DOI:
10.3399/bjgp18X696185

Document Version
Peer reviewed version

Cluster randomised controlled trial of a nurse-led psychological intervention for type 2 diabetes: Diabetes-6 study

Khalida Ismail, Kirsty Winkley, Nicola de Zoysa, Anita Patel, Margaret Heslin, Helen Graves, Stephen Thomas, Dominic Stringer, Daniel Stahl, Stephanie A Amiel

Corresponding author:

Khalida Ismail

Institute of Psychiatry, Psychology and Neuroscience, King's College London

Weston Education Centre, 10 Cutcombe Road

London SE5 9RJ

Email: khalida.2.ismail@kcl.ac.uk

Telephone: 020 7848 5131

14

Abstract

Background

Suboptimal glycaemic control in type 2 diabetes (T2D) is common and associated with psychological barriers.

Aim

We tested whether it was possible to train practice nurses in six psychological skills (Diabetes 6 (D6)) based on motivational interviewing (MI) and basic cognitive behaviour therapy (CBT) and whether integrating these with diabetes care was associated with improved glycaemic control over 18 months compared to standard care.

Design and Setting

A two-arm, single-blind, parallel cluster randomised controlled trial conducted in primary care practices (n=24) (ISRCTN trial registration: ISRCTN75776892).

Method

Adult participants (n=334) with T2D and HbA1c ≥69.4 mmol/mol (lowered to ≥64 mmol/mol midstudy to increase recruitment) at least once in previous 18 months and at recruitment were randomised to receive 12 sessions of either the D6 intervention or standard care over 12 months. The practices nurses were trained in the six psychological skills and their competencies were measured by standardised rating scales. All sessions were audiotaped. The primary outcome was change in HbA1c at 18 months from randomisation; secondary outcomes were change in systolic and diastolic blood pressure, body mass index, waist circumference, depressive symptoms, harmful alcohol intake, diabetes-specific distress, and cost-effectiveness.

Results

Using intention-to-treat analysis, there was no significant difference between D6 intervention and standard care in HbA1c (absolute mean difference -0.79 mmol/mol, 95% CI -5.75–4.18) or for any of the secondary outcomes. The competency level of D6 nurses was below the beginner proficiency level and similar to the standard care nurses.

Conclusion

Training nurses in MI and basic CBT to support self-management did not lead to improvements in glycaemic control or other secondary outcomes in people with T2D at 18 months. It was also unlikely to be cost-effective. Furthermore, the increased contact with standard care nurses did not improve glycaemic control.

Keywords: Type 2 diabetes, Self-management, Motivational interviewing, Cognitive behavioural therapy, Glycaemic control

How this fits in

The evidence that low intensity psychological interventions to support self-management in people with poorly controlled type 2 diabetes in primary care setting is limited.

It is not known whether practice nurses can be trained to deliver low intensity psychological treatments to support self-management in type 2 diabetes.

Training on low intensity psychological interventions based on motivational interviewing and basic cognitive behaviour therapy led to basic proficiency in these skills but this was not maintained.

Offering more sessions with practice nurses to support self-management in people with persistent hyperglycaemia does not lead to improvement in glycaemic control in type 2 diabetes.

Introduction

Around half of people with type 2 diabetes (T2D) have persistent suboptimal glycaemic control despite evidence based pathways based on national guidance.[1–3] Psychological factors, such as depressive symptoms and diabetes-specific fears are common in T2D and associated with reduced self-management.[4,5] Addressing these psychological barriers could lead to improvement in glycaemic control.

Common psychological interventions include motivational interviewing (MI)[6] and cognitive behaviour therapy (CBT).[7,8] Recent randomised controlled trials (RCT) suggest that the effect of low-intensity psychological interventions on glycaemic control is lower than reported in systematic reviews.[9–11]

One of the roles of the practice nurse is to support diabetes self-management. Hospital diabetes specialist nurses can be trained to competently deliver MI and basic CBT skills with improvement in glycaemic control in type 1 diabetes[12] and psychological interventions could be delivered by nurses in research settings.[13] We defined a package of six psychological skillsets for T2D (Diabetes 6 (D6)) of similar intensity to low-level psychological treatments for common mental disorders in the NHS.[14] We tested in a cluster RCT whether training practice nurses in D6 skills was associated with increased competency than nurses not receive the training, and whether the D6 intervention was more effective than standard care in improving suboptimal glycaemic control in people with T2D over 18 months and in improving secondary outcomes (such as lipids, depressive symptoms), and if it was cost-effective.

Method

Trial design

D6 was a pragmatic parallel two-arm cluster RCT design for 18 months. GP practices with ≥6000 patients registered in the Lambeth, Southwark, Lewisham, Wandsworth, and Bexley Clinical Commissioning Groups (representing a resident population of 1.43 million), were invited to participate if they had a practice nurse delivering diabetes care. Recruitment of patients began after each practice consented to randomisation. Randomisation of clusters was conducted in two phases, as recruitment of practices and patients had slowed down following the organisational uncertainties preceding the implementation of the Health and Social Care Act 2012. This Act re-organised the UK's National Health Service (NHS), dismantling current organisational structures and creating new ones for funding, management, accountability and regulation.[15]

Patients

Inclusion criteria were: adults aged 18–79 years, duration of T2D for ≥2 years, persistent suboptimal glycaemic control defined as International Federation of Clinical Chemistry (IFCC) HbA1c ≥69.4 mmol/mol (National Glycohemoglobin Standardization Program (NGSP) 8.5%) on two occasions (at least once in the preceding 18 months and the second one at recruitment) while on at least two oral diabetes medication (metformin and one other), and/or requiring insulin therapy to ensure that efforts to optimise medical care had been offered to the patient.[15] The IFCC HbA1c was lowered to ≥64 mmol/mol (NGSP 8%) in Phase 2 to increase recruitment.

Exclusion criteria were: severe mental disorders; terminal illnesses and end-stage diabetes complications; morbid obesity (body mass index (BMI) >40 kg/m^2 in Phase 1 and >50 kg/m^2 in Phase 2); non-ambulatory; no phone/internet access; non-English-speaking; and receiving psychological treatments elsewhere. Patients who had Patient Health Questionnaire-9 (PHQ-9) depressive scores >20 were excluded if they had psychotic depression or active suicidal ideation.[16]

Baseline measures

Baselines measures before randomisation were: age, gender, self-reported ethnicity, occupation, employment status, and smoking status. Complication status included: neuropathic ulcer risk by perception of 10g monofilament; retinopathy coding of the most recent annual standardised digital retinal photography; nephropathy using the urinary albumin:creatinine ratio (ACR); and history of macrovascular complications.

Randomisation

Randomisation of practices (unit of cluster) was conducted by an independent statistician using a random number generator to assign equal numbers of practices to each arm at each phase. For allocation concealment, an independent manager held the randomisation list in password-locked computer.

Intervention

Group 1: Standard care

The nurse delivered diabetes care in both groups as recommended by national guidance, which included diabetes self-management education, monitoring of biomedical status, and giving clinical information and advice.[17] To control for attention, standard care nurses offered the same number of sessions as D6. This consisted of 12 sessions, each 30 minutes in duration, over 12 months. The sessions were held in routine primary care clinics and audiotaped.

Group 2: Standard care plus Diabetes 6

The theory underlying MI is that the patient's state of ambivalence (resistance versus willingness to make lifestyle changes) is the core psychological construct that needs addressing.[6] MI is a directive, counselling style which encourages patients to change behaviours using collaborative, non-judgmental, and affirming communications. The theory underlying CBT is that barriers to diabetes self-management are maintained by unhelpful thoughts (e.g., *if I can't cure diabetes, what's the point?*), unhelpful behaviours (e.g., missing insulin doses), and distressing emotions (e.g., low mood/anxiety when seeing a high blood glucose reading).[18,19] Identifying and challenging these cognitive barriers are effective in changing behaviours.[20] The D6 nurses were trained to integrate diabetes care with six skills drawn from MI and CBT, as follows : 1. Active listening; 2. Managing resistance; 3. Directing change; 4. Supporting self-efficacy; 5. Addressing health beliefs; and 6. Shaping behaviours. This consisted of 12 sessions, each 30 minutes in duration, over 12 months. The sessions were held in routine primary care clinics and were audiotaped.

The Motivational Interviewing Treatment Integrity (MITI) Scale (version 3.1.1)[21] and Behaviour Change Counselling Index (BECCI)[22] were used to compare competencies in both groups. The middle 20 minutes of sessions were rated by two independent psychologists trained in MITI and the BECCI was rated by a clinical psychologist, blind to treatment allocation.

Outcomes

The follow-up was reduced from 24 to 18 months secondary to the delays in recruitment. The primary outcome was change in HbA1c (mmol/mol) from cluster randomisation to 18 months measured centrally (King's College Hospital NHS Foundation Trust) by affinity chromatography (Primus Ultra2, Kansas City, USA). If the study HbA1c were missing at 18-month, we included the 15-month HbA1c as this clinically overlaps with the 3-month window for 18-month HbA1c. The following secondary outcomes were change in systolic and diastolic blood pressure using an electronic sphygmomanometer; BMI, and waist circumference (cm); depressive symptoms using the PHQ-9;[16] the Alcohol Use Disorders Identification Test (AUDIT);[23] and the Diabetes Distress Scale, which measures diabetes-specific psychological burden.[24] A fasting blood sample was used for HbA1c, total cholesterol, and triglycerides.

Sample size

An IFCC HbA1c 10.9 mmol/mol (NGSP HbA1c 1%) difference in D6 compared to standard care was the minimal clinically significant reduction at 18 months, considering that standard care may produce a 2.2 mmol/mol (NGSP HbA1c 0.2%) reduction in HbA1c (equivalent to a moderate effect size of d=0.55). Assuming 20% dropout, we needed 360 patients to achieve

80% power at a two-sided alpha-level of 5%, with 20 practices with 18 patients each per arm. We assumed two practices per arm would dropout, thus requiring 24 practices with a total patient sample of 24x18=432 patients. After adjusting for clustering by practice (clustering intra-correlation coefficient (ICC)=0.05) and an inflation factor of 1.7, the final required sample size was 81x1.7=138 patients per arm.

We recruited 334 patients of which 231 had at least one follow-up in 24 clusters. The average cluster size was therefore 10 patients per cluster, smaller than our assumed size of 15 patients per cluster with a post-hoc power of 77% at two-sided alpha-level of 5%.[25]

Statistical analysis

Data were analysed using STATA 13. The sample characteristics were described as means (standard deviation (SD)) or as proportions (percentage). A comparison of patient list size and Index of Multiple Deprivation (IMD) 2010 rank score by practices that participated versus those that did not was conducted using Student's t-test. The IMD 2010 score is a composite index of relative deprivation at a small area level, based on seven domains of deprivation: income, employment, health deprivation and disability, education, skills and training, barriers to housing and services, crime and disorder, and living environment.[26] A linear mixed-effects model estimated group differences in HbA1c levels between D6 and standard care groups at 18 months. Nurse was included as a random effect as the unit of randomisation. Secondary outcomes were also analysed using linear mixed models to estimate group differences at 18 months.

Twenty-nine participants with HbA1c <64 mmol/mol were mistakenly recruited because of coding errors by the research team during assessment of eligibility and this mistake was only

discovered after randomisation. Therefore, they were retained for the ITT. We performed a sensitivity analysis by including a binary covariate of this protocol violation using maximum likelihood under the missing at random assumption. Sensitivity to missingness in HbA1c was assessed by investigating and including predictors of missingness in the model and by using multiple imputation for the missing values of HbA1c.

For further details of the protocol, including the economic evaluation, see Appendix 1.

Results

We invited 116 practices, 26 agreed to participate and two dropped out before randomisation (Figure 1; Appendix2:Table 1) and 995 potentially eligible participants. Of the 451 who consented for eligibility, 334 were recruited. Twelve practice clusters were randomly assigned to standard care (n=164 participants) and 12 to standard care plus D6 (n=170). One D6 practice dropped out after randomisation, before the nurse received the training, and before all patients were recruited (those who consented remained in the ITT analysis). Invited practices that participated (n=24) compared to those that did not (n=89) had higher mean patient list sizes (12180 (SD=5099) vs. 10091 (SD=3894), p=0.03) but no difference in IMD score (10049 (SD=6910) versus 12441 (SD=7785), p=0.17). Table 1 presents the baseline characteristics of the sample.

Figure 1 here; Table 1 here

The mean number of sessions attended was 7.42 (SD=4.4) and 8.20 (SD=4.4) in the D6 and standard care groups, respectively.

Primary outcome data at 18-month follow-up were collected for 219 (65.6%) participants and a further 12 had 15-month HbA1c data, providing 231 participants. There was a non-significant larger proportion with missing HbA1c in the D6 group compared to standard care (35.9% versus 32.9%, respectively) (Appendix 2:Table 2) and more likely to be African/Caribbean or Asian/Other ethnicity. In the ITT analysis, there was no significant difference in mean HbA1c at follow-up in the D6 group compared to the standard care group (table 2). The ICC for the clustering effect of nurse was 0.02 (95% CI 0.001–0.37). Linear mixed models showed no significant effects of the intervention on the secondary outcomes including BMI, blood pressure, fasting triglyceride, or psychological distress (table 2).

Table 2 here

Results were similar for the sensitivity analyses when: using practice as the clustering variable in place of nurse as cluster; including a binary covariate for the 29 participants with baseline HbA1c <64 mmol/mol; including ethnicity and history of stroke as predictor of missingness at follow-up; or using multiple imputation to account for missingness in HbA1c (Appendix 2:Table 2). There was no evidence of an association between the number of D6 sessions attended and HbA1c at 18 months within the D6 group (-0.44 mmol per additional session attended, 95% CI -1.28–0.41).

Intervention costs were higher in the D6 group (mean difference £276, 95% CI £225–£327) (Table 3) due to greater training costs but there were no differences in mean total health and social care costs (adjusted mean difference £150, 95% CI -£34–£333) or QALY gains at 18 months (Appendix 4).

Table 3 here

The inter-rater reliability for the MITI global domains of spirit and empathy was 0.87 and 0.91 respectively so we combined both sets of ratings and derived the mean score for each domain. We rated 69 sessions (4.0% of all available recordings) for fidelity from 33/170 and 36/164 patients from the D6 and standard care groups respectively (Table 4). The level of competency in the D6 group was below the beginner proficiency level in all the scales for MI and BECCI. Except for a slightly higher proportion of open questions in D6, and a slightly larger reflection/question ratio in standard care, there were no statistically significant differences in the remaining mean MI domain scores or BECCI scores.

Table 4 here

There were 43 serious adverse events (cardiovascular (n=11), injury (n=5), cancer (n=4), infection (n=5), diabetes-related (n=3), psychiatric (n=2), and other (n=10)), reported after 18 months for 38 different participants (D6 n=14; standard care n=24) and 2 deaths from cancer, with no difference between the two groups

Discussion

Summary

Training nurses in MI and basic CBT to support self-management did not lead to improvements in glycaemic control, or any other secondary outcomes, in people with T2D and persistent hyperglycaemia compared to attention control at 18 months from randomisation. Further, it was unlikely to be cost-effective.

Strengths and limitations

This was a pragmatic design set in real-world, inner-city, primary care representing the ethnic and social diversity of people with T2D.[27] Only a few other RCTs have achieved similar ethnicity distributions.[28–34] This was a high risk group for diabetes complications. We selected a cluster design to reduce contamination of the intervention in the control group. Contamination is the process whereby an intervention intended for members of the trial (intervention or treatment) arm of a study is received by members of another (control) arm leading to a risk of under estimation of the effect.[35] We assessed contamination by comparing the competencies in the intervention and control group. The hypothesis was that the control group would have lower competencies than the D6 group. As both groups had similar and borderline beginner proficiency competencies (which is probably the pre-training level of competency) we concluded it was unlikely there was contamination. We developed a theoretically informed intervention and an evidence-based manual. We measured fidelity (which is the same measure as competency in this study) to the intervention. We controlled for the non-specific effect of receiving more attention by D6 by offering similar number of sessions to patients randomised to the control group. We were only slightly underpowered at 77% power compared to the 80% originally proposed. The upper limit of the 95% confidence interval of the estimated treatment effect for HbA1c (4.8 mmol/mol) was less than estimated treatment reductions in meta-analyses.[36] The comprehensive within-trial economic evaluation assessed all relevant health and social care costs.

The limitations of D6 included a 20% uptake of practice participation, despite the offer of generous backfill payments. The main reasons given by the practices when feedback was informally asked were the pressures to deliver current services with limited resources exacerbated by co-incidental national restructuring of primary care services creating organisational uncertainty. Data missingness for the economic analyses was high, however,

imputing missing data confirmed the lack of cost-effectiveness of D6. We did not obtain sufficient repeated measures of HbA1c. We failed to achieve a minimum level of beginner proficiency in motivational interviewing in the D6 group therefore unable to conclude that motivational interviewing is not effective in supporting self-management.

Comparison with existing literature

Although there have been over 40 RCTs in this field since the last review,[36] only three had defined poor glycaemic control (HbA1c ≥64 mmol/mol) as an inclusion criterion and showed no benefit from psychological support andonly one of these was delivered by nurse care managers.[37–39] Recent pragmatic RCTs of similar interventions included samples with near optimal glycaemic control with less room for improvement in the primary outcome.[10,11,40] Our sample had sustained high HbA1c so we may have selected a more severe group not suitable for practitioners with lower levels of psychological skill competencies.[28–34]

We are one of a handful of RCTs to include fidelity and competency (a complex, laborious, and expensive process evaluation).[41,42] On average patients attended only 50% of sessions in either group. This is a common observation in psychological interventions.[43] However, no dose-response relationship was observed.

Implications for research and/or practice

There are several potential nurse, patient and methodological reasons for the non-significant effect of D6. The nurses did not self-select and may not have had the generic psychotherapist factors often attributed as the active ingredients in psychological treatments.[44] D6 nurses had concerns about over-stepping their professional roles, lacking confidence, and/or resented the

297 extra workload. [45] The low competencies in most MI and CBT domains suggest that practice
298 nurses may need longer periods of training or should self-select for generic psychotherapist
299 skills in advance. Our findings may also reflect the difficulty of engaging this high risk
300 clinical group but with low levels of worry. Even offering more nurse support in the form of
301 more frequent sessions did not lead to improved glycaemic control. In exit interviews,
302 patients stated they lacked time (although the majority was not employed) and difficulties in
303 establishing a rapport with the nurses as reasons for dropout (unpublished observations). One
304 methodological explanation is that we selected HbA1c, strongly associated to the levels of
305 glycaemia, as a surrogate outcome for diabetes complications. However, a landmark RCT[46]
306 and a meta-analysis of RCTs[47] aimed at intensive glycaemic control have failed to observe
307 consistently a positive effect on reduction of complications of diabetes or global mortality
308 and there may be even a negative effect of increased mortality when tight glycaemic control
309 is the aim. Perhaps these negative findings represent an opportunity to focus on psychological
310 interventions to improve other outcomes such as blood pressure, lipids or a composite
311 outcome. Another methodological implication is whether the duration of the intervention and
312 the follow up was too short. Brief psychological interventions are designed to be exactly that,
313 with the added advantage of being cheap and not too demanding on the patient. However, our
314 patients had a long history of poor self-management and may have needed a longer duration
315 of therapy. Whether longer therapy would be pragmatic to be funded as a RCT or in the NHS
316 is to be debated and is showing promise for chronic depression.[48]

317 The implication for clinical practice is that low-intensity psychological interventions
318 delivered at low level of competencies may not be as effective in supporting self-
319 management in people with T2D and longstanding suboptimal glycaemic control as
320 previously thought.

A conceptual dilemma is that theoretical frameworks for MI and CBT assume that mental health conditions remit (alcohol problems, smoking, depression) and this assumption does not apply to T2D which progressively worsen.[49]

We urgently need to reconsider what skills, what competencies, which workforce are the most effective in delivering psychological interventions to improve glycaemic control in people with T2D [50] before investing sparse funds into low intensity psychological treatments for improving glycaemic control in T2D.[51]

330

331 **Author degrees, positions, and affiliations:**

332 Khalida Ismail, MRCPsych, PhD, professor, Institute of Psychiatry, Psychology and
333 Neuroscience, King's College London, London, SE5 9RJ, UK

334 Kirsty Winkley, PhD, senior lecturer, Institute of Psychiatry, Psychology and Neuroscience,
335 King's College London, London, SE5 9RJ, UK

336 Nicole de Zoysa, DClinPsych, clinical psychologist, Diabetes Centre, King's College
337 Hospital NHS Foundation Trust, London, SE5 9RS, UK

338 Anita Patel, PhD, visiting professor, Institute of Psychiatry, Psychology and Neuroscience,
339 King's College London, London, SE5 8AF UK & director, Anita Patel Health Economics
340 Consulting Ltd, London, EC1V 2NX, UK

341 Margaret Heslin, PhD, research fellow, Institute of Psychiatry, Psychology and Neuroscience,
342 King's College London, London, SE5 8AF, UK

343 Helen Graves, PhD candidate, Institute of Psychiatry, Psychology and Neuroscience, King's
344 College London, London, SE5 9RJ, UK

345 Stephen Thomas, MRCP, MD, physician, Guys and St Thomas' NHS Foundation Trust SE1
346 9RT

347 Dominic Stringer, MSc, medical statistician, Institute of Psychiatry, Psychology and
348 Neuroscience, King's College London, London, SE5 8AF, UK

349 Daniel Stahl, PhD, reader and medical statistician, Institute of Psychiatry, Psychology and
350 Neuroscience, King's College London, London, SE5 8AF, UK

Stephanie A Amiel, FRCP, professor, Division of Diabetes and Nutritional Sciences, King's College London, London, UK SE1 9NH

Author Contributions

KI, SAA, DStahl, AP, SMT developed the hypotheses. SAA and KI led the conduct of the study; KW project managed and contributed to analysis, training and assessment of nurses; NDZ developed the Diabetes 6 manual, the protocol for fidelity and did the training and supervision of the nurses; DStashl was the senior trial statistician and led the statistical plan and DStringer conducted the statistical analysis; AP designed and led the economic evaluation and MH conducted the economic analysis. KI drafted the manuscript and all authors contributed to the drafts and approved final version.

Competing Interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf. KI has received honorarium from Eli-Lilly, Sanofi, Janssen and Sunovion for lectures at educational events. KW received honorarium from Atlantis Healthcare and NIHR grants. NDZ has received honorarium paid to employer by Eli Lilly for educational lecture.

Trial Funding

This research was part funded by the National Institute for Health Research (NIHR; Programme Grant for Applied Research RP-PG-0606-1142). KI, D Stahl, D Stringer were part funded by the NIHR Mental Health Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Ethical Approval

Ethical approval was granted by the King's College Hospital Research Ethics Committee (reference 09/H0808/97) and Primary Care Trusts (references RDLSLBex 534 and 2010/403/W). Changes to the protocol were approved by the Trial Steering Committee and the Research Ethics Committee. All participants gave written, informed consent and the trial was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki.

Acknowledgements

We would like to thank the practices and their nurses who gave so much of their time during a period of organisational insecurity, and to all the patients for participating. We would also like to thank the independent raters of the audiotapes, Pam Macdonald, Amy Harrison and Emma Shuttleworth, the members of the Independent Trial Steering Committee (Ms Shiela Burston, Dr Tim Clayton, Prof Simon Gilbody (Chair), Prof Simon Heller and Ms Lynne Priest) and Data Monitoring Ethics Committee (Professor Holman (Chair), Professor King and Dr Bartlett) and to Nicholas Magill NIHR Doctoral Fellow for help with the fidelity analysis, Rebecca Upsher PhD student for conducting the meta-analysis in the Appendix, the research assistants (Sara Mann, Robert Turner) and Kurtis Stewart for administrative support.

The corresponding author (KI) had full access to all the data in the study and had final responsibility for the decision to submit for publication. We attest that we have obtained appropriate permissions and paid any required fees for use of copyright protected materials.

Data Sharing

The protocol and patient-level data are available from the corresponding author upon request.

References

1. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS). Lancet. 1998;352:837–53.
2. Gaede P, Vedel P, Parving H-H, Pedersen O. Intensified multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: The Steno type 2 randomised study. Lancet. 1999;353:617–22.
3. Ryan AM, Krinsky S, Kontopantelis E, Doran T. Long-term evidence for the effect of pay-for-performance in primary care on mortality in the UK: A population study. Lancet. 2016;388:268–74.
4. Snoek FJ, Bremmer MA, Hermanns N. Constructs of depression and distress in diabetes: Time for an appraisal. Lancet Diabetes Endocrinol. 2015;3:450–60.
5. Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. Arch Intern Med. 2000;160:3278–85.
6. Miller W, Rollnick S. Motivational interviewing: helping people change. 3rd ed. New York: Guilford Press; 2013.
7. Beck AT. Thinking and depression: I. Idiosyncratic content and cognitive distortions. Arch Gen Psychiatry. 1963;9:324–33.
8. Beck AT. Cognitive therapy and the emotional disorders. New York: Meridian; 1976.
9. Ismail K, Winkley K, Rabe-Hesketh S. Systematic review and meta-analysis of randomised controlled trials of psychological interventions to improve glycaemic control in patients with type 2 diabetes. Lancet. 2004;363:1589–97.

10. Juul L, Maindal HT, Zoffmann V, Frydenberg M, Sandbaek A. Effectiveness of a Training Course for General Practice Nurses in Motivation Support in Type 2 Diabetes Care: A Cluster-Randomised Trial. PLoS One. 2014;9:e96683.

11. Heinrich E, Candel MJJM, Schaper NC, de Vries NK. Effect evaluation of a Motivational Interviewing based counselling strategy in diabetes care. Diabetes Res Clin Pract. 2010;90:270–8.

12. Ismail K, SM T, Maissi E, Al E. Motivational enhancement therapy with and without cognitive behavior therapy to treat type 1 diabetes: A randomized trial. Ann Intern Med. 2008;149:708–19.

13. Alam R, Sturt J, Lall R, Winkley K. An updated meta-analysis to assess the effectiveness of psychological interventions delivered by psychological specialists and generalist clinicians on glycaemic control and on psychological status. Patient Educ Couns. 2009;75:25–36.

14. NHS England. Adult Improving Access to Psychological Therapies programme [Internet]. 2015 [cited 2016 Sep 10]. Available from: https://www.england.nhs.uk/mental-health/adults/iapt/

15. Department of Health. Health and Social Care Act 2012: Chapter 7 [Internet]. United Kingdom; 2012. Available from: http://www.legislation.gov.uk/ukpga/2012/7/contents/enacted

16. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. JAMA. 1999;282:1737–44.

17. National Institute for Health and Care Excellence. Type 2 diabetes [Internet]. London: National Institute for Clinical Excellence; 2008. Available from: http://guidance.nice.org.uk/CG66

18. Beck J. Cognitive therapy: Basics and beyond. New York, NY: Guildford Press; 1995.

19. Hawton K, Salkovskis PM, Kirk J, Clark DM. Cognitive behaviour therapy for psychiatric problems: A practical guide. Oxford: Oxford Medical Publications; 1989.

20. Hofmann SG, Asnaani A, Vonk IJJ, Sawyer AT, Fang A. The efficacy of cognitive behavioral therapy: A review of meta-analyses. Cognit Ther Res. 2012;36:427–40.

21. Moyers T, Martin T, Manuel J, Miller W, Ernst D. Revised global scales: Motivational interviewing treatment integrity 3.1.1 (MITI 3.1.1). Unpubl manuscript, Univ New Mex Albuquerque, NM. 2010;

22. Lane C, Huws-Thomas M V, Hood K, Rollnick S, Edwards K, Robling M. Measuring adaptations of motivational interviewing: The development and validation of the behavior change counseling index (BECCI). Patient Educ Couns. 2005;56:166–73.

23. Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption-II. Addiction. 1993;88:791–804.

24. Polonsky WH, Fisher L, Earles J, Dudl RJ, Lees J, Mullan J, et al. Assessing psychosocial distress in diabetes: Development of the Diabetes Distress Scale. Diabetes Care. 2005;28:626–31.

25. Batistatou E, Roberts C, Roberts S. Sample size and power calculations for trials and quasi-experimental studies with clustering. Stata J. 2014;14:159–75.

26. Department for Communities and Local Government. Indices of Multiple Deprivation, Borough [Internet]. 2010 [cited 2016 Sep 1]. Available from: https://data.london.gov.uk/dataset/indices-multiple-deprivation-borough

27. Gulliford MC, Naithani S, Morgan M. Continuity of care and intermediate outcomes

of type 2 diabetes mellitus. Fam Pract. 2007;245–51.

28. Penckofer SM, Ferrans C, Mumby P, Byrn M, Emanuele MA, Harrison PR, et al. A psychoeducational intervention (SWEEP) for depressed women with diabetes. Ann Behav Med. 2012;44:192–206.

29. Piette JD, Richardson C, Himle J, Duffy S, Torres T, Vogel M, et al. A Randomized Trial of Telephonic Counseling Plus Walking for Depressed Diabetes Patients. Med Care. 2011;49:641–8.

30. Pladevall M, Divine G, Wells KE, Resnicow K, Williams LK. A Randomized Controlled Trial to Provide Adherence Information and Motivational Interviewing to Improve Diabetes and Lipid Control. Diabetes Educ. 2015;41:136–46.

31. Plotnikoff RC, Karunamuni N, Courneya KS, Sigal RJ, Johnson JA, Johnson ST. The Alberta Diabetes and Physical Activity Trial (ADAPT):A Randomized Trial Evaluating Theory-Based Interventions to Increase Physical Activity in Adults with Type 2 Diabetes. Ann Behav Med. 2012;45:45–56.

32. Sacco WP, Malone JI, Morrison AD, Friedman A, Wells K. Effect of a brief, regular telephone intervention by paraprofessionals for type 2 diabetes. J Behav Med. 2009;32:349–59.

33. Safren SA, Gonzalez JS, Wexler DJ, Psaros C, Delahanty LM, Blashill AJ, et al. A Randomized Controlled Trial of Cognitive Behavioral Therapy for Adherence and Depression (CBT-AD) in Patients With Uncontrolled Type 2 Diabetes. Diabetes Care. 2013;37:625–33.

34. Wolever RQ, Dreusicke M, Fikkan J, Hawkins T V, Yeung S, Wakefield J, et al. Integrative Health Coaching for Patients With Type 2 Diabetes. Diabetes Educ. 2010;36:629–39.

35. Keogh-Brown MR, Bachmann MO, Shepstone L, Hewitt C, Howe A, Ramsay CR, et al. Contamination in trials of educational interventions. Health Technol Assess [Internet]. 2007;11:iii, ix-107. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17935683

36. Ismail K, Maissi E, Thomas S, Chalder T, Schmidt U, Bartlett J, et al. A randomised controlled trial of cognitive behaviour therapy and motivational interviewing for people with Type 1 diabetes mellitus with persistent sub-optimal glycaemic control: A Diabetes and Psychological Therapies (ADaPT) study. Heal Technol Assess. 2010;14:1–101, iii–iv.

37. Keogh KM, Smith SM, White P, McGilloway S, Kelly A, Gibney J, et al. Psychological family intervention for poorly controlled type 2 diabetes. Am J Manag Care. 2011;17:105–13.

38. Li M, Li T, Shi BY, Gao CX. Impact of motivational interviewing on the quality of life and its related factors in type 2 diabetes mellitus patients with poor long-term glycemic control. Int J Nurs Sci. 2014;1:250–4.

39. Gabbay RA, Añel-Tiangco RM, Dellasega C, Mauger DT, Adelman A, Van Horn DHA. Diabetes nurse case management and motivational interviewing for change (DYNAMIC): Results of a 2-year randomized controlled pragmatic trial. J Diabetes. 2013;5:349–57.

40. Jansink R, Braspenning J, Keizer E, van der Weijden T, Elwyn G, Grol R. No identifiable Hb1Ac or lifestyle change after a comprehensive diabetes programme including motivational interviewing: A cluster randomised trial. Scand J Prim Health Care. 2013;31:119–27.

41. Waker CL. Effects of Motivational Interviewing on Diabetes Self-Management

Behaviors and Glycemic Control in Type 2 Diabetes: A Translational Study. University of Cincinnati; 2012.

42. Welch G, Zagarins SE, Feinberg RG, Garb JL. Motivational interviewing delivered by diabetes educators: does it improve blood glucose control among poorly controlled type 2 diabetes patients? Diabetes Res Clin Pract. 2011;91:54–60.

43. Community and Mental Health Team, Health and Social Care Information Centre. Psychological Therapies: Annual Report on the use of IAPT services: England 2014/15 [Internet]. 2015. Available from: http://content.digital.nhs.uk/catalogue/PUB19098/psyc-ther-ann-rep-2014-15.pdf

44. Baskin TW, Tierney SC, Minami T, Wampold BE. Establishing specificity in psychotherapy: A meta-analysis of structural equivalence of placebo controls. J Consult Clin Psychol. 2003;71:973–9.

45. Graves H, Garrett C, Amiel SA, Ismail K, Winkley K. Psychological skills training to support diabetes self-management: Qualitative assessment of nurses' experiences. Prim Care Diabetes. 2016;10:376–82.

46. Action to Control Cardiovascular Risk in Diabetes Study Group, Gerstein HC, Miller ME, Byington RP, Goff DC, Bigger JT, et al. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008;358:2545–59.

47. Hemmingsen B, Lund SS, Gluud C, Vaag A, Almdal T, Hemmingsen C, et al. Targeting intensive glycaemic control versus targeting conventional glycaemic control for type 2 diabetes mellitus. Cochrane database Syst Rev. 2011;CD008143.

48. Fonagy P, Rost F, Carlyle J, McPherson S, Thomas R, Pasco Fearon RM, et al. Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study (TADS). World

Psychiatry. 2015;14:312–21.

49. Mulder BC, Lokhorst AM, Rutten GEHM, van Woerkum CMJ. Effective Nurse Communication With Type 2 Diabetes Patients. West J Nurs Res. 2015;37:1100–31.

50. Young-Hyman D, de Groot M, Hill-Briggs F, Gonzalez JS, Hood K, Peyrot M. Psychosocial Care for People With Diabetes: A Position Statement of the American Diabetes Association. Diabetes Care. 2016;39:2126–40.

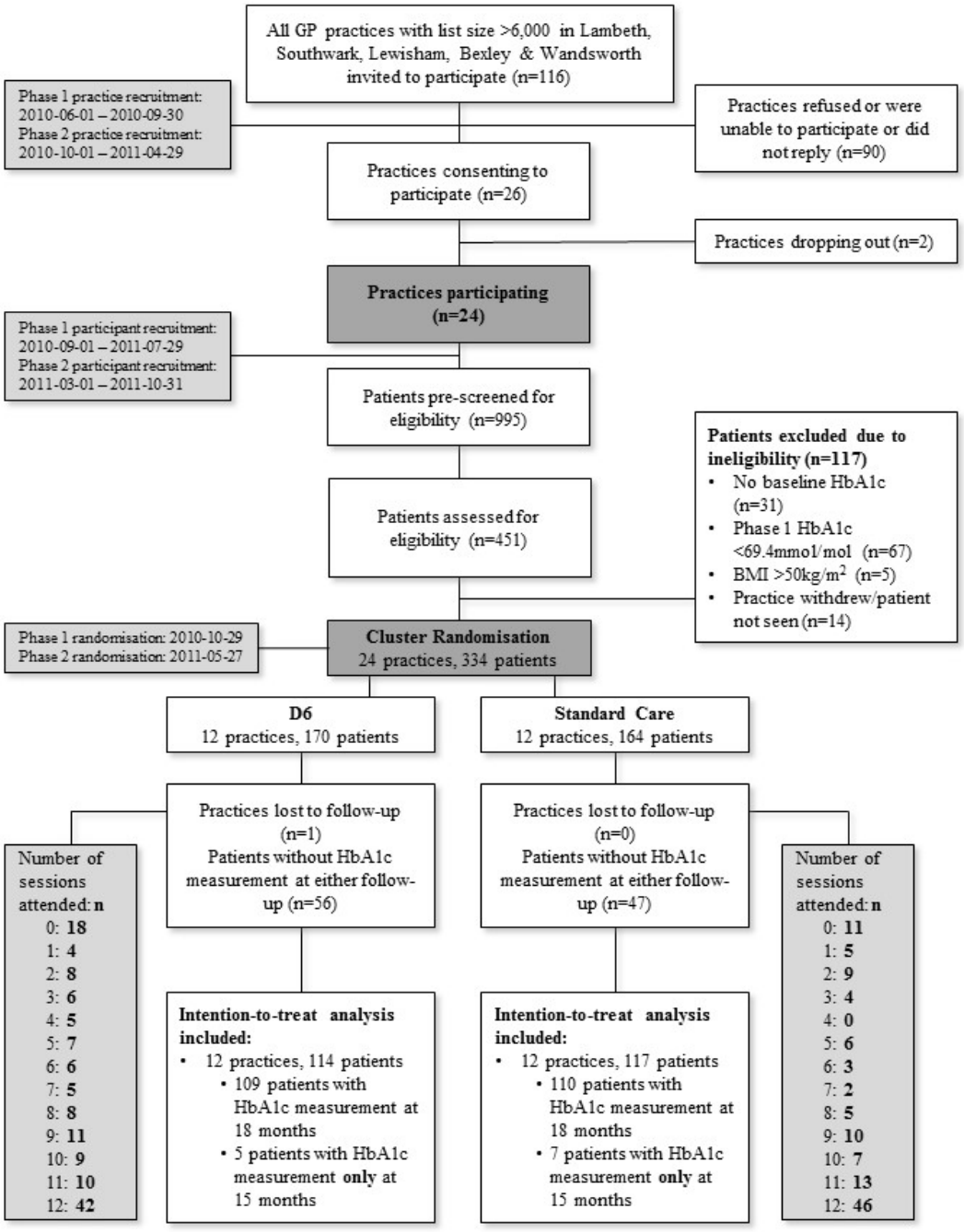
51. Donovan HS, Kwekkeboom KL, Rosenzweig MQ, Ward SE. Non-specific effects in psycho-educational intervention research. West J Nurs Res. 2009;31:983–98.

52. Ware J, Kosinski M, Keller SD. A 12-Item short-form health survey: Construction of scales and preliminary tests of reliability and validity. Med Care. 1996;34:220–33.

53. Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. J Health Econ. 2002;21:271–92.

552 **Figures**

553 **Figure 1. Diabetes 6 (D6) study flow chart**



554

555 **Tables**

Table 1. Baseline characteristics of participants randomly assigned to receive D6 or standard care.

Variable*	D6 (n=164)	Standard Care (n=170)	Total
Age (years)	59.0 (11.1)	58.9 (11.4)	58.9 (11.2)
Gender			
Male	82 (50.0%)	81 (47.7%)	163 (48.8%)
Female	82 (50.0%)	89 (52.4%)	171 (51.2%)
Ethnicity			
White	60 (36.8%)	74 (43.8%)	134 (40.4%)
African/Caribbean	81 (49.7%)	62 (36.7%)	143 (43.1%)
Asian/Other	22 (13.5%)	33 (19.5%)	55 (16.6%)
Relationship status			
Married or Cohabiting	82 (50.3%)	89 (52.7%)	171 (51.5%)
Separated/Divorced/Widowed	52 (31.9%)	45 (26.6%)	97 (29.2%)
Single	29 (17.8%)	35 (20.7%)	64 (19.3%)
Education level			
A-level or higher	47 (29.2%)	43 (25.8%)	90 (27.4%)
O-level or GCSE equivalent	68 (42.2%)	48 (28.7%)	116 (35.4%)
No formal qualifications	46 (28.6%)	76 (45.5%)	122 (37.2%)
Employment			
Yes[1]	69 (42.1%)	70 (41.2%)	139 (41.6%)
No[2]	95 (57.9%)	100 (58.8%)	195 (58.4%)
Borough			
Lambeth	83 (50.6%)	42 (24.7%)	125 (37.4%)
Southwark	25 (15.2%)	40 (23.5%)	65 (19.5%)
Lewisham	19 (11.6%)	52 (30.6%)	71 (21.3%)
Wandsworth	37 (22.6%)	24 (14.1%)	61 (18.3%)
Bexley	0 (0.0%)	12 (7.1%)	12 (3.6%)
Diabetes duration (years)	10 (7–13)	9 (5–12)	9 (6–12)
HbA1c (mmol/mol)	81.0 (17.1)	80.1 (19.1)	80.5 (18.1)
Body mass index (kg/m^2)	32.0 (5.6)	31.9 (6.6)	31.9 (6.1)
Systolic blood pressure (mm/Hg)	135.2 (16.9)	133.2 (17.3)	134.2 (17.1)
Diastolic blood pressure (mm/Hg)	79.5 (9.8)	79.0 (10.3)	79.2 (10.1)
Total cholesterol (mmol/L)	4.3 (1.1)	4.2 (1.2)	4.2 (1.2)
Fasting triglycerides (mmol/L)	1.7 (1.2)	1.7 (1.3)	1.7 (1.3)
Taking insulin			
Yes	75 (46.3%)	66 (39.8%)	141 (43.0%)
No	87 (53.7%)	100 (60.3%)	187 (57.0%)
Any retinopathy			
Yes	59 (35.9%)	65 (38.2%)	124 (37.1%)
No	105 (64.0%)	105 (61.8%)	210 (62.9%)
Albumin:Creatinine ratio			

Negative	65 (59.1%)	83 (69.8%)	148 (64.6%)
Positive	45 (40.9%)	36 (30.3%)	81 (35.4%)
Protein:Creatinine ratio			
Negative	33 (76.7%)	17 (77.3%)	50 (76.9%)
Positive	10 (23.3%)	5 (22.7%)	15 (23.1%)
Foot ulcers			
Yes	9 (5.6%)	12 (7.1%)	21 (6.4%)
No	152 (94.4%)	157 (92.9%)	309 (93.6%)
Macrovascular disease			
Yes	61 (37.2%)	55 (32.4%)	116 (34.7%)
No	103 (62.8%)	115 (67.7%)	218 (65.3%)
Patient Health Questionnaire-9 score			
≥10	31 (20.4%)	35 (22.4%)	66 (21.4%)
<10	121 (79.6%)	121 (77.6%)	242 (78.6%)
Diabetes Distress Scale (mean item score)	2.1 (1.7–2.7)	2.0 (1.6–2.7)	2.1 (1.6–2.7)

Data are n (%), median (IQR), or mean (SD), as appropriate.
[1]Yes = full-time, part-time, student or self-employed; [2]No = retired/unemployed/not seeking employment
***Values missing for age (n=1), ethnicity (n=2), relationship status (n=2), education level (n=6), diabetes duration (n=20), body mass index (n=5), systolic blood pressure (n=25), diastolic blood pressure (n=26), HbA1c (n=1), total cholesterol (n=53), fasting triglycerides (n=58), insulin (n=6), albumin:creatinine ratio (n=105), protein:creatinine ratio (n=269), foot ulcers (n=2), Patient Health Questionnaire-9 (n=26), diabetes distress scale (n=27).**

558

559

Table 2. Results from primary and secondary outcomes.			
Outcome at 18 months	**Participants with baseline measurements**	**Participants with measurements at 18 months**	**Estimated Mean Difference: D6 vs standard care (95% CI)**
Primary			
HbA1c (mol/mmol)*	332	231	-0.79 (-5.75–4.18)
Secondary			
Body mass index (kg/m^2)*	329	152	-0.08 (-1.12–0.97)
Total cholesterol*	281	140	-0.08 (-0.42–0.27)
Systolic blood pressure (mm/Hg)*	309	198	-1.35 (-6.85–4.14)
Diastolic blood pressure (mm/Hg)*	308	198	1.22 (-1.87–4.32)
Fasting triglycerides**	276	135	0.02 (-0.22–0.26)
Patient Health Questionnaire-9 Score***	308	114	-0.18 (-1.30–0.94)

*Estimates based on linear combination from linear mixed-effects model with fixed effects of time (15 or 18 months), an interaction between time and randomisation group, randomisation phase, borough and baseline values of the outcome, a random effect for GP practice nurse clustering and with unstructured covariance matrix to account for dependency of repeated observations.
**Estimates based on linear combination from linear mixed-effects model with fixed effects of time (15 months or 18 months), an interaction between time and randomisation group, randomisation phase, borough and baseline values of the outcome, a random effect for GP practice nurse clustering and with independent covariance structure due to convergence issues when estimating non-zero covariances.
***Collected at 18 months only. Estimates based on linear combination from linear mixed model with fixed effects of randomisation phase, borough, baseline value and random within-cluster effect of nurse with unstructured covariance matrix to account for dependency of repeated observations.
D6=Diabetes 6

560

561

562

563

564

Table 3. Mean costs (for the previous 6 months, £ sterling, 2011/12 prices), SF-12-based utility scores and QALY gains at baseline and/or 18 months.

Costs at baseline	D6			Standard care			UMD*	95% CI	AMD**	95% CI*
	valid n	*Mean £*	*SD*	*valid n*	*Mean £*	*SD*				
Health and social care costs	157	847	847	161	976	760	-129	-301–44	-96	-293–101
Costs at 18 months										
Health and social care costs, excluding intervention, without discounting	133	707	579	137	793	558	-85	-252–81	-71	-242–100
Health and social costs, excluding intervention, with discounting	133	684	560	137	766	540	-82	-243–78	-69	-234–96
Intervention costs	121	451	99	139	167	100	285	240–329	276	225–327
Health and social care costs, including intervention costs, with discounting for non-intervention costs	92	1184	572	107	1025	573	159	-39–357	150	-34–333
SF-12-based utility scores at baseline										
Utility	157	0.75	0.16	159	0.74	0.16	0.01	-0.03–0.04	0.01	-0.03–0.00
SF-12-based utility scores and QALY gains at 18 months										
Utility	60	0.79	0.13	53	0.75	0.13	0.04	-0.01–0.08	0.01	-0.03–0.06
QALY gain since baseline, without discounting	58	1.15	0.20	48	1.11	0.18	0.03	-0.04–0.10	0.01	-0.03–0.05
QALY gain since baseline, with discounting and interpolation to match 6-month period for cost data	58	0.37	0.06	48	0.36	0.06	0.01	-0.01–0.03	0.00	-0.01–0.02

SF-12 = Short Form 12; QALY = quality-adjusted life year; D6 = Diabetes 6; UMD=Unadjusted mean difference; AMD=adjusted mean difference.
*Intervention minus control. Comparisons include clustering for nurse.
**Intervention minus control. Cost comparisons account for clustering for nurse plus covariates for baseline cost, age, gender, marital status, ethnicity, duration of diabetes and baseline utility. QALY comparisons account for clustering for nurse plus covariates for age, gender, marital status, ethnicity, duration of diabetes and baseline utility.

565

566

567

568
569

Table 4. Group comparison for fidelity to MI and CBT.

MI domain[a]	D6	Standard care	*p*-value*
Global Spirit	3.23 (1.13)	2.87 (0.87)	0.14
Global Empathy	3.00 (2.00–4.00)	2.50 (2.00–3.00)	0.19
Proportion Complex Reflections	0.35 (0.20)	0.40 (0.17)	0.25
Proportion Open Questions	0.36 (0.17)	0.25 (0.10)	**<0.01**
Reflection/Question Ratio	0.57 (0.47–0.72)	0.74 (0.53–1.19)	**0.03**
Proportion Motivational Interviewing Adherent	0.58 (0.32)	0.54 (0.28)	0.51
CBT skills			
BECCI score	1.33 (0.56)	1.12 (0.55)	0.12

Data are mean (standard deviation), or median (interquartile range), as appropriate.
MI=Motivational interviewing; CBT=Cognitive behavour therapy; D6=Diabets 6; BECCI=Behaviour Change Counselling Index.
*Based on result of either a t-test or Mann-Whitney U-test.
[a]The MITI guidance indicates that to reach proficiency, a practitioner must achieve an average global spirit rating of 3.5, a reflection to question ratio of ≥1, ≥0.5 open questions relative to all questions, ≥0.4 complex reflections relative to all reflections, and ≥0.9 MI adherent.

570
571

572

573 **Appendices**
574 Appendices to: Cluster randomised controlled trial of a psychological intervention for type 2
575 diabetes.

576 **Table of Contents**

577

587

588

1 Full description of the study's methods

Trial design

D6 was a pragmatic parallel two-arm cluster RCT design for 18 months. Ethical approval was granted by the King's College Hospital Research Ethics Committee (reference 09/H0808/97) and by the respective Primary Care Trusts (reference RDLSLBex 534 and 2010/403/W). Changes to the protocol were approved by the Trial Steering Committee and the Research Ethics Committee. All participants gave informed consent, including access to their medical records.

All moderate-to-large GP practices (≥6000 patients registered) in the Lambeth, Southwark, Lewisham, Wandsworth, and Bexley Clinical Commissioning Groups, representing a resident population of 1.43 million in south London, UK, were invited to participate if they had a practice nurse delivering diabetes care. Practices were reimbursed £10k for seconding their nurse for one day/week for 15 months. We began recruiting patients after each practice consented to randomisation. The study was conducted in two phases as recruitment had slowed down significantly secondary to organisational uncertainties caused by the Health and Social Care Act 2012. This Act reorganised the UK's National Health Service (NHS), dismantling current organisational structures and creating new ones for funding, management, accountability, and regulation.[15]

Patients

The target population was adults with T2D who had persistent suboptimal glycaemic control despite care pathways based on national guidance,[17] therefore a group likely to have barriers to achieving optimal self-management. The study population was patients on diabetes registers of consenting practices. Using standardised search strategies, a list of potentially eligible patients based on the HbA1c (current and preceding 18 months) was generated by each practice and invited to participate. Three practices were eligible and willing to participate but did not have a nurse to second. A protocol change was made in Phase 2, which allowed a consenting practice without a nurse to amalgamate with an adjacent consenting practice which had a nurse, and each pair formed one cluster. The rationale was that the

patient catchment area was likely to be similar and that both practices used the same clinical guidance for diabetes care.

Inclusion criteria were adults aged 18–79 years, duration of T2D for ≥2 years, persistent suboptimal glycaemic control defined as HbA1c ≥69.4 mmol/mol on two occasions (at least once in the preceding 18 months and at recruitment) while on at least two oral diabetes medications (metformin and one other), and/or requiring insulin therapy. The HbA1c was lowered to ≥64 mmol/mol in Phase 2 to increase recruitment. These lower cut-offs for HbA1c was selected to maximise the proportion of patients who could potentially benefit. The minimum requirement of being prescribed at least two classes of oral diabetes medications was to ensure that efforts to optimise and intensify medical care according to national guidance had been offered to the patient before randomisation. Exclusion criteria were: severe mental disorders; terminal illnesses and end-stage diabetes complications; morbid obesity with a BMI >40 kg/m^2 in Phase 1, which was raised to >50 kg/m^2 in Phase 2 to enhance recruitment; non-ambulatory as patients had to be able to attend the clinic; no phone/internet access; non-English-speaking as therapy was delivered in English; and currently receiving psychological treatments from elsewhere. Patients who had Patient Health Questionnaire-9 (PHQ-9) depressive scores >20 were excluded if they had psychotic depression or active suicidal ideation.[16]

Randomisation

Randomisation of practices (unit of cluster) was conducted after baseline data were collected by an independent statistician using a random number generator to assign equal numbers of practices to each arm at each phase. Allocation concealment was conducted by holding the randomisation list by an independent manager in password-locked computer. The trial manager was only able to reveal to themselves, and then to one D6 researcher, the allocation after entering the details of the practice.

Randomisation of clusters was intended to take place after all the patients had been recruited but this was leading to unacceptable delays in training the nurses. Therefore, some patients were recruited after randomisation of clusters but remained blind to allocation until the interventions were offered in both groups.

Procedures

Baseline measures

Baselines measures were: age, gender, self-reported ethnicity, occupation, employment status, and smoking status. HbA1c was measured centrally (King's College Hospital NHS Foundation Trust) by affinity chromatography (Primus Ultra2, Kansas City, USA) and reported in mmol/mol. Complication status was assessed before randomisaton by the research assistant as follows: neuropathic ulcer risk was assessed by perception of 10g monofilament; retinopathy coding e was taken from the most recent of annual standardised digital retinal photography documented in the community-based Diabetic Eye Complications Screening Service (DECS), with a new appointment arranged if one had been missed; urine was collected to assess nephropathy using the urinary albumin:creatinine ratio (ACR); and history of macrovascular complications collected from the medical records.

In addition, the following secondary outcomes were measured: systolic and diastolic blood pressure using an electronic sphygmomanometer; body mass index (BMI) (kg/m^2) and waist circumference (cm); depressive symptoms using the Patient Health Questionnaire-9 questionnaire;[16] the Alcohol Use Disorders Identification Test (AUDIT);[23] and the Diabetes Distress Scale, which measures diabetes specific psychological burden (in the protocol we had proposed a similar but longer scale).[24] A fasting blood sample was sent for measurement of HbA1c, total cholesterol, and triglycerides.

Intervention

Group 1: Standard care

The nurse delivered diabetes care in both groups as recommended by national guidance.[17] To control for attention, standard care nurses offered the same number of sessions as in D6. The sessions were audio-taped for assessment of contamination bias.

Group 2: Standard care plus D6

D6 aimed to provide the nurses with skills based on MI and CBT to address psychological barriers maintaining poor self-management. The theory underlying MI is that the patient's state of ambivalence (resistance versus willingness to make lifestyle changes) is the core psychological construct that needs addressing.[6] MI is a directive, person-centered counselling style which encourages patients to change behaviours using collaborative, non-judgmental, and affirming communications. The theory underlying CBT is that barriers to diabetes self-

management are maintained by unhelpful thoughts (e.g., *if I can't cure diabetes, what's the point?*), unhelpful behaviours (e.g., missing insulin doses), and distressing emotions (e.g., low mood/anxiety when seeing a high blood glucose reading).[18,19] Identifying and challenging these cognitive barriers are effective in changing behaviours.[20]

The D6 nurses were trained in six skills drawn from MI and CBT: 1. Active listening; 2. Managing resistance; 3. Directing change; 4. Supporting self-efficacy; 5. Addressing health beliefs; and, 6. Shaping behaviours. These skills were applied to common barriers around diabetes such as medication adherence, self-testing, physical activity and dietary changes. The training was conducted by a senior diabetes-experienced clinical psychologist and lasted three months. It comprised three hours per week, interactive classroom activities, a training caseload (average 3-5 non-study patients), and weekly supervision of audiotaped sessions. We produced a manual containing the rationale for D6, the six psychological skills, case examples, strategies to manage clinician's own resistance, and for 'troubleshooting' common clinical obstacles. D6 nurses were expected to apply the skills flexibly to different situations (e.g., weight loss, medication adherence) using visual aids and worksheets. The format was 12 face-to-face individual sessions (sessions 1-4 fortnightly during months 1-2, sessions 5-6 monthly during months 3-6, and sessions 7-12 during months 7-12). Monthly group supervision by a senior clinical psychologist was provided. The sessions were audio-taped for assessment of fidelity.

The Motivational Interviewing Treatment Integrity (MITI) Scale (version 3.1.1)[21] and Behaviour Change Counselling Index (BECCI)[22] were used to assess treatment fidelity of D6, and to compare competencies in both groups. The MITI assesses: global spirit and global empathy with scores ≥ 3.5 (range 1-5); percentage of complex reflections, open questions, and MI adherent behaviours with scores of ≥40%, 50%, and 90% respectively; and ratio of reflections to closed questions scores with ≥1 as proficient. The middle 20 minutes of sessions were rated by two independent psychologists trained in MITI and blind to treatment allocation. The BECCI consists of 11 items with 5-point Likert scales to rate the frequency or the strength of the nurse skill, ranging from 0 (not at all) to 4 (a great extent). A clinical psychologist, blind to treatment allocation, rated the BECCI. We stratified sessions by nurse and patient and then randomly selected tapes (that lasted ≥20 minutes) for 3 different patients for each nurse from either session 2, 3 and 4. Three nurses did not have three tapes lasting 20 minutes or more and, for these, the three longest tapes were chosen.

Outcomes

As the recruitment and follow-up was delayed by the NHS restructuring and patient attrition, the protocol was changed from 24 months follow-up to 18 months. The primary outcome was change in HbA1c from cluster randomisation to 18 months. If the study HbA1c data were missing at 18-month, we used routinely collected HbA1c data if it was collected within the 15-month follow-up window. Secondary outcomes were change in lipids, blood pressure, BMI and depressive symptoms at 18 months. Research assistants were blind to allocation when collecting follow-up data.

Sample size

A 10.9 mmol/mol difference in HbA1c in D6 compared to standard care was the minimal clinically acceptable reduction at 18 months, considering: (a) baseline HbA1c and (b) that standard care may produce a 2.2 mmol/mol (equivalent to 0.2%) reduction in HbA1c for the placebo effect of participating in a RCT (actual difference between groups 8.8 mmol/mol (equivalent to 0.8%), equivalent to a moderate effect size of d=0.55). Assuming 20% dropout, we needed 360 patients to achieve 80% power at a two-sided alpha-level of 5%, with 20 practices with 18 patients each per arm. We then took account of clustering by practice and we assumed two practices per arm dropped out. Therefore, we needed 24 practices with a total patient size of 24x18=432 patients. The required sample size adjusted for a clustering intra-correlation coefficient (ICC) effect of 0.05 was 81x1.7=138 patients per arm (inflation factor 1.7).

We recruited 334 patients of which 231 had at least one follow-up in 24 clusters. The average cluster size was therefore 10 patients per cluster, smaller than our assumed size of 15 patients per cluster with a post-hoc power of 77% (STATA 13 *clsampsi* function) at two-sided alpha-level of 5%.[25]

Statistical analysis

Data were analysed using STATA 13. The sample characteristics were described as means (standard deviation (SD)) or as proportions (percentage). A comparison of patient list size and Index of Multiple Deprivation rank score by practices that participated versus those that did not was conducted using Student's t-test.[26] A linear mixed-effects model estimated group differences in HbA1c levels between D6 and standard care groups at 18 months. We included

741 the 15-month HbA1c as this clinically just overlaps with the 3-month window for 18-month
742 HbA1c and to include more patients with at least one follow-up measure. Data were analysed
743 as intention-to-treat (ITT). Time (with two levels: 15 and 18 months), treatment group, an
744 interaction between treatment group and time, Primary Care Trust (as a possible prognostic
745 factor), recruitment phase, and baseline HbA1c were included as fixed covariates. The
746 dependency of the repeated observations of the same subjects was modeled on the covariance
747 between the residuals using an unstructured covariance pattern model. Nurse was included as
748 a random effect as the unit of randomisation.

749 Observations from the same nurse cluster were likely to be more similar than observations
750 from two different clusters. However, in three cases, a practice was twinned with an adjacent
751 practice and one nurse covered both practices. Therefore, two types of clustering could occur:
752 within practice and within nurse. We assumed that nurse clustering would have a stronger
753 effect than practice clustering. We therefore treated the twinned practices as one unit which is
754 equivalent to treating nurse as the primary clustering unit. However, we repeated the model
755 using 'practice' as the main clustering unit in a sensitivity analysis.

756 Secondary outcomes were analysed in the same way using linear mixed models to estimate
757 group differences at 18 months (including15 months). An independent covariance structure
758 pattern was used for the triglycerides as the model did not converge using unstructured
759 covariance.

760 Twenty-nine participants with HbA1c <64 mmol/mol contrary to the study criteria were
761 included and this was a protocol violation. We performed a sensitivity analysis by including a
762 binary covariate of this protocol violation (yes/no) in the model.

763 The analyses were conducted using maximum likelihood under the missing at random
764 assumption. Sensitivity analyses were carried out to assess sensitivity to missingness in
765 HbA1c using several approaches: by investigating and including predictors of missingness in
766 the model and by using multiple imputation for the missing values of HbA1c (50 imputations
767 using *mi* impute command in STATA 13 with all variables from the mixed-effects model
768 included in the imputation model, as well as age, ethnicity, gender, baseline BMI, total
769 cholesterol, triglycerides, blood pressure, and PHQ-9 score).

770 The Data Monitoring Committee oversaw the study.

Fidelity

To assess IRR for each fidelity measure, absolute agreement was measured by estimating the ICC from a two-way mixed model or using Spearman's rank correlation coefficient if residuals from the mixed model were not normally distributed. A t-test or Mann-Whitney U-test was used to compare the skills of D6 versus standard care nurses, using STATA 14.

Role of funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or reporting. The authors had full access to all data and final responsibility for submission for publication and acted independently from the funding source.

Patient Involvement

We included a person with type 1 diabetes from our local community who also was an active member of the local and national Diabetes UK. This person was instrumental in guiding us to use NHS practice nurses rather than research diabetes nurses to deliver the intervention. This person inputted into the importance of quality of life and psychological well-being as outcome measures alongside glycaemic control. For the process evaluation, we invited participants to give us feedback of the intervention in terms of the perception of burden as patients. We included a person with type 1 diabetes on the Trial Steering Committee.

Transparency Declaration

The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; there were discrepancies from the study as planned and these have been explained.

2 Additional Tables

Table 1. Breakdown of patients attending each practice and primary outcome follow-up rates by group.

D6		Standard care	
Practice*	**Proportion with HbA1c data at 18 months (%)**	**Practice***	**Proportion with HbA1c data at 18 months (%)**
1	14/18 (77.8)	2	11/12 (91.7)
3	13/19 (72.2)	4	14/19 (73.7)
5	7/16(64.3)	6	11/18 (61.1)
7	6/9 (66.7)	8	12/17 (70.6)
9	15/16 (93.8)	10	6/12 (50.0)
11	6/12 (50.0)	12	13/13 (100.0)
13	6/9 (66.7)	14	13/17 (76.5)
15**	9/18 (50.0)	16	13/17 (76.5)
17	9/13 (69.2)	18	5/8 (62.5)
19**	12/14 (85.7)	20***	1/4 (25.0)
21	8/14 (57.1)	22	5/11 (45.5)
23**	4/12 (33.3)	24	6/16 (37.5)
Total	**109/170 (64.1%)**	**Total**	**110/164 (67.1%)**

* Practices 1-6 are from Phase 1 (HbA1c $\geq$ 69.4 mmol/mol and BMI $\leq$ 40kg/m^2). Practices 7-24 are from Phase 2 (HbA1c $\geq$ 64 mmol/mol, BMI $\leq$ 50kg/m^2, and twinned practices).
** Two practices twinned and covered by 1 nurse.
*** Practice dropped out post-randomisation.
D6=Diabetes 6

796

Table 2. Comparison of missingness in HbA1c at 18 months.			
Variable	**HbA1c measured at 18 months (n=219)**	**Missing HbA1c at 18 months (n=115)**	**Test of independence (t-test or Pearson χ^2-test)**
Age (years)	58·9 (11·4)	59·0 (11·0)	*t*=0·045, *p*=0·964
Ethnicity			
White	72 (33·0)	62 (54·4)	**$\chi^2(3)$=14·854, *p*=0·001**
African/Caribbean	103 (47·3)	40 (35·1)	
Asian/Other	43 (19·7)	12 (10·5)	
Gender			
Male	104 (47·5)	59 (51·3)	$\chi^2(1)$=0·439, *p*=0·507
Female	115 (52·5)	56 (48·7)	
Education level			
A levels or higher	60 (27·9)	30 (26·6)	$\chi^2(2)$=0·091, *p*=0·956
O level or GCSE equivalent	75 (34·9)	41 (36·3)	
No formal qualifications	80 (37·2)	42 (37·2)	
Relationship status			
Married or Cohabiting	112 (51·3)	59 (51·3)	$\chi^2(2)$=1·221, *p*=0·543
Separated/Divorced/Widowed	60 (27·7)	37 (32·2)	
Single	45 (20·7)	19 (16·5)	
Employment			
Yes	92 (42·0)	47 (40·9)	$\chi^2(1)$=0·040, *p*=0·841
No	127 (58·0)	68 (59·1)	
BMI (kg/m^2)	32·1 (6·0)	31·5 (6·4)	*t*=-0·839, *p*=0·402
Systolic BP (mm/Hg)	133·6 (17·2)	135·3 (16·9)	*t*=-0·823, *p*=0·411
Diastolic BP (mm/Hg)	79·2 (10·0)	79·2 (10·3)	*t*=-0·052, *p*=0·958
HbA1c (mmol/mol)	79·1 (17·4)	83·2 (19·3)	*t*=-1·96, *p*=0·051
Total Cholesterol (mmol/L)	4·2 (1·1)	4·3 (1·3)	*t*=-0.501, *p*=0.617
Fasting triglycerides (mmol/L)	1·6 (1·2)	1·9 (1·4)	*t*=-1.631, *p*=0.104
Diabetes duration (years)	10·5 (6·1)	10·0 (6·7)	*t*=-0.694, *p*=0.488
DDS (mean item score)	2·2 (0·8)	2·3 (0·8)	*t*=0.959, *p*=0.338

Data are n (%) or mean (SD), as appropriate.
[1] Yes = full time, part-time, student or self-employed
[2] No = retired/unemployed/not seeking employment
BMI = Body mass index; BP = blood pressure; DDS = Diabetes Distress Scale

797

798

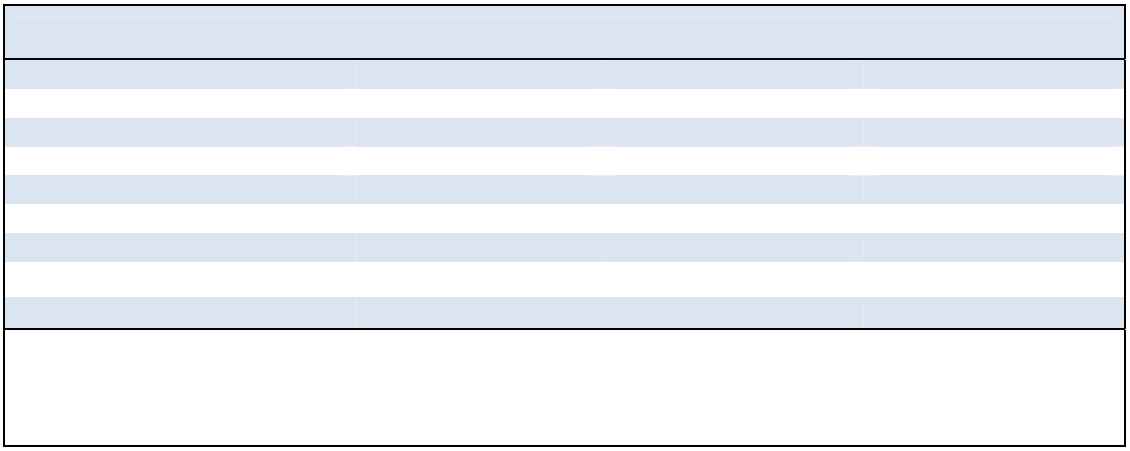
Table 3. Inter-rater reliability for each MI domain.	
MI Domain	**Inter-rater reliability***
Global Spirit (ICC)	0·87
Global Empathy (Spearman's rho)	0·91
% Complex Reflections (ICC)	0·86
% Open Questions (ICC)	0·92
Reflection/Question Ratio (Spearman's rho)	0·88
% MI Adherent (ICC)	0·90

MI=Motivational interviewing; ICC=Intra-class correlation coefficient
*Reliability was calculated as an ICC if the distribution was normal and a Spearman's rho if non-normal.

799

800 We rated 69 sessions (4.0% of all available recordings) for fidelity from 33/170 and 36/164
801 patients from the D6 and standard care groups, respectively. The level of competency in the
802 D6 group was below the beginner proficiency level in all the scales for MI and BECCI.
803 Except for a slightly higher proportion of open questions in D6, and a slightly larger
804 reflection/question ratio in standard care, there were no statistically significant differences in
805 the remaining mean MI domain scores or BECCI scores.

806



807

808

809

810 **3 CONSORT 2010 checklist of information for reporting a cluster randomised**
811 **trial**

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Page No *
Title and abstract				
	1a	Identification as a randomised trial in the title	Identification as a cluster randomised trial in the title	**1**
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)[i,ii]	See table 2	**2**
Introduction				
Background and objectives	2a	Scientific background and explanation of rationale	Rationale for using a cluster design	**4-5**
	2b	Specific objectives or hypotheses	Whether objectives pertain to the the cluster level, the individual participant level or both	**4**
Methods				
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Definition of cluster and description of how the design features apply to the clusters	**5-6**
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		**Appendix**
Participants	4a	Eligibility criteria for participants	Eligibility criteria for clusters	**5**
	4b	Settings and locations where the data were collected		**5**
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Whether interventions pertain to the cluster level, the individual participant level or both	**6-7**
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Whether outcome measures pertain to the cluster level, the individual participant level or both	**7-8**
	6b	Any changes to trial outcomes after the trial commenced, with reasons		**7-8, Appendix**
Sample size	7a	How sample size was determined	Method of calculation, number of clusters(s) (and whether equal or unequal cluster sizes are assumed), cluster size, a coefficient of intracluster correlation (ICC or *k*), and an indication of its uncertainty	**8, Appendix**
	7b	When applicable,		**NA**

		explanation of any interim analyses and stopping guidelines		
Randomisation:				
Sequence generation	8a	Method used to generate the random allocation sequence		**6, Appendix**
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Details of stratification or matching if used	**6, Appendix**
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Specification that allocation was based on clusters rather than individuals and whether allocation concealment (if any) was at the cluster level, the individual participant level or both	**6, Appendix**
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Replace by 10a, 10b and 10c	
	10a		Who generated the random allocation sequence, who enrolled clusters, and who assigned clusters to interventions	**6, Appendix**
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete enumeration, random sampling)	**6, Appendix**
	10c		From whom consent was sought (representatives of the cluster, or individual cluster members, or both), and whether consent was sought before or after randomisation	**5-6,18, Appendix**
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		**8**
	11b	If relevant, description of the similarity of interventions		**6-7**
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	How clustering was taken into account	**8-9, Appendix**
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		**8-9, Appendix**

Results				
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	For each group, the numbers of clusters that were randomly assigned, received intended treatment, and were analysed for the primary outcome	**9-10, Figure 1, Appendix 3 Table 1**
	13b	For each group, losses and exclusions after randomisation, together with reasons	For each group, losses and exclusions for both clusters and individual cluster members	**9-10, Figure 1, Appendix 3 Table 1**
Recruitment	14a	Dates defining the periods of recruitment and follow-up		**Figure 1, Appendix**
	14b	Why the trial ended or was stopped		**NA**
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Baseline characteristics for the individual and cluster levels as applicable for each group	**Table 1**
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	For each group, number of clusters included in each analysis	**10, Figure 1**
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Results at the individual or cluster level as applicable and a coefficient of intracluster correlation (ICC or k) for each primary outcome	**10-11**
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		**NA**
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		**10-11, Appendix**
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms[iii])		**12**
Discussion				
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses		**12-15**
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	**12-15**
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant		**12-15**

		evidence	
Other information			
Registration	23	Registration number and name of trial registry	**2**
Protocol	24	Where the full trial protocol can be accessed, if available	**NA**
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	**17**

** Note: page numbers optional depending on journal requirements*

4 Supplementary Data from the Economic Evaluation

Correspondence to: Professor Anita Patel anitapatelconsulting@gmail.com

4.1 Summary of methods

A within-trial economic evaluation assessed the cost-effectiveness of D6 from a health and social care perspective at 18 months. This linked individual-level costs with HbA1c and quality-adjusted life year (QALY) gains estimated from the Short Form 12 (SF-12) version 2.[52,53] We calculated individual-level total costs (English pounds sterling, £, 2011–12 prices) by attaching unit costs from national sources to individual-level (all-cause) resource use quantities covering a retrospective 6-month period at baseline and 18 months. Use of hospital services was assessed by retrospective review of hospital records. Use of out-of-area hospital services, community-based services, and medications were measured by self-report using a specifically developed proforma. Cost estimates for D6 included the full costs of staff training/supervision/assessment and time spent on delivery to patients. Outcomes and costs at 18 months were discounted by 3.5%.

Costs and QALY gains at 18 months were compared using non-parametric bootstrap regressions (10000 repetitions) with baseline covariates and adjustment for nurse. We only calculated incremental cost-effectiveness ratios where either group showed statistically greater costs and outcomes. The probability of cost-effectiveness for D6 was assessed by constructing cost-effectiveness acceptability curves (10000 bootstrap repetitions) for threshold ranges of £0–£50,000 per QALY gain/point improvement in HbA1c. Sensitivity analyses explored the impact on cost and/or outcome differences when: (a) missing data due to loss of follow-up were imputed (using multiple imputation in STATA 11.2) rather than excluded, (b) the unit cost of the D6 intervention was lowered by assuming 50% more people received D6, (c) accounting for the inadvertent inclusion of 29 individuals with HbA1c <64 mmol/mol by including a binary covariate for this, and (d) accounting for clustering at practice rather than nurse level.

4.2 Intervention Costs

Table S1: D6 intervention costs (English pounds sterling, £, 2011–12 prices; total costs rounded to nearest £)

Intervention Component	Description	Resources	Resource and cost details	Total cost	Unit cost per participant (n164)
Training	One training session (three hours) per week for 12 weeks, for 11 trainees. Delivered by one clinical psychologist over two training courses.	Trainer's time	1 band 8a clinical psychologist for 4 hours (3 hour training plus 1 hour preparation) for 12 weeks for 2 courses (1 * 4 * 12 * 2 * £60[1]) £5,760	£20,074	£122
		Trainees' time	11 trainees (primary care nurses) for 3 hours for 12 weeks (11 * 3 * 12 * £35[2]) £13,860.		
		Capital/materials	Room to train in: 3 hours training for 12 weeks for 2 courses (3 * 12 * 2 * £3.10 per hour[3]) £223.20. Printing of 11 D6 psychology skills handbook: (11 * £11.94[4]) £131.34. Printing of 10 A4 PowerPoint presentations for 12 session for 11 trainees (10 * 12 * 11 * £0.06[5]) £79.20. Use of 1 video camera: £19.99[6]		
Supervision	Supervision for trainees provided in two hour group sessions by a clinical psychologist.	Trainer's time	1 band 8a clinical psychologist for 3 hours (2 hour supervision plus 1 hour preparation) for a total of 35 group supervision sessions (1 * 3 * 35 * £60[1]) £6,300. 1 band 8a clinical psychologist for 30 minutes for transcription of 131 taped trainee sessions (0.5 * 131 * £60[1]) £3,930.	£23,449	£143
		Trainees' time	1 trainee (primary care nurse) for 2 hours for 140 trainee attendances at group sessions (1 * 2 * 140 * £35[2]) £9,800.		
		Transcription	Transcription of 131 30-minute sessions: (131 * 30 * 0.80) £3,144[7].		
		Materials	1 audio recorder per trainee: (11 * £24.99[8]) £274.89.		
Assessment	One 30-minute assessment by band 8a nurse per trainee	Assessor's time	1 band 8a nurse for 30-minutes, for 11 assessments (1 * 0.5 * 11 * £60[9]) £330	£330	£2

Total for training				£43,853	£267
Intervention	Participants offered 12 sessions over twelve months.	Trainees' time	Individually calculated for each case based on number of sessions attended (assume 30 minute session): (30 minutes * £0.75 per minute[10]) £22.50 per session.	Cost per patient	Mean £301

Sources and details (all pounds sterling (£), 2011/12 prices):

1. Curtis L. 2012. Unit Costs of Health and Social Care 2012. Personal Social Services Research Unit: University of Kent. Based on £60 per hour, band 8a clinical psychologist.
2. Curtis L. 2012. Unit Costs of Health and Social Care 2012. Personal Social Services Research Unit: University of Kent. Based on £35 per hour excluding qualifications.
3. Hurley MV, Walsh NE, Mitchell HL, Pimm J, Williamson E, Jones RH, Reeves BC, Dieppe PA, Patel A. Economic evaluation of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain. Arthritis & Rheumatism (Arthritis Care & Research) 2007; 57 (7): 1220-122. Obtained further details via correspondence with the authors. Based on capital costs of a gym (£5.10 per hour, 2003/4 prices), halved to give more appropriate sized room (£2.55), inflated to 2011/12 prices (£3.10), (inflation source: Curtis L. 2012. Unit Costs of Health and Social Care 2012. Personal Social Services Research Unit: University of Kent, The Hospital & Community Health Services (HCHS) index – annual percentage prices increase).
4. Information from the clinical team: £11.94 each.
5. Rymans photocopying. Available at: http://www.ryman.co.uk/photocopying [accessed: 13/02/2015]: £0.06 per copy for 100+ pages
6. Argos camcorder. Available at: http://www.argos.co.uk/static/Product/partNumber/2268077.htm [accessed: 13/02/2015]: £19.99 for the lowest priced camcorder.
7. Transcript Divas Transcription Services. Available at: http://transcriptdivas.co.uk/ [accessed: 13/02/15] Based on £0.80 per minute of recording data.
8. Argos voice recorder. Available at: http://www.argos.co.uk/static/Product/partNumber/3071452.htm [accessed: 13/02/2015]: £24.99 for the lowest priced voice recorder.
9. Curtis L. 2012. Unit Costs of Health and Social Care 2012. Personal Social Services Research Unit: University of Kent. Based on £46,600 median full-time equivalent total earnings for a band 8a nurse, with proportions of a band 7 nurse for per hour cost applied (£40,200 - £52 per hour): £60 per hour.
10. Curtis L. 2012. Unit Costs of Health and Social Care 2012. Personal Social Services Research Unit: University of Kent. Based on £45 per hour of face-to-face contact excluding qualifications.

4.3 Other Unit Costs

Table S2: Unit costs

Item	Unit	Unit cost (£) 2011-12 prices	Source	Notes
Inpatient services				
Nervous System	bed day	368	1	NHS reference cost - Code A
Eyes & Periorbital	bed day	606	1	NHS reference cost - Code B
Mouth, head, neck & ears	bed day	519	1	NHS reference cost - Code C
Respiratory system	bed day	326	1	NHS reference cost - Code D
Cardiac Surgery & Primary Cardiac Conditions	bed day	452	1	NHS reference cost - Code E
Digestive System	bed day	428	1	NHS reference cost - Code F
Hepato-biliary and Pancreatic Systems	bed day	398	1	NHS reference cost - Code G
Musculoskeletal System	bed day	486	1	NHS reference cost - Code H
Skin, Breast & Burns	bed day	404	1	NHS reference cost - Code J
Endocrine & Metabolic System	bed day	327	1	NHS reference cost - Code K
Urinary Tract & Male Reproductive Systems	bed day	350	1	NHS reference cost - Code L
Female Reproductive System & Assisted Reproduction	bed day	599	1	NHS reference cost - Code M
Obstetrics	bed day	818	1	NHS reference cost - Code N
Diseases of Childhood & Neonates	bed day	577	1	NHS reference cost - Code P
Vascular System	bed day	472	1	NHS reference cost - Code Q
Radiology and Nuclear Medicine	bed day	513	1	NHS reference cost - Code R
Haematology, Chemotherapy, Radiotherapy & Specialist Palliative Care	bed day	448	1	NHS reference cost - Code S
Multiple Trauma, Emergency Medicine and Rehabilitation	bed day	458	1	NHS reference cost - Code T
Immunology, Infectious Diseases & other contacts	bed day	360	1	NHS reference cost - Code W
General inpatient	bed day	439	1	NHS reference cost - Overall inpatient
A&E	bed day	112	1	TAandEMSNA - Accident and Emergency Services: Not Leading to Admitted
Outpatient services				
Diabetes clinic	visit	134	1	307 - diabetic medicine on Total-OPATT tab
Diabetes foot clinic	visit	134	1	cost as diabetes clinic
Diabetes eye clinic	visit	134	1	cost as diabetes clinic
Ophthalmology	visit	86	1	130 - ophthalmology on Total-OPATT tab
Blood tests / phlebotomy	visit	3	1	DAP839 - Phlebotomy: on TDAPS tab (Pathology services)
Dietetics	visit	57	1	Total - OPATT Tab: Service code 654A - Adult dietetics
General medical outpatient	visit	158	1	300 - general medicine on Total-OPATT tab
Day surgery centre	visit	123	1	Total OPATT (Outpatient Attendances Data) tab - code 100 - general surgery
A&E	visit	110	1	180 - A&E on Total-OPATT tab
X-ray (x-ray only)	visit	30	1	Total - OPATT Tab: Direct Access Plain Film - DAPF
Community based professionals				
GP at surgery	contact	36	2	P183 - PSSRU - per patient contact lasting 11.7 minutes - Excludes qualification costs, including direct care staff costs.
GP at home	contact	92	2	P183 - PSSRU - per patient out of surgery visit lasting 23.4 minutes - Excludes qualification costs, including direct care staff costs.
GP telephone	contact	22	2	P183 - PSSRU - per telephone contact lasting 7.2 minutes - Excludes qualification costs, including direct care staff costs.
Diabetes specialist nurse at surgery	contact	11.11	2	p178 - PSSRU - Nurse specialist - £43 per hour excluding qualifications, assuming 15.5 (specified on p180 for practice nurse) min appointment
Diabetes specialist nurse at home	contact	16.11	2	p178 - PSSRU - Nurse specialist - £43 per hour excluding qualifications, - using per hour of home visiting from community nurse (p175) - £61:£42 = 1.45 SO - 11.11*1.45=16.11
Diabetes specialist nurse telephone	contact	6.78	2	p178 - PSSRU - Nurse specialist - £43 per hour

				excluding qualifications, assume same proportion of costs as a GP telephone call (61% (*0.61)) - 11.11*.61=6.78
Practice nurse at surgery	contact	11.63	2	P180 - PSSRU - £45 per hour of face-to-face contact excluding qualifications assuming 15.5 (specified on p180) min appointment
Practice nurse at home	contact	16.166	2	based on practice nurse surgery visit cost above but use the proportion of district nurse home visit hour / clinic hour proportion from PSSRU 2010 (68/49=139%)
Practice nurse telephone	contact	7.0943	2	assume same proportion of costs as a GP telephone call (61% (*0.61))
Chiropodist/podiatrist at surgery	contact	48.529	1	TOCS tab - N910 Podiatry services - £47 per activity
Chiropodist/podiatrist at home	contact	70.367	1	TOCS tab - N910 Podiatry services - £47 per activity - with proportions of home visit from community nurse (p175, PSSRU) - £61:£42 = 1.45 SO - 47*1.45=68.15
Chiropodist/podiatrist telephone	contact	29.603	1	assume same proportion of costs as a GP telephone call (61% (*0.61))
Optician at surgery	contact	20.7	3	"The fee paid to an optical contractor for carrying out an NHS sight test by the governments of England, Wales, and Northern Ireland remains at £20.70 for the year 1 April 2011 to 31 March 2012"
Optician at home	contact	28.773	2	based on surgery visit cost above but use the proportion of district nurse home visit hour / clinic hour proportion from PSSRU 2010 (68/49=139%)
Optician telephone	contact	12.627	2	assume same proportion of costs as a GP telephone call (61% (*0.61))
District nurse at surgery	contact	11.347	2	based on district nurse home visit cost above but use the proportion of clinic hour / home visit hour proportion from PSSRU 2010 (49/68=72%)
District nurse at home	contact	15.76	2	P175 - PSSRU - Community nurse including district - £61 per hour of home visiting including travel, excluding quals, assume 15.5 (see page 180) min appointment
District nurse telephone	contact	9.6136	2	assume same proportion of costs as a GP telephone call (61% (*0.61))
Dietician at surgery	contact	72.277	1	TOCS tab - N800 Dietetics services - £70 per activity
Dietician at home	contact	104.8	1	Cost combines price from 2011/12 (above) but with proportions of home visit from community nurse (p175, PSSRU) - £61:£42 = 1.45 SO - 70*1.45=101.5
Dietician telephone	contact	44.089	1	assume same proportion of costs as a GP telephone call (61% (*0.61))
Physiotherapist at surgery	contact	48.529	1	TCSCT tab (community based therapy services) - N5A1 - Community Physiotherapy Services : Adult - One-to-One Services - £47
Physiotherapist at home	contact	70.367	1	TCSCT tab (community based therapy services) - N5A1 - Community Physiotherapy Services : Adult - One-to-One Services - £47 - but with proportions of home visit from community nurse (p175, PSSRU) - £61:£42 = 1.45 SO - 47*1.45=68.15
Physiotherapist telephone	contact	29.603	1	assume same proportion of costs as a GP telephone call (61% (*0.61))
Occupational therapist at surgery	contact	30	2	p168 - pssru - NHS community OT - £30 per hour - assume 1 hour meeting, Excludes qualification costs.
Occupational therapist at home	contact	54.78	2	Cost combines price from 2011/12 (above) but with proportions of client time set down in 2009-10 (p152) book (£42 per home visit / £23 per hour = 182.61%). £30 per hour (excluding qualifications) multiplied by 182.61%
Occupational therapist telephone	contact	18.3	2	assume same proportion of costs as a GP telephone call (61% (*0.61))
Psychiatrist at surgery	contact	171.4	1	TMHCSOPFUAF tab (Mental Health Consultant Services (Outpatient Setting) - Follow-up Attendance Face to Face) - MHOPFUA2 (Adult other services)
Psychiatrist at home	contact	248.53	1	based on psychiatrist visit cost above but use the proportion of home visiting from community nurse (p175, PSSRU) - £61:£42 = 1.45 SO - 166*1.45=240.70
Psychiatrist telephone	contact	51.626	1	TMHCSOPFUANF tab (Mental Health Consultant

				Services (Outpatient Setting) - Follow-up Attendance Non Face to Face) - MHOPFUA2 (Adult other services)
Psychologist at surgery	contact	136	2	p171 PSSRU - £136 per hour of client contact - assume 1 hour appointment, Excludes qualification costs.
Psychologist at home	contact	189.04	2	based on psychologist visit cost above but use the proportion of district nurse home visit hour / clinic hour proportion from PSSRU 2010 (68/49=139%)
Psychologist telephone	contact	40.8	2	assume same proportion of costs as a psychiatrist face to face v non face to face (30% (*0.30))
Psychotherapist at surgery	contact	136	2	Assume same as a psychologist. "A psychotherapist may be a psychiatrist, social worker, psychologist, mental health nurse or other mental health professional who has had further specialist training in psychotherapy. Increasingly, there are a number of psychotherapists who do not have backgrounds in these fields but who have undertaken in-depth training in this area. " - from http://www.nhscareers.nhs.uk/explore-by-career/psychological-therapies/careers-in-psychological-therapies/psychotherapist/ - accessed 16April2013
Psychotherapist at home	contact	189.04	2	based on psychotherapist visit cost above but use the proportion of district nurse home visit hour / clinic hour proportion from PSSRU 2010 (68/49=139%)
Psychotherapist telephone	contact	40.8	2	assume same proportion of costs as a psychiatrist face to face v non face to face (30% (*0.30))
Counsellor at surgery	contact	59	2	P53 Pssru - £59 per consultation
Counsellor at home	contact	82.01	2	based on surgery visit cost above but use the proportion of district nurse home visit hour / clinic hour proportion from PSSRU 2010 (68/49=139%)
Counsellor telephone	contact	35.99	2	assume same proportion of costs as a GP telephone call (61% (*0.61))
Social worker at surgery	contact	78	2	P190 - PSSRU - social worker adult services - £156 per hour of face to face contact - assume 30 min appointment - excludes qualifications.
Social worker at home	contact	108.42	2	based on social worker visit cost above but use the proportion of district nurse home visit hour / clinic hour proportion from PSSRU 2010 (68/49=139%)
Social worker telephone	contact	23.4	2	assume same proportion of costs as a psychiatrist face to face v non face to face (30% (*0.30))
Home help/ care worker at surgery	contact	11.58	2	same as surgery
Home help/ care worker at home	contact	11.58	2	P193 PSSRU - Home care worker per hour of face to face contact, Weighted average accounting for different rates for day/evening/weekday/weekends. Plus, info that over 50% of visits are for 30 minutes so accounting for this (23.16/2= £11.58)
Home help/ care worker telephone	contact	7.0638	2	assume same proportion of costs as a GP telephone call (61% (*0.61))
Meals on Wheels at surgery	contact	5	2	same as home visit
Meals on Wheels at home	contact	5	2	P125 PSSRU - £6 local authority meal v £4 independent sector cost per day
Meals on Wheels telephone	contact	3.05	2	assume same proportion of costs as a GP telephone call (61% (*0.61))
Pharmacist for advice at surgery	contact	4.17	2	p172 PSSRU - £50 - assume 5 min consultation - Excludes qualification costs.
Pharmacist for advice at home	contact	4.17	2	same as home visit
Pharmacist for advice telephone	contact	4.17	2	Assume same as a pharmacist surgery consult
NHS direct at surgery	contact	22.358	4	cost as telephone
NHS direct at home	contact	22.358	4	cost as telephone
NHS direct telephone	contact	22.358	4	21.02 in 2009/10 so inflate up to 2011/12
Insulin equipment				
Blood glucose monitor / metre	item	12	5	
Blood glucose testing strips	100-pack	30.1	6	per 100: p459 - accu-chek mobile - n100
Insulin pen	item	15.7	6	per 1 pen: p446 - autopen 24
Insulin pump	item	2375	7	
Needle	100-pack	2.79	1	per 100: p447 - hypodermic needle - n100
Syringe	10-pack	1.35	6	per 10; p447 - U100 syringe with needle - 10 needles - 1.35
Finger prick device	200-pack	2.94	6	p446 - unilet eco – 200

Sources

1. NHS. NHS trust reference cost schedules 2010-11, inflated up to 2011-12 prices using the retail price inflation percentage from PSSRU 2012/13. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_131140 Last accessed 19/02/13.
2. PSSRU. Unit Costs of Health & Social Care 2012. http://www.pssru.ac.uk/archive/pdf/uc/uc2012/full-with-covers.pdf Last accessed 27/02/13.
3. Optical Confederation. Optics at a Glance. Dec 2011. http://www.fodo.com/downloads/Optics-at-a-glance_Dec2011_web.pdf Last accessed 03/05/13.
4. NHS Direct. NHS Direct Business Plan 2010-11. http://www.nhsdirect.nhs.uk/CorporateInformation/OperatingStatistics/AnnualReport2010-2011 Last accessed 03/05/13.
5. Boots. Blood glucose metre. http://www.boots.com/en/iBGStar-blood-glucose-meter_1253400/ Last accessed 23/06/14.
6. Joint Formulary Committee. British National Formulary. March 2012. 63rd edition. London: BMJ Group and Pharmaceutical Press.
7. Diabetes.co.uk. Cost of Insulin Pumps. http://www.diabetes.co.uk/insulin-pumps/buying-an-insulin-pump.html Last accessed 23/06/14.

851
852
853

854

4.4 Sensitivity Analyses

Table S11: Total costs at baseline and 18 months including intervention costs based on sensitivity analyses (2011/12 prices; all 18 month costs except intervention costs discounted)

	Control			Intervention			Unadjusted mean difference[$]	95% C.I.	Adjusted mean difference[$$]	95% C.I.[$]
	valid n	*Mean £*	*SD*	*valid n*	*Mean £*	*SD*				
Costs at 18 months										
Per protocol										
Health & social care costs including intervention costs	107	1025	573	92	1184	572	159	-39 to 357	151	-32 to 334
GP Clustering										
Health & social care costs including intervention costs	107	1025	573	92	1184	572	159	-39 to 357	150	-30 to 329
Alternative intervention cost										
Health & social care costs including intervention costs	107	1025	573	92	1095	572	70	-128 to 268	61	-123 to 244
Intention to treat										
Health & social care costs including intervention costs – intention to treat	170	1052	497	164	1126	473	74	-42 to 190	107	7 to 207*

[$]Comparisons include clustering for nurse. [$$]Comparisons include clustering for nurse plus covariates for baseline cost, age, gender, marital status, ethnicity, duration of diabetes and baseline utility. * Statistically significant

Table S12: Outcomes at baseline and 18 months interpolated to a six month period to match the cost data based on sensitivity analyses

	Control			Intervention			Unadjusted mean difference[$]	95% C.I.	Adjusted mean difference[$$]	95% C.I.[$]
	valid n	*Mean £*	*SD*	*valid n*	*Mean £*	*SD*				
Outcomes at 18 months										
Per protocol										
HbA1c (discounted)	109	71.31	19.22	110	71.60	18.11	0.29	-5.40 to 5.98	0.00	-6.08 to 6.09
SF12 based QALY (discounted and interpolated)	48	0.36	0.06	58	0.37	0.06	0.01	-0.01 to 0.03	0.00	-0.01 to 0.02
GP cluster										
HbA1c (discounted)	109	71.31	19.22	110	71.60	18.11	0.29	-5.38 to 5.97	0.66	-5.43 to 6.75
SF12 based QALY (discounted and interpolated)	48	0.36	0.06	58	0.37	0.06	0.01	-0.01 to 0.03	0.00	-0.01 to 0.00
Intention to treat										
HbA1c (discounted)	170	72.16	16.74	164	72.19	15.61	0.02	-4.34 to 4.39	0.47	-4.75 to 3.82
SF12 based QALY (discounted	170	0.36	0.06	164	0.37	0.06	0.00	-0.01 to 0.02	0.00	-0.00 to 0.01

and interpolated)

[$]Comparisons include clustering for nurse. [$$]Comparisons include clustering for nurse plus covariates for age, gender, marital status, ethnicity, duration of diabetes and baseline utility. * Statistically significant

4.5 Cost-effectiveness

For the economic analysis, 139 (42%) and 85 (25%) participants had the two necessary combinations of cost/HbA1c/covariate and cost/SF-12/covariate data, respectively; characteristics of those with and without data were comparable.

Based on QALYs, probabilities of cost-effectiveness for the D6 group at 18 months did not exceed 35% at the examined willingness to pay thresholds. However, based on HbA1c, probabilities of cost-effectiveness were around 5% at a willingness to pay threshold of £0, rising to (and remaining at) around 65% at thresholds of £5000–£50000. However, willingness to pay for a point improvement in HbA1c is unknown, and such a small improvement is unlikely to be clinically meaningful. Based on QALYs, probabilities of cost-effectiveness for the D6 group at 18 months did not exceed 35% at the examined willingness to pay thresholds. However, based on HbA1c, probabilities of cost-effectiveness were around 5% at a willingness to pay threshold of £0, rising to (and remaining at) around 65% at thresholds of £5000–£50000. However, willingness to pay for a point improvement in HbA1c is unknown, and such a small improvement is unlikely to be clinically meaningful.

Figure S1: Cost-effectiveness plane for HbA1c changes at 18 months from a health & social care perspective

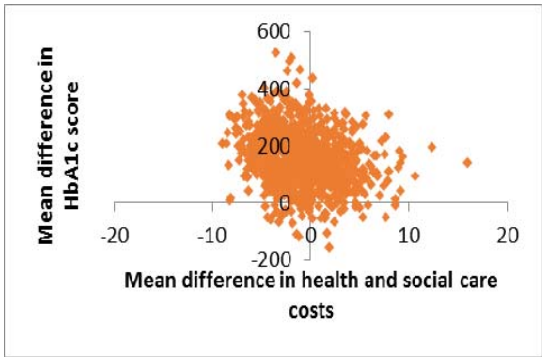


Figure S2: Cost-effectiveness plane for QALY gains at 18 months from a health & social care perspective

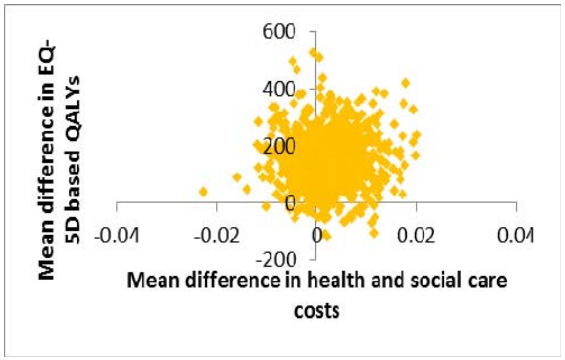


Figure S3: Cost-effectiveness acceptability curve for HbA1c point improvements at 18 months from a health & social care perspective

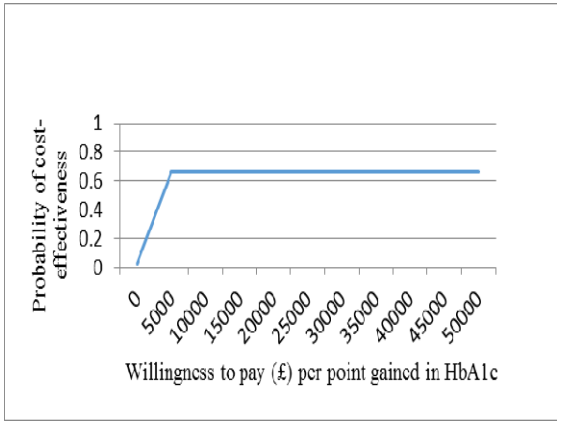
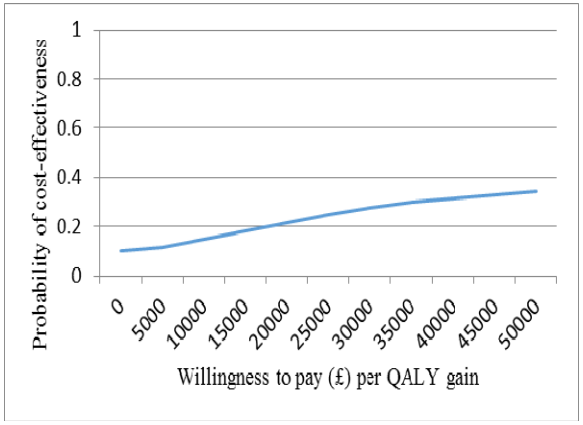


Figure S4: Cost-effectiveness acceptability curve QALY gains at 18 months from a health & social care perspective



878

879

880

881

882 The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, a worldwide license to the
883 Publishers and its licensees in perpetuity, in all forms, formats and media (whether known now or created in the future), to i) publish, reproduce,
884 distribute, display and store the Contribution, ii) translate the Contribution into other languages, create adaptations, reprints, include within
885 collections and create summaries, extracts and/or, abstracts of the Contribution, iii) create any other derivative work(s) based on the
886 Contribution, iv) to exploit all subsidiary rights in the Contribution, v) the inclusion of electronic links from the Contribution to third party
887 material where-ever it may be located; and, vi) license any third party to do any or all of the above.
888

---

[i] Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG, et al. CONSORT for reporting randomised trials in journal and conference abstracts. *Lancet* 2008, 371:281-283

[ii] Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG at al (2008) CONSORT for reporting randomized controlled trials in journal and conference abstracts: explanation and elaboration. *PLoS Med* 5(1): e20

[iii] Ioannidis JP, Evans SJ, Gotzsche PC, O'Neill RT, Altman DG, Schulz K, Moher D. Better reporting of harms in randomized trials: an extension of the CONSORT statement. *Ann Intern Med* 2004; 141(10):781-788.