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| 1  | Cluster randomised controlled trial of a nurse-led psychological intervention for type 2 |
|----|--|
| 2  | diabetes: Diabetes-6 study   |
| 3  |  |
| 4  | Khalida Ismail, Kirsty Winkley, Nicola de Zoysa, Anita Patel, Margaret Heslin, Helen     |
| 5  | Graves, Stephen Thomas, Dominic Stringer, Daniel Stahl, Stephanie A Amiel                |
| 6  | Corresponding author:  |
| 7  | Khalida Ismail   |
| 8  | Institute of Psychiatry, Psychology and Neuroscience, King's College London              |
| 9  | Weston Education Centre, 10 Cutcombe Road  |
| 10 | London SE5 9RJ   |
| 11 | Email: khalida.2.ismail@kcl.ac.uk  |
| 12 | Telephone: 020 7848 5131   |

| 15 | Abstract |
|----|----------|
|    |          |

## 16 Background

17 Suboptimal glycaemic control in type 2 diabetes (T2D) is common and associated with

18 psychological barriers.

19 Aim

20 We tested whether it was possible to train practice nurses in six psychological skills

21 (Diabetes 6 (D6)) based on motivational interviewing (MI) and basic cognitive behaviour

therapy (CBT) and whether integrating these with diabetes care was associated with

23 improved glycaemic control over 18 months compared to standard care.

# 24 Design and Setting

25 A two-arm, single-blind, parallel cluster randomised controlled trial conducted in primary

26 care practices (n=24) (ISRCTN trial registration: ISRCTN75776892).

# 27 Method

Adult participants (n=334) with T2D and HbA1c  $\geq$ 69.4 mmol/mol (lowered to  $\geq$ 64

29 mmol/mol midstudy to increase recruitment) at least once in previous 18 months and at

30 recruitment were randomised to receive 12 sessions of either the D6 intervention or standard

- 31 care over 12 months. The practices nurses were trained in the six psychological skills and
- 32 their competencies were measured by standardised rating scales. All sessions were

audiotaped. The primary outcome was change in HbA1c at 18 months from randomisation;

34 secondary outcomes were change in systolic and diastolic blood pressure, body mass index,

35 waist circumference, depressive symptoms, harmful alcohol intake, diabetes-specific distress,

36 and cost-effectiveness.

37

# 38 **Results**

| 39 | Using intention-to-treat analysis, there was no significant difference between D6 intervention |
|----|--|
| 40 | and standard care in HbA1c (absolute mean difference -0.79 mmol/mol, 95% CI -5.75-4.18)        |
| 41 | or for any of the secondary outcomes. The competency level of D6 nurses was below the          |
| 42 | beginner proficiency level and similar to the standard care nurses.                            |
| 43 | Conclusion   |
| 44 | Training nurses in MI and basic CBT to support self-management did not lead to                 |
| 45 | improvements in glycaemic control or other secondary outcomes in people with T2D at 18         |
| 46 | months. It was also unlikely to be cost-effective. Furthermore, the increased contact with     |
| 47 | standard care nurses did not improve glycaemic control.  |
| 48 |  |
| 49 | Keywords: Type 2 diabetes, Self-management, Motivational interviewing, Cognitive               |
| 50 | behavioural therapy, Glycaemic control   |
| 51 |  |
| 52 | How this fits in   |
| 53 | The evidence that low intensity psychological interventions to support self-management in      |
| 54 | people with poorly controlled type 2 diabetes in primary care setting is limited.              |
| 55 | It is not known whether practice nurses can be trained to deliver low intensity psychological  |
| 56 | treatments to support self-management in type 2 diabetes.                                      |
| 57 | Training on low intensity psychological interventions based on motivational interviewing and   |
| 58 | basic cognitive behaviour therapy led to basic proficiency in these skills but this was not    |
| 59 | maintained.  |

60 Offering more sessions with practice nurses to support self-management in people with

61 persistent hyperglycaemia does not lead to improvement in glycaemic control in type 262 diabetes.

# 64 Introduction

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

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

74 One of the roles of the practice nurse is to support diabetes self-management. Hospital 75 diabetes specialist nurses can be trained to competently deliver MI and basic CBT skills with improvement in glycaemic control in type 1 diabetes<sup>12</sup> and psychological interventions could 76 be delivered by nurses in research settings.<sup>13</sup> We defined a package of six psychological 77 78 skillsets for T2D (Diabetes 6 (D6)) of similar intensity to low-level psychological treatments for common mental disorders in the NHS.<sup>14</sup> We tested in a cluster RCT whether training 79 80 practice nurses in D6 skills was associated with increased competency than nurses not receive 81 the training, and whether the D6 intervention was more effective than standard care in 82 improving suboptimal glycaemic control in people with T2D over 18 months and in 83 improving secondary outcomes (such as lipids, depressive symptoms), and if it was cost-84 effective.

