps per day at all time points, with a significant effect seen at 12, 36 months and overall.

Subsidiary analyses

In the per-protocol analysis, significant reductions at 36 months were seen for fasting (−0.12 mmol/l), 2-hour (−0.35 mmol/l) and HbA1c (−0.11%) in the intervention compared to standard-care (Table 4). The increase in step count in the intervention group compared to standard-care was increased in the per-protocol analysis. For the intention-to-treat analysis, the interpretation of the results for the secondary outcomes assessed did not change.

Discussion

To our knowledge, this is the first study investigating the effectiveness of a T2DM prevention programme within primary care in the UK. We have shown that a pragmatic, low-resource, three-year T2DM prevention programme, based on a 6 h , group-based, structured-education session followed by two annual group-based sessions and nine telephone contacts, can lead to improvements in markers of metabolic health, psychosocial well-being, and health behaviour. The primary outcome of the study was reduction in progression to T2DM; although non-significant, a modest 25% reduction in progression was observed in those receiving the education intervention, which increased

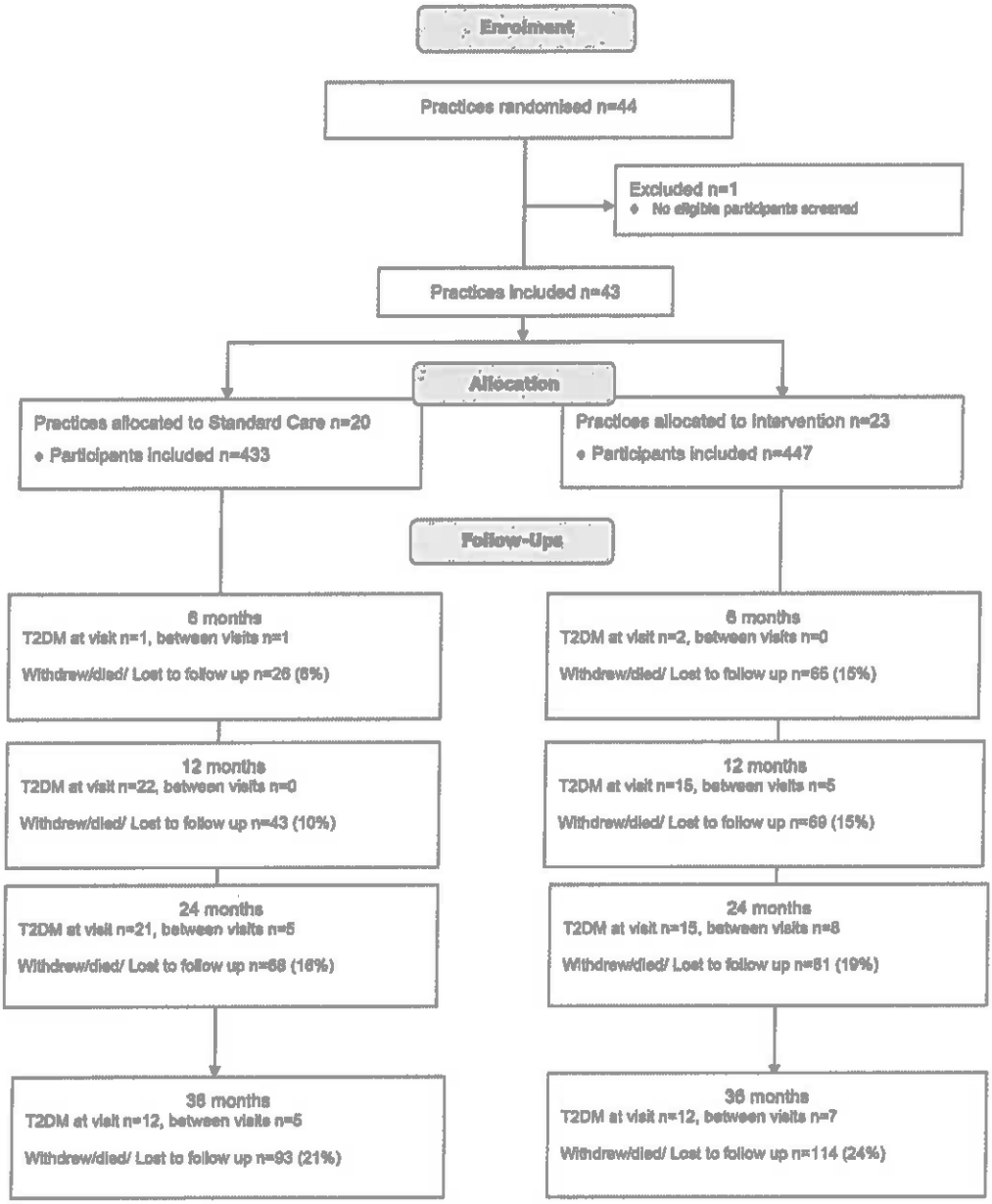

Fig. 1. Flow of practices and participants through the trial.

to 35% when excluding those who did not attend the first education session.

Our study has several strengths and limitations. The strengths include using a rigorous design to evaluate the effectiveness of the programme specially developed for delivery within a multiethnic primary care setting. The primary limitation was that this study was underpowered due to the discrepancy between predicted and observed incidence rates of T2DM. The observed incidence rate of 63.16 events per 1000 person years in the standard-care arm was substantially lower than anticipated, and consistent with those observed in non-intervention settings (Morris et al., 2013). This acted to substantially reduce the study power, resulting in wider confidence intervals and a greater likelihood of a type 2 error. In addition, the variation in cluster size was greater than planned (the number of participants recruited per practice ranged from 2 to 49), further diluting power. However, the estimates of the ICC (0.05) and the inflation for dropout (25%) used were adequate (0.02 and 24% respectively). Although the reduction in the risk of T2DM was not statistically significant, the effect size was similar to the Indian Diabetes Prevention programme, which reported a 28.9% reduction in the risk of T2DM following a lifestyle intervention (Ramachandran et al., 2006). Limitations inherent in cluster randomised studies were also observed here, particularly achieving a balance in participant characteristics across groups: important differences at baseline were observed, with the intervention group having higher levels of social deprivation and smoking rates, but with lower levels of BMI and waist circumference. These differences could have acted to confound the result. Finally, the generalisability of the findings should be assessed cautiously. Of those invited for screening, 19% attended (Gray et al., 2012b). Although this uptake rate is consistent with other studies in similar populations (Aujla et al., 2010; Webb et al., 2011) and reflects the difficulty of recruiting a multiethnic urban population into prevention studies, it may limit the generalisability of the findings. Higher rates of uptake would be expected in a non-research setting: for example, the NHS Health Checks programme has 40% uptake (Dalton et al., 2011). Due

Table 1
Baseline characteristics.
Data given as mean (SD) unless otherwise stated.

	Standard care	Intervention
Individual level		
Number of participants	433	447
Age	63.9 (7.9)	63.9 (7.6)
Male *n* (%)	278 (64.2)	282 (63.1)
White European, *n* (%)	363 (84.3)	377 (84.5)
Deprivation, median (IQR)	10.1 (6.3, 18.1)	13.4 (8.4, 24.4)*
Current smoker, *n* (%)	22 (5.1)	38 (8.5)*
Prescribed statins, *n* (%)	171 (43.3)	184 (44.2)
Prescribed antihypertensives, *n* (%)	270 (62.4)	275 (61.5)
History CVD, *n* (%)	78 (18.0)	75 (16.8)
HbA1c (%)	6.1 (0.4)	6.1 (0.4)
HbA1c (mmol/mol)	42.8 (4.6)	43.2 (4.7)
Fasting glucose	5.6 (0.7)	5.7 (0.7)
2-hour glucose	8.8 (1.6)	8.9 (1.7)
Total cholesterol (mmol/l)	5.1 (1.1)	5.0 (1.0)
HDL cholesterol (mmol/l)	1.4 (0.5)	1.4 (0.5)
LDL cholesterol (mmol/l)	3.0 (0.9)	3.0 (0.9)
Triglycerides (mmol/l)	1.7 (1.0)	1.7 (0.9)
Systolic blood pressure (mmHg)	147.7 (17.7)	147.9 (20.7)
Diastolic blood pressure (mmHg)	86.2 (10.6)	86.6 (11.0)
Heart rate (bmp)	69.1 (12.1)	68.3 (13.1)
Weight (kg)	94.4 (18.9)	89.9 (16.6)*
BMI (kg/m^2)	33.1 (5.8)	32.0 (5.2)*
Waist circumference (cm)	111.3 (13.2)	108.0 (12.4)*
Average steps per day	6308.12 (3094.44)	6137.97 (2791.02)
IFG only, *n* (%)	51 (11.8)	57 (12.8)
IGT only, *n* (%)	308 (71.1)	301 (67.3)
IFG and IGT, *n* (%)	74 (17.1)	89 (19.9)
HbA1c 6.0%–6.4% (%)	216 (50.1)	205 (46.7)
CHD 10 year risk***	14.5 (8.6)	14.5 (8.5)
CVD 10 year risk***	20.2 (11.8)	20.3 (11.9)
Cluster level		
Number of practices	20**	23
Median participants per practice (IQR)	23 (8, 34)	17 (7, 30)
Range participants per practice	2–41	3–49
Median practice size (IQR)	6932 (4008, 10,069)	5429 (3356, 8780)
High South Asian population, *n* (%)	2 (10.0)	4 (17.4)

HDL: High-density lipoprotein; LDL: Low-density lipoprotein; IGT: Impaired glucose tolerance; IFG: Impaired fasting glucose; CHD: Coronary heart disease; CVD: Cardiovascular disease; IQR: Inter-quartile range.

* Groups differ significantly ($p < 0.05$).

** One practice randomised to standard care had no eligible participants.

*** Only calculated for those of WE or SA ethnicity between the ages of 35 and 75.

to ethical constraints, no data were extracted from primary care regarding those invited for screening. Therefore we cannot compare the characteristics of the invited cohort to those who attended to establish if there was any potential for bias. A study of similar design conducted in the same area screening for T2DM found that the 22% who attended the screening were older and more likely to be female compared to non-attenders (Webb et al., 2011). Only 77% of the intervention group attended the initial education, ad-hoc analyses suggest that the intervention effect can be increased as attendance increases. Future studies should focus on strategies to increase uptake to screening and attendance/compliance with the programme.

We observed several improvements in secondary outcomes. Importantly, there was evidence that the programme reduced threatening perceptions of PDM, anxiety and improved overall quality of life. This is consistent with other structured-education programmes (Davies et al., 2008). These benefits were mirrored by modest improvements in health behaviour. For example, the intervention group reported healthier dietary fat profile, sitting on average for 26 min less per day and undertaking 498 more steps per day compared to standard-care. This change equates to an increase of 35 min of purposeful walking per week (Tudor-Locke and Bassett, 2004). This is similar to that reported in the Early Activity in Diabetes (ACTID) diet and physical activity intervention for those with newly diagnosed T2DM, which was also conducted in primary care (Andrews et al., 2015). The protocol defined a priori number secondary outcomes (Gray et al., 2012c), and this reflects the nature of the intervention, which targets a number of aspects of health and well-being. We have not adjusted for multiple testing, which may have increased the type 1 error rate (Freemantle, 2001). The results seen here reflect those seen in other similar trials (Ramachandran et al., 2006; Lindström et al., 2003), and have been interpreted in terms of clinical as well as statistical importance.

Our study extends evidence for efficacy of lifestyle interventions in the prevention of T2DM into in a primary care setting. There is now evidence internationally that T2DM prevention programmes can be tailored for, and translated into, primary health care and community settings, with modest short-term effects on markers of health status, such as body weight (Dunkley et al., 2014). However, longer-term studies designed to quantify effectiveness on reducing progression to T2DM are lacking. This has resulted in a lack of evidence-based solutions that might enable primary care organisations to conform to NICE guidance for the prevention of T2DM (National Institute of Health and Clinical Excellence, 2012). By utilising structured education, Let's Prevent was purposefully designed to harness existing infrastructure within routine primary care. Structured education has been recommended in the management of T2DM by NICE since 2003 (National Institute for Health and Clinical Excellence, 2003). DESMOND is one of the most prominent nationally available T2DM structured-education programme, and the only UK programme tested within a multi-centred RCT to quantify effectiveness and cost-effectiveness (Davies et al., 2008; Gillett et al., 2015). Here we show that this approach can be adapted to the prevention of T2DM within a diverse multiethnic PDM population whilst using less than 25% of the contact time seen in other efficacy trials. Future research is needed to investigate how the approach used in Let's Prevent can be tailored to individual preferences concerning the frequency and format of contact. In particular, utilising web-based platforms is likely to receive a growing focus in the future.

A separate paper assesses the cost effectiveness of the intervention. In brief, this showed that the education programme was associated with higher costs (£168) and higher quality of life (0.046 QALYs) compared to the standard care group over 3 years. Therefore, the Let's Prevent programme is likely to be cost effective at a willingness to pay a threshold of £20,000 per QALY gained (Leal et al., 2015).

Conclusion

We have shown that a relatively low-resource, pragmatic T2DM prevention programme can lead to modest improvements to biomedical, lifestyle and psychosocial outcomes without significantly reducing the risk of T2DM. The findings have important implications for future research and primary care.

Funding and ethics

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Contributor statements

MJD is the principal investigator for the Let's Prevent programme grant, initiated the project, commented on the drafts of the paper and approved the final version. MJD is the guarantor for the paper and affirms that the manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the

Table 2
Development of T2DM overall and by PDM diagnosis.
HR (95% CI) takes into account clustering.

	Standard care	Intervention	HR	95% CI	p value
Intention to treat[a]			0.74	0.48, 1.14	0.18
Events, n (%)	67 (15.5)	64 (14.3)			
Rate per 1000 person years (95% CI)	63.16 (49.71, 80.24)	57.60 (45.09, 73.59)			
Per protocol			0.65	0.41, 1.03	0.07
Events, n (%)	67 (15.5)	51 (14.7)			
Rate per 1000 person years (95% CI)	63.16 (49.71, 80.24)	53.04 (40.31, 69.80)			
PDM subgroup					
IGT alone	34 (11.2)	32 (10.7)	0.79	0.45, 1.38	0.41
IFG alone	7 (14.3)	6 (10.5)	0.52	0.15, 1.83	0.31
IGT and IFG	26 (32.9)	26 (28.3)	0.51	0.22, 1.16	0.11
HbA1c 6.0–6.4	36 (15.2)	27 (11.9)	0.65	0.38, 1.12	0.12

[a] This is the same as complete case as there are no missing data for the primary outcome.

study have been omitted, and that any discrepancies from the study as planned (and, if relevant, registered) have been explained. LJG wrote the statistical analysis plan, cleaned and analysed the data, and drafted and revised the paper. JT developed the Let's Prevent programme, commented on the drafts of the paper and approved the final version. AG had input into the design of the study, the collection of data, led the cost effectiveness analysis, commented on the drafts of the paper and approved the final version. JTu had input into the design of the

Table 3
Secondary outcomes.
Coefficients show the mean effect of the intervention compared to standard care adjusted for baseline value and cluster (full table given in Tables A3–6).

	6 months	12 months	24 months	36 months	Overall
Fasting glucose	NR	0.001 (−0.10, 0.10)	−0.06 (−0.16, 0.04)	−0.05 (−0.18, 0.07)	0.0004 (−0.10, 0.10)
2-hour glucose	NR	0.08 (−0.23, 0.39)	−0.07 (−0.37, 0.22)	−0.14 (−0.46, 0.18)	−0.03 (−0.28, 0.22)
HbA1c (%)	−0.07 (−0.12, −0.01)*	−0.04 (−0.10, 0.02)	−0.10 (−0.20, −0.004)*	−0.07 (−0.18, 0.04)	−0.06 (−0.11, −0.01)*
Total cholesterol (mmol/l)	−0.06 (−0.18, 0.05)	−0.07 (−0.16, 0.02)	−0.02 (−0.12, 0.08)	−0.11 (−0.23, 0.02)	−0.06 (−0.14, 0.01)
HDL cholesterol (mmol/l)	0.003 (−0.05, 0.06)	−0.01 (−0.07, 0.05)	0.004 (−0.06, 0.07)	−0.02 (−0.08, 0.05)	0.01 (−0.04, 0.05)
LDL cholesterol (mmol/l)	−0.06 (−0.15, 0.04)	−0.10 (−0.018, −0.02)*	−0.02 (−0.09, 0.05)	−0.09 (−0.19, 0.01)	−0.08 (−0.15, −0.01)*
Triglyceride (mmol/l)	−0.01 (−0.16, 0.14)	0.05 (−0.05, 0.15)	−0.05 (−0.15, 0.05)	−0.06 (−0.17, 0.06)	−0.001 (−0.08, 0.08)
Body weight (kg)	−0.10 (−0.72, 0.51)	−0.27 (−1.17, 0.63)	−0.49 (−1.48, 0.50)	−0.26 (−1.17, 0.65)	−0.10 (−0.85, 0.66)
BMI (kg/m^2)	−0.03 (−0.24, 0.19)	−0.11 (−0.42, 0.21)	−0.14 (−0.50, 0.21)	−0.05 (−0.38, 0.27)	−0.02 (−0.28, 0.25)
Waist circumference (cm)	−0.91 (−2.03, 0.20)	−0.11 (−1.37, 1.15)	−0.82 (−2.03, 0.40)	−0.79 (−1.73, 0.14)	−0.45 (−1.32, 0.42)
Systolic BP (mmHg)	1.17 (−1.45, 3.79)	1.22 (−0.85, 3.30)	−1.26 (−3.79, 1.28)	0.55 (−2.09, 3.19)	0.81 (−0.97, 2.60)
Diastolic BP (mmHg)	−0.22 (−1.90, 1.46)	0.80 (−0.66, 2.26)	−0.37 (−1.92, 1.19)	−0.49 (−2.15, 1.17)	0.24 (−0.82, 1.30)
Heart rate (bpm)	−1.31 (−2.90, 0.28)	−0.61 (−1.84, 0.61)	−0.68 (−2.00, 0.65)	−0.52 (−1.83, 0.78)	−0.66 (−1.58, 0.27)
CHD 10-year risk	−0.18 (−0.84, 0.48)	−0.14 (−0.73, 0.45)	−0.68 (−1.40, 0.04)	−0.23 (−1.07, 0.60)	−0.35 (−0.81, 0.11)
CVD 10-year risk	0.28 (−0.77, 1.32)	0.01 (−0.74, 0.76)	−0.74 (−1.64, 0.15)	0.04 (−1.07, 1.14)	−0.14 (−0.64, 0.35)
Metabolic syndrome[a]	NR	1.05 (0.78, 1.43)	0.81 (0.60, 1.09)	1.10 (0.83, 1.46)	1.10 (0.83, 1.46)
Illness perception score (BIPQ)[b]	−1.46 (−3.13, 0.21)	−2.06 (−4.03, −0.09)*	−2.47 (−4.16, −0.78)**	−1.16 (−2.69, 0.37)	−1.61 (−2.92, −0.30)*
Quality of life score (15D)[c]	0.01 (−0.001, 0.01)	0.01 (−0.002, 0.02)	0.01 (−0.002, 0.02)	0.02 (0.01, 0.03)**	0.01 (0.001, 0.02)*
Anxiety score (HADS)[d]	−0.21 (−0.57, 0.15)	−0.40 (−0.77, −0.03)*	−0.09 (−0.40, 0.21)	−0.11 (−0.44, 0.23)	−0.28 (−0.54, −0.02)*
Depression score (HADS)[d]	−0.08 (−0.42, 0.26)	−0.34 (−0.81, 0.14)	−0.09 (−0.45, 0.27)	−0.05 (−0.44, 0.35)	−0.21 (−0.57, 0.16)
Diet (DINE):					
Fibre intake	−1.69 (−4.68, 1.29)	0.97 (−1.27, 3.21)	−1.64 (−4.68, 1.39)	1.53 (−0.94, 4.00)	−1.01 (−3.11, 1.08)
Fat intake	−1.41 (−4.60, 1.77)	0.45 (−2.62, 3.51)	−0.55 (−4.04, 2.95)	−3.60 (−7.52, 0.31)	−0.72 (−2.92, 1.48)
Unsaturated fat intake	0.18 (−0.12, 0.48)	0.32 (0.05, 0.58)*	0.50 (0.24, 0.76)***	0.38 (0.12, 0.63)**	0.33 (0.15, 0.51)***
Subjective physical activity (IPAQ):					
Total METS	352.71 (−570.24, 1275.65)	447.31 (−220.84, 1115.46)	415.06 (−234.47, 1064.59)	−19.82 (−568.05, 528.41)	428.37 (−175.19, 1031.93)
Sitting time (min)	−27.26 (−63.34, 8.83)	−25.94 (−49.95, −1.92)*	−38.96 (−66.15, −11.78)**	−20.15 (−43.91, 3.60)	−26.29 (−45.26, −7.32)**
Objective physical activity:					
Average steps per day	591.38 (63.61, 1119.16)*	551.76 (117.27, 986.25)*	466.30 (−65.50, 998.10)	535.76 (12.71, 1058.81)*	498.15 (162.10, 834.20)**
Sleep:					
Hours slept last night	NR	0.04 (−0.15, 0.22)	−0.05 (−0.18, 0.09)	−0.10 (−0.26, 0.06)	−0.05 (−0.18, 0.08)
Average hours asleep in 24 h	NR	0.10 (−0.16, 0.35)	−0.03 (−0.23, 0.17)	0.11 (−0.06, 0.27)	0.01 (−0.16, 0.18)

HDL: High-density lipoprotein; LDL: Low-density lipoprotein; BMI: Body mass index; IGT: Impaired glucose tolerance; IFG: Impaired fasting glucose; CHD: Coronary heart disease; CVD: Cardiovascular disease; BIPQ: Brief Illness Perception Questionnaire; 15D: 15-dimensional; HADS: Hospital Anxiety and Depression Scale; DINE: Dietary Instrument for Nutrition Education; IPAQ: International Physical Activity Questionnaire; METS: Metabolic equivalents.

[a] Data shown OR (95% CI).
[b] Higher score reflects a more threatening view of illness.
[c] Higher score reflects better quality of life.
[d] Higher score reflects worse levels of anxiety/depression.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

Table 4
Key secondary outcomes – subsidiary analysis.
Coefficients show intervention effect adjusted for baseline value and cluster. Complete case – data analysed according to randomised group; those with missing data excluded on a case-by-case basis. Per protocol – those randomised to the intervention who did not attend the initial education are excluded. Intention to treat – data analysed according to randomised group, all randomised participants included. Missing data imputed using multiple imputations.

	Complete case		Per protocol		Intention to treat	
	12 months	36 months	12 months	36 months	12 months	36 months
Fasting glucose	0.001 (−0.10, 0.10)	−0.05 (−0.18, 0.07)	0.03 (−0.14, 0.08)	−0.12 (−0.23, −0.01)*	0.02 (−0.09, 0.13)	−0.02 (−0.13, 0.08)
2-hour glucose	0.08 (−0.23, 0.39)	−0.14 (−0.46, 0.18)	0.03 (−0.30, 0.36)	−0.35 (−0.61, −0.09)**	0.10 (−0.22, 0.42)	−0.10 (−0.45, 0.25)
HbA1c (%)	−0.04 (−0.10, 0.02)	−0.07 (−0.18, 0.04)	−0.04 (−0.10, 0.02)	−0.11 (−0.21, −0.01)*	−0.02 (−0.08, 0.04)	−0.07 (−0.17, 0.04)
CHD 10-year risk	−0.14 (−0.73, 0.45)	−0.23 (−1.07, 0.60)	−0.11 (−0.75, 0.53)	−0.15 (−1.05, 0.75)	−0.16 (−0.81, 0.49)	−0.48 (−1.34, 0.37)
CVD 10-year risk	0.01 (−0.74, 0.76)	0.04 (−1.07, 1.14)	−0.02 (−0.77, 0.73)	0.12 (−1.03, 1.28)	−0.12 (−0.96, 0.72)	−0.55 (−1.50, 0.39)
Metabolic syndrome	1.05 (0.78, 1.43)	1.10 (0.83, 1.46)	0.74 (0.52, 1.05)	0.77 (0.56, 1.04)	1.05 (0.78, 1.43)	1.10 (0.83, 1.46)
Average steps per day	551.76 (117.27, 986.25)*	535.76 (12.71, 1058.81)*	777.48 (336.66, 1218.31)**	634.27 (1419.41, 2665.56)*	576.47 (110.37, 1042.56)*	469.52 (29.47, 909.57)*

CHD: Coronary heart disease; CVD: Cardiovascular disease.
* $p < 0.05$.
** $p < 0.01$.

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Conflicts of interests

Laura J Gray, Jacqui Troughton, Alastair Gray, Jaakko Tuomilehto and Azhar Farooqi declare no support from any organisation for the submitted work, no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years, and no other relationships or activities that could appear to have influenced the submitted work. Melanie J Davies, Kamlesh Khunti and Thomas Yates declare no support from any organisation for the submitted work and no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; MJD, KK and TY were members (KK chair) of the NICE PH 38 (Preventing type 2 diabetes: risk identification and interventions for individuals at high risk) Programme Development Group.

Transparency document

The transparency document associated with this article can be found, in the online version.

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Appendix A. Supplementary data

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