# 85 Method

# 86 Trial design

| 87 | D6 was a pragmatic parallel two-arm cluster RCT design for 18 months. GP practices with      |
|----|--|
| 88 | ≥6000 patients registered in the Lambeth, Southwark, Lewisham, Wandsworth, and Bexley        |
| 89 | Clinical Commissioning Groups (representing a resident population of 1.43 million), were     |
| 90 | invited to participate if they had a practice nurse delivering diabetes care. Recruitment of |
| 91 | patients began after each practice consented to randomisation. Randomisation of clusters was |
| 92 | conducted in two phases, as recruitment of practices and patients had slowed down following  |
| 93 | the organisational uncertainties preceding the implementation of the Health and Social Care  |
| 94 | Act 2012. This Act re-organised the UK's National Health Service (NHS), dismantling          |
| 95 | current organisational structures and creating new ones for funding, management,             |
| 96 | accountability and regulation. <sup>15</sup>   |

# 97 **Patients**

98 Inclusion criteria were: adults aged 18–79 years, duration of T2D for ≥2 years, persistent

99 suboptimal glycaemic control defined as International Federation of Clinical Chemistry

100 (IFCC) HbA1c ≥69.4 mmol/mol (National Glycohemoglobin Standardization Program

101 (NGSP) 8.5%) on two occasions (at least once in the preceding 18 months and the second one

102 at recruitment) while on at least two oral diabetes medication (metformin and one other),

103 and/or requiring insulin therapy to ensure that efforts to optimise medical care had been

104 offered to the patient.<sup>15</sup> The IFCC HbA1c was lowered to  $\geq 64$  mmol/mol (NGSP 8%) in

105 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<sup>2</sup> in Phase 1 and >50 kg/m<sup>2</sup> 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.<sup>16</sup>

# 112 **Baseline measures**

- 113 Baselines measures before randomisation were: age, gender, self-reported ethnicity,
- 114 occupation, employment status, and smoking status. Complication status included:
- 115 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.

# 118 **Randomisation**

119 Randomisation of practices (unit of cluster) was conducted by an independent statistician

120 using a random number generator to assign equal numbers of practices to each arm at each

- 121 phase. For allocation concealment, an independent manager held the randomisation list in
- 122 password-locked computer.

# 123 Intervention

# 124 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.<sup>17</sup> 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.

131

## 132 Group 2: Standard care plus Diabetes 6

133 The theory underlying MI is that the patient's state of ambivalence (resistance versus 134 willingness to make lifestyle changes) is the core psychological construct that needs 135 addressing.<sup>6</sup> MI is a directive, counselling style which encourages patients to change 136 behaviours using collaborative, non-judgmental, and affirming communications. The theory 137 underlying CBT is that barriers to diabetes self-management are maintained by unhelpful 138 thoughts (e.g., if I can't cure diabetes, what's the point?), unhelpful behaviours (e.g., missing 139 insulin doses), and distressing emotions (e.g., low mood/anxiety when seeing a high blood glucose reading).<sup>18,19</sup> Identifying and challenging these cognitive barriers are effective in 140 changing behaviours.<sup>20</sup> The D6 nurses were trained to integrate diabetes care with six skills 141 142 drawn from MI and CBT, as follows : 1. Active listening; 2. Managing resistance; 3. 143 Directing change; 4. Supporting self-efficacy; 5. Addressing health beliefs; and 6. Shaping 144 behaviours. This consisted of 12 sessions, each 30 minutes in duration, over 12 months. The 145 sessions were held in routine primary care clinics and were audiotaped.

146 The Motivational Interviewing Treatment Integrity (MITI) Scale (version 3.1.1)<sup>21</sup> and

147 Behaviour Change Counselling Index (BECCI)<sup>22</sup> were used to compare competencies in both

148 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.

# 151 Outcomes

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

161 specific psychological burden.<sup>24</sup> A fasting blood sample was used for HbA1c, total

162 cholesterol, and triglycerides.

# 163 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 168 80% power at a two-sided alpha-level of 5%, with 20 practices with 18 patients each per arm.

169 We assumed two practices per arm would dropout, thus requiring 24 practices with a total

170 patient sample of 24x18=432 patients. After adjusting for clustering by practice (clustering

171 intra-correlation coefficient (ICC)=0.05) and an inflation factor of 1.7, the final required

172 sample size was 81x1.7=138 patients per arm.

173 We recruited 334 patients of which 231 had at least one follow-up in 24 clusters. The average

174 cluster size was therefore 10 patients per cluster, smaller than our assumed size of 15 patients

175 per cluster with a post-hoc power of 77% at two-sided alpha-level of 5%.<sup>25</sup>

# 176 Statistical analysis

177 Data were analysed using STATA 13. The sample characteristics were described as means 178 (standard deviation (SD)) or as proportions (percentage). A comparison of patient list size 179 and Index of Multiple Deprivation (IMD) 2010 rank score by practices that participated 180 versus those that did not was conducted using Student's t-test. The IMD 2010 score is a 181 composite index of relative deprivation at a small area level, based on seven domains of 182 deprivation: income, employment, health deprivation and disability, education, skills and training, barriers to housing and services, crime and disorder, and living environment.<sup>26</sup> A 183 184 linear mixed-effects model estimated group differences in HbA1c levels between D6 and 185 standard care groups at 18 months. Nurse was included as a random effect as the unit of 186 randomisation. Secondary outcomes were also analysed using linear mixed models to 187 estimate group differences at 18 months.

188 Twenty-nine participants with HbA1c <64 mmol/mol were mistakenly recruited because of 189 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.

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

# 196 **Results**

- 197 We invited 116 practices, 26 agreed to participate and two dropped out before randomisation
- 198 (Figure 1; Appendix2:Table 1) and 995 potentially eligible participants. Of the 451 who
- 199 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
- 201 D6 practice dropped out after randomisation, before the nurse received the training, and
- 202 before all patients were recruited (those who consented remained in the ITT analysis). Invited
- 203 practices that participated (n=24) compared to those that did not (n=89) had higher mean
- 204 patient list sizes (12180 (SD=5099) vs. 10091 (SD=3894), p=0.03) but no difference in IMD
- 205 score (10049 (SD=6910) versus 12441 (SD=7785), *p*=0.17). Table 1 presents the baseline
- characteristics of the sample.
- 207 Figure 1 here; Table 1 here
- 208 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.

210 Primary outcome data at 18-month follow-up were collected for 219 (65.6%) participants and 211 a further 12 had 15-month HbA1c data, providing 231 participants. There was a non-212 significant larger proportion with missing HbA1c in the D6 group compared to standard care 213 (35.9% versus 32.9%, respectively) (Appendix 2:Table 2) and more likely to be 214 African/Caribbean or Asian/Other ethnicity. In the ITT analysis, there was no significant 215 difference in mean HbA1c at follow-up in the D6 group compared to the standard care group 216 (table 2). The ICC for the clustering effect of nurse was 0.02 (95% CI 0.001-0.37). Linear 217 mixed models showed no significant effects of the intervention on the secondary outcomes 218 including BMI, blood pressure, fasting triglyceride, or psychological distress (table 2).

219 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).

231 Table 3 here

232 The inter-rater reliability for the MITI global domains of spirit and empathy was 0.87 and 233 0.91 respectively so we combined both sets of ratings and derived the mean score for each 234 domain. We rated 69 sessions (4.0% of all available recordings) for fidelity from 33/170 and 235 36/164 patients from the D6 and standard care groups respectively (Table 4). The level of 236 competency in the D6 group was below the beginner proficiency level in all the scales for MI 237 and BECCI. Except for a slightly higher proportion of open questions in D6, and a slightly 238 larger reflection/question ratio in standard care, there were no statistically significant 239 differences in the remaining mean MI domain scores or BECCI scores.

240 Table 4 here

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

# 245 Discussion

# 246 Summary

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

# 251 Strengths and limitations

252 This was a pragmatic design set in real-world, inner-city, primary care representing the ethnic and social diversity of people with T2D.<sup>27</sup> Only a few other RCTs have achieved similar 253 ethnicity distributions.<sup>28–34</sup> This was a high risk group for diabetes complications. We 254 255 selected a cluster design to reduce contamination of the intervention in the control group. 256 Contamination is the process whereby an intervention intended for members of the trial 257 (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.<sup>35</sup> We assessed contamination by comparing 258 259 the competencies in the intervention and control group. The hypothesis was that the control 260 group would have lower competencies than the D6 group. As both groups had similar and 261 borderline beginner proficiency competencies (which is probably the pre-training level of 262 competency) we concluded it was unlikely there was contamination. We developed a 263 theoretically informed intervention and an evidence-based manual. We measured fidelity 264 (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 265 266 sessions to patients randomised to the control group. We were only slightly underpowered at 267 77% power compared to the 80% originally proposed. The upper limit of the 95% confidence 268 interval of the estimated treatment effect for HbA1c (4.8 mmol/mol) was less than estimated treatment reductions in meta-analyses.<sup>36</sup> The comprehensive within-trial economic evaluation 269 270 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,

276 imputing missing data confirmed the lack of cost-effectiveness of D6. We did not obtain

277 sufficient repeated measures of HbA1c. We failed to achieve a minimum level of beginner

278 proficiency in motivational interviewing in the D6 group therefore unable to conclude that

279 motivational interviewing is not effective in supporting self-management.

# 280 **Comparison with existing literature**

- 281 Although there have been over 40 RCTs in this field since the last review,<sup>36</sup> only three had
- defined poor glycaemic control (HbA1c ≥64 mmol/mol) as an inclusion criterion and showed
- 283 no benefit from psychological support and only one of these was delivered by nurse care
- 284 managers.<sup>37–39</sup> Recent pragmatic RCTs of similar interventions included samples with near
- optimal glycaemic control with less room for improvement in the primary outcome.<sup>10,11,40</sup>
- 286 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.<sup>28–34</sup>
- 288 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
- 290 either group. This is a common observation in psychological interventions.<sup>43</sup> However, no
- 291 dose-response relationship was observed.

# 292 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.<sup>44</sup> D6 nurses had concerns about over-stepping their professional roles, lacking confidence, and/or resented the

extra workload.<sup>45</sup> The low competencies in most MI and CBT domains suggest that practice 297 298 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 glycaemia, as a surrogate outcome for diabetes complications. However, a landmark RCT<sup>46</sup> 305 and a meta-analysis of RCTs<sup>47</sup> aimed at intensive glycaemic control have failed to observe 306 307 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.<sup>48</sup>

The implication for clinical practice is that low-intensity psychological interventions delivered at low level of competencies may not be as effective in supporting selfmanagement in people with T2D and longstanding suboptimal glycaemic control as 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.<sup>49</sup>
- 325 We urgently need to reconsider what skills, what competencies, which workforce are the
- 326 most effective in delivering psychological interventions to improve glycaemic control in
- 327 people with T2D <sup>50</sup> before investing sparse funds into low intensity psychological treatments
- 328 for improving glycaemic control in T2D.<sup>51</sup>

# 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
- 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 SE1346 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

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

# 353 Author Contributions

- 354 KI, SAA, DStahl, AP, SMT developed the hypotheses. SAA and KI led the conduct of the
- 355 study; KW project managed and contributed to analysis, training and assessment of nurses;
- 356 NDZ developed the Diabetes 6 manual, the protocol for fidelity and did the training and
- 357 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
- 359 evaluation and MH conducted the economic analysis. KI drafted the manuscript and all
- 360 authors contributed to the drafts and approved final version.

# 361 **Competing Interests**

- 362 All authors have completed the ICMJE uniform disclosure form at
- 363 <u>www.icmje.org/coi\_disclosure.pdf</u>. KI has received honorarium from Eli-Lilly, Sanofi,
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# 373 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.

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# 393 Data Sharing

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

395

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# 552 Figures

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



### 555 Tables

| Table 1. Baseline characteristics of participants randomly assigned to receive D6 or standard care. |               |                             |              |  |
|---|---------------|-----------------------------|--------------|--|
| Variable*   | D6<br>(n=164) | Standard<br>Care<br>(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 <sup>1</sup>  | 69 (42.1%)    | 70 (41.2%)                  | 139 (41.6%)  |  |
| No <sup>2</sup>   | 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 <sup>2</sup> )  | 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.

<sup>1</sup>Yes = full-time, part-time, student or self-employed; <sup>2</sup>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).

556

| Table 2. Results from primary and secondary outcomes. |  |     |   |  |  |  |  |
|---|--|-----|---|--|--|--|--|
| Outcome at 18 months                                  | ParticipantsParticipantswith baselinewithmeasurements18 months |     | Estimated Mean Difference:<br>D6 vs standard care (95%<br>CI) |  |  |  |  |
| Primary   |  |     |   |  |  |  |  |
| HbA1c (mol/mmol)*                                     | 332  | 231 | -0.79 (-5.75-4.18)  |  |  |  |  |
| Secondary   |  |     |   |  |  |  |  |
| Body mass index (kg/m <sup>2</sup> )*                 | 329  | 152 | -0.08 (-1.12-0.97)  |  |  |  |  |
| Total cholesterol*                                    | 281  | 140 | -0.08 (-0.42-0.27)  |  |  |  |  |
| Systolic blood pressure<br>(mm/Hg)*                   | 309  | 198 | -1.35 (-6.85–4.14)  |  |  |  |  |
| Diastolic blood pressure<br>(mm/Hg)*                  | 308  | 198 | 1.22 (-1.87–4.32)   |  |  |  |  |
| Fasting triglycerides**                               | 276  | 135 | 0.02 (-0.22-0.26)   |  |  |  |  |
| Patient Health Questionnaire-<br>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

# 

|  | D6         |            |         | Sta        | ndard o    | care |      |            |       |            |
|--|------------|------------|---------|------------|------------|------|------|------------|-------|------------|
| Costs at baseline  | valid<br>n | Mea<br>n £ | SD      | valid<br>n | Mea<br>n £ | SD   | UMD* | 95% CI     | AMD** | 95% CI*    |
| Health and social care costs   | 157        | 847        | 847     | 161        | 976        | 760  | -129 | -301-44    | -96   | -293-101   |
| Costs at 18 months   |            |            |         |            |            |      |      |            |       |            |
| Health and social<br>care costs,<br>excluding<br>intervention,<br>without discounting<br>Health and social | 133        | 707        | 579     | 137        | 793        | 558  | -85  | -25281     | -71   | -242-100   |
| costs, excluding<br>intervention, with<br>discounting  | 133        | 684        | 560     | 137        | 766        | 540  | -82  | -243-78    | -69   | -234—96    |
| Intervention costs<br>Health and social  | 121        | 451        | 99      | 139        | 167        | 100  | 285  | 240-329    | 276   | 225-327    |
| care costs,<br>including<br>intervention costs,<br>with discounting for<br>non-intervention<br>costs       | 92         | 1184       | 572     | 107        | 1025       | 573  | 159  | -39–357    | 150   | -34–333    |
| SF-12-based utility s  | cores a    | t baseliı  | ne      |            |            |      |      |            |       |            |
| 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 s  | cores a    | nd QAI     | .Y gain | s at 18 r  | nonths     |      |      |            |       |            |
| Utility<br>OALY gain since   | 60         | 0.79       | 0.13    | 53         | 0.75       | 0.13 | 0.04 | -0.01-0.08 | 0.01  | -0.03-0.06 |
| baseline, without<br>discounting<br>QALY gain since  | 58         | 1.15       | 0.20    | 48         | 1.11       | 0.18 | 0.03 | -0.04-0.10 | 0.01  | -0.03-0.05 |
| baseline, with<br>discounting and<br>interpolation to<br>match 6-month                                     | 58         | 0.37       | 0.06    | 48         | 0.36       | 0.06 | 0.01 | -0.01-0.03 | 0.00  | -0.01-0.02 |

\*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.

# 

| Table 4. Group comparison for fidelity to MI and CBT. |                            |                          |                  |  |  |  |
|---|----------------------------|--------------------------|------------------|--|--|--|
| MI domain <sup>a</sup>                                | D6                         | Standard care            | <i>p</i> -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<br>Reflections                     | 0.35 (0.20)                | 0.40 (0.17)              | 0.25             |  |  |  |
| Proportion Open Questions                             | 0.36 (0.17)                | 0.25 (0.10)              | <0.01            |  |  |  |
| <b>Reflection/Question Ratio</b>                      | 0.57 (0.47-0.72)           | 0.74 (0.53-1.19)         | 0.03             |  |  |  |
| Proportion Motivational<br>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 deviati                       | on) or median (interquarti | le range) as appropriate |                  |  |  |  |

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. \*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  $\geq 1$ ,  $\geq 0.5$  open questions relative to all questions,  $\geq 0.4$  complex reflections relative to all reflections, and  $\geq 0.9$  MI adherent.

| Appen<br>Append | dices<br>dices to: Cluster randomised controlled trial of a psychological intervention for type  | 2   |
|-----------------|--|---|
| diabete         | S.   |   |
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|                 |  |   |
|                 |  |   |
|                 | Append         Append         diabete         Table of         1       Fu         2       Ac         3       CC         4       Su         4.1       4.2         4.3       4.4         4.5 | Appendices         Appendices to: Cluster randomised controlled trial of a psychological intervention for type diabetes. <b>Table of Contents</b> 1       Full description of the study's methods |

# 590 1 Full description of the study's methods

591

# 592 Trial design

593 D6 was a pragmatic parallel two-arm cluster RCT design for 18 months. Ethical approval was 594 granted by the King's College Hospital Research Ethics Committee (reference 09/H0808/97) 595 and by the respective Primary Care Trusts (reference RDLSLBex 534 and 2010/403/W). 596 Changes to the protocol were approved by the Trial Steering Committee and the Research 597 Ethics Committee. All participants gave informed consent, including access to their medical 598 records.

599 All moderate-to-large GP practices (≥6000 patients registered) in the Lambeth, Southwark,

600 Lewisham, Wandsworth, and Bexley Clinical Commissioning Groups, representing a resident

601 population of 1.43 million in south London, UK, were invited to participate if they had a

602 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

604 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

606 Social Care Act 2012. This Act reorganised the UK's National Health Service (NHS),

607 dismantling current organisational structures and creating new ones for funding,

608 management, accountability, and regulation.<sup>15</sup>

# 609 Patients

610 The target population was adults with T2D who had persistent suboptimal glycaemic control

611 despite care pathways based on national guidance,<sup>17</sup> therefore a group likely to have barriers

to achieving optimal self-management. The study population was patients on diabetes

613 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

615 each practice and invited to participate. Three practices were eligible and willing to

616 participate but did not have a nurse to second. A protocol change was made in Phase 2, which

617 allowed a consenting practice without a nurse to amalgamate with an adjacent consenting

618 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 clinicalguidance for diabetes care.

621 Inclusion criteria were adults aged 18–79 years, duration of T2D for  $\geq$ 2 years, persistent 622 suboptimal glycaemic control defined as HbA1c  $\geq$ 69.4 mmol/mol on two occasions (at least 623 once in the preceding 18 months and at recruitment) while on at least two oral diabetes 624 medications (metformin and one other), and/or requiring insulin therapy. The HbA1c was 625 lowered to  $\geq 64$  mmol/mol in Phase 2 to increase recruitment. These lower cut-offs for HbA1c 626 was selected to maximise the proportion of patients who could potentially benefit. The 627 minimum requirement of being prescribed at least two classes of oral diabetes medications 628 was to ensure that efforts to optimise and intensify medical care according to national 629 guidance had been offered to the patient before randomisation. Exclusion criteria were: 630 severe mental disorders; terminal illnesses and end-stage diabetes complications; morbid 631 obesity with a BMI >40 kg/m<sup>2</sup> in Phase 1, which was raised to >50 kg/m<sup>2</sup> in Phase 2 to 632 enhance recruitment; non-ambulatory as patients had to be able to attend the clinic; no 633 phone/internet access; non-English-speaking as therapy was delivered in English; and 634 currently receiving psychological treatments from elsewhere. Patients who had Patient Health 635 Questionnaire-9 (PHQ-9) depressive scores >20 were excluded if they had psychotic depression or active suicidal ideation.<sup>16</sup> 636

# 637 Randomisation

638 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

640 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

642 manager was only able to reveal to themselves, and then to one D6 researcher, the allocation

643 after entering the details of the practice.

644 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

646 were recruited after randomisation of clusters but remained blind to allocation until the

647 interventions were offered in both groups.

# 648 **Procedures**

# 649 **Baseline measures**

- 650 Baselines measures were: age, gender, self-reported ethnicity, occupation, employment
- status, and smoking status. HbA1c was measured centrally (King's College Hospital NHS
- 652 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
- 656 photography documented in the community-based Diabetic Eye Complications Screening
- 657 Service (DECS), with a new appointment arranged if one had been missed; urine was
- 658 collected to assess nephropathy using the urinary albumin:creatinine ratio (ACR); and history
- of macrovascular complications collected from the medical records.
- 660 In addition, the following secondary outcomes were measured: systolic and diastolic blood
- 661 pressure using an electronic sphygmomanometer; body mass index (BMI) (kg/m<sup>2</sup>) and waist
- 662 circumference (cm); depressive symptoms using the Patient Health Questionnaire-9
- questionnaire;<sup>16</sup> the Alcohol Use Disorders Identification Test (AUDIT);<sup>23</sup> and the Diabetes
- 664 Distress Scale, which measures diabetes specific psychological burden (in the protocol we
- had proposed a similar but longer scale).<sup>24</sup> A fasting blood sample was sent for measurement
- 666 of HbA1c, total cholesterol, and triglycerides.

# 667 Intervention

# 668 Group 1: Standard care

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

# 672 Group 2: Standard care plus D6

673 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
- 675 state of ambivalence (resistance versus willingness to make lifestyle changes) is the core
- 676 psychological construct that needs addressing.<sup>6</sup> MI is a directive, person-centered counselling
- 677 style which encourages patients to change behaviours using collaborative, non-judgmental,
- and affirming communications. The theory underlying CBT is that barriers to diabetes self-

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

683 The D6 nurses were trained in six skills drawn from MI and CBT: 1. Active listening; 2. 684 Managing resistance; 3. Directing change; 4. Supporting self-efficacy; 5. Addressing health 685 beliefs; and, 6. Shaping behaviours. These skills were applied to common barriers around 686 diabetes such as medication adherence, self-testing, physical activity and dietary changes. 687 The training was conducted by a senior diabetes-experienced clinical psychologist and lasted 688 three months. It comprised three hours per week, interactive classroom activities, a training 689 caseload (average 3-5 non-study patients), and weekly supervision of audiotaped sessions. 690 We produced a manual containing the rationale for D6, the six psychological skills, case 691 examples, strategies to manage clinician's own resistance, and for 'troubleshooting' common 692 clinical obstacles. D6 nurses were expected to apply the skills flexibly to different situations 693 (e.g., weight loss, medication adherence) using visual aids and worksheets. The format was 694 12 face-to-face individual sessions (sessions 1-4 fortnightly during months 1-2, sessions 5-6 695 monthly during months 3-6, and sessions 7-12 during months 7-12). Monthly group 696 supervision by a senior clinical psychologist was provided. The sessions were audio-taped for 697 assessment of fidelity.

- 698 The Motivational Interviewing Treatment Integrity (MITI) Scale (version 3.1.1)<sup>21</sup> and
- 699 Behaviour Change Counselling Index (BECCI)<sup>22</sup> were used to assess treatment fidelity of D6,
- and to compare competencies in both groups. The MITI assesses: global spirit and global
- rot empathy with scores  $\geq$  3.5 (range 1-5); percentage of complex reflections, open questions,
- and MI adherent behaviours with scores of  $\geq$ 40%, 50%, and 90% respectively; and ratio of
- reflections to closed questions scores with  $\geq 1$  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
- 707 psychologist, blind to treatment allocation, rated the BECCI. We stratified sessions by nurse
- and patient and then randomly selected tapes (that lasted  $\geq 20$  minutes) for 3 different patients
- for each nurse from either session 2, 3 and 4. Three nurses did not have three tapes lasting 20
- 710 minutes or more and, for these, the three longest tapes were chosen.

# 711 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

715 missing at 18-month, we used routinely collected HbA1c data if it was collected within the

716 15-month follow-up window. Secondary outcomes were change in lipids, blood pressure,

717 BMI and depressive symptoms at 18 months. Research assistants were blind to allocation

718 when collecting follow-up data.

# 719 Sample size

720 A 10.9 mmol/mol difference in HbA1c in D6 compared to standard care was the minimal 721 clinically acceptable reduction at 18 months, considering: (a) baseline HbA1c and (b) that 722 standard care may produce a 2.2 mmol/mol (equivalent to 0.2%) reduction in HbA1c for the 723 placebo effect of participating in a RCT (actual difference between groups 8.8 mmol/mol 724 (equivalent to 0.8%), equivalent to a moderate effect size of d=0.55). Assuming 20% 725 dropout, we needed 360 patients to achieve 80% power at a two-sided alpha-level of 5%, 726 with 20 practices with 18 patients each per arm. We then took account of clustering by 727 practice and we assumed two practices per arm dropped out. Therefore, we needed 24 728 practices with a total patient size of 24x18=432 patients. The required sample size adjusted 729 for a clustering intra-correlation coefficient (ICC) effect of 0.05 was 81x1.7=138 patients per 730 arm (inflation factor 1.7).

731 We recruited 334 patients of which 231 had at least one follow-up in 24 clusters. The average

r 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-

734 level of 5%.<sup>25</sup>

# 735 Statistical analysis

736 Data were analysed using STATA 13. The sample characteristics were described as means

737 (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

739 did not was conducted using Student's t-test.<sup>26</sup> A linear mixed-effects model estimated group

740 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.

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

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

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

included and this was a protocol violation. We performed a sensitivity analysis by including a

binary covariate of this protocol violation (yes/no) in the model.

763 The analyses were conducted using maximum likelihood under the missing at random

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

the model and by using multiple imputation for the missing values of HbA1c (50 imputations

vising *mi* impute command in STATA 13 with all variables from the mixed-effects model

included in the imputation model, as well as age, ethnicity, gender, baseline BMI, total

cholesterol, triglycerides, blood pressure, and PHQ-9 score).

The Data Monitoring Committee oversaw the study.

# 771 Fidelity

- To assess IRR for each fidelity measure, absolute agreement was measured by estimating the
- 773 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.

# 776 Role of funding source

- 777 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.

# 780 **Patient Involvement**

- 781 We included a person with type 1 diabetes from our local community who also was an active
- 782 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.
- 784 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.

# 788 Transparency Declaration

- 789 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
- 791 discrepancies from the study as planned and these have been explained.

### Additional Tables

| Table 1. Breakdown of patients attending each practice and primary outcome follow-up rates by group. |   |                    |   |  |  |
|--|---|--------------------|---|--|--|
|  | D6  | Standard care      |   |  |  |
| Practice*  | Proportion with<br>HbA1c data at 18<br>months (%) | Practice*          | Proportion with<br>HbA1c data at 18<br>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 a  | are from Phase 1 (HbA1c $\ge 6$                   | 9.4 mmol/mol and E | $3MI \le 40 \text{kg/m}^2$ ). Practices 7-        |  |  |

24 are from Phase 2 (HbA1c  $\geq$  64 mmol/mol, BMI  $\leq$  50kg/m<sup>2</sup>, and twinned practices). \*\* Two practices twinned and covered by 1 nurse. \*\*\* Practice dropped out post-randomisation.

D6=Diabetes 6

| Table 2. Comparison of missingness in H  | HbA1c at 18 months.                    |  |   |
|--|--|--|---|
| Variable   | HbA1c measured at<br>18 months (n=219) | Missing HbA1c<br>at 18 months<br>(n=115) | Test of<br>independence (t-test<br>or Pearson χ <sup>2-</sup> 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)                                | $\chi^2(3)=14.854,$   |
| African/Caribbean  | 103 (47·3)                             | 40 (35.1)                                | <i>p</i> =0·001   |
| 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)                                | 2(2) 0.001 0.056  |
| O level or GCSE equivalent   | 75 (34.9)                              | 41 (36·3)                                | $\chi$ (2)=0.091, p=0.956   |
| No formal qualifications   | 80 (37.2)                              | 42 (37·2)                                |   |
| Relationship status  |  |  |   |
| Married or Cohabiting  | 112 (51.3)                             | 59 (51.3)                                | 2(2) 1 221 0 5 42   |
| Separated/Divorced/Widowed   | 60 (27.7)                              | 37 (32·2)                                | $\chi^{-}(2)=1.221, p=0.543$  |
| 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 <sup>2</sup> )   | 32.1 (6.0)                             | 31.5 (6.4)                               | <i>t</i> =-0·839, <i>p</i> =0·402                                   |
| Systolic BP (mm/Hg)  | 133.6 (17.2)                           | 135.3 (16.9)                             | <i>t</i> =-0·823, <i>p</i> =0·411                                   |
| Diastolic BP (mm/Hg)   | 79.2 (10.0)                            | 79.2 (10.3)                              | <i>t</i> =-0·052, <i>p</i> =0·958                                   |
| HbA1c (mmol/mol)   | 79.1 (17.4)                            | 83.2 (19.3)                              | <i>t</i> =-1·96, <i>p</i> =0·051                                    |
| Total Cholesterol (mmol/L)   | 4.2 (1.1)                              | 4.3 (1.3)                                | <i>t</i> =-0.501, <i>p</i> =0.617                                   |
| Fasting triglycerides (mmol/L)   | 1.6 (1.2)                              | 1.9 (1.4)                                | <i>t</i> =-1.631, <i>p</i> =0.104                                   |
| Diabetes duration (years)  | 10.5 (6.1)                             | 10.0 (6.7)                               | <i>t</i> =-0.694, <i>p</i> =0.488                                   |
| DDS (mean item score)  | 2.2 (0.8)                              | 2.3 (0.8)                                | <i>t</i> =0.959, <i>p</i> =0.338                                    |
| Data are n (%) or mean (SD), as appropria<br><sup>1</sup> Yes = full time, part-time, student or self<br><sup>2</sup> No = retired/unemployed/not seeking em | te.<br>-employed<br>ployment           |  |   |

BMI = Body mass index; BP = blood pressure; DDS = Diabetes Distress Scale

| 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<br>(Spearman's rho)   | 0.88                     |  |  |  |
| % MI Adherent (ICC)   | 0.90                     |  |  |  |
| MI=Motivational interviewing; ICC=Intra-class correlation coefficient<br>*Reliability was calculated as an ICC if the distribution was normal and a |                          |  |  |  |

- 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.



# **3 CONSORT 2010 checklist of information for reporting a cluster randomised**

trial

| Section/Topic                | Item | Standard Checklist item  | Extension for   | Page          |
|------------------------------|------|--|---|---------------|
| Title and abstract           | NO   |  | cluster designs   | NO *          |
|                              | 1a   | Identification as a  | Identification as a cluster   | 1             |
|                              | 14   | randomised trial in the title  | randomised trial in the title   | 1             |
|                              | 1b   | Structured summary of<br>trial design, methods,<br>results, and conclusions  | See table 2   | 2             |
|                              |      | (for specific guidance see<br>CONSORT for abstracts) <sup>i,ii</sup>   |   |               |
| Introduction                 | _    |  | · · · · · · · · · · · · · · · · · · ·   |               |
| Background and<br>objectives | 2a   | Scientific background and explanation of rationale   | Rationale for using a cluster design  | 4-5           |
|                              | 2b   | Specific objectives or<br>hypotheses   | Whether objectives pertain to<br>the the cluster level, the<br>individual participant level or<br>both  | 4             |
| Methods                      |      |  |   |               |
| Trial design                 | 3a   | Description of trial design<br>(such as parallel, factorial)<br>including allocation ratio   | Definition of cluster and<br>description of how the design<br>features apply to the clusters  | 5-6           |
|                              | 3b   | Important changes to<br>methods after trial<br>commencement (such as<br>eligibility criteria), with<br>reasons                                       |   | Appendix      |
| Participants                 | 4a   | Eligibility criteria for<br>participants   | Eligibility criteria for clusters   | 5             |
|                              | 4b   | Settings and locations<br>where the data were<br>collected   |   | 5             |
| Interventions                | 5    | The interventions for each<br>group with sufficient<br>details to allow replication,<br>including how and when<br>they were actually<br>administered | Whether interventions pertain<br>to the cluster level, the<br>individual participant level or<br>both   | 6-7           |
| Outcomes                     | ба   | Completely defined pre-<br>specified primary and<br>secondary outcome<br>measures, including how<br>and when they were<br>assessed                   | Whether outcome measures<br>pertain to the cluster level, the<br>individual participant level or<br>both  | 7-8           |
|                              | 6b   | Any changes to trial<br>outcomes after the trial<br>commenced, with reasons  |   | 7-8, Appendix |
| Sample size                  | 7a   | How sample size was<br>determined  | Method of calculation, number<br>of clusters(s) (and whether<br>equal or unequal cluster sizes<br>are assumed), cluster size, a<br>coefficient of intracluster<br>correlation (ICC or k), and an<br>indication of its uncertainty | 8, Appendix   |
|                              | 7b   | When applicable,   |   | NA            |

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

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

|                     |          | evidence   |    |
|---------------------|----------|--|----|
| Other information   |          |  |    |
| Registration        | 23       | Registration number and<br>name of trial registry  | 2  |
| Protocol            | 24       | Where the full trial<br>protocol can be accessed, if<br>available                        | NA |
| Funding             | 25       | Sources of funding and<br>other support (such as<br>supply of drugs), role of<br>funders | 17 |
| * Note: page number | rs optio | nal depending on journal requirements  |    |

# 815 4 Supplementary Data from the Economic Evaluation

- 816 Correspondence to: Professor Anita Patel anitapatelconsulting@gmail.com
- 817

# 4.1 Summary of methods

818

819 A within-trial economic evaluation assessed the cost-effectiveness of D6 from a health and 820 social care perspective at 18 months. This linked individual-level costs with HbA1c and 821 quality-adjusted life year (QALY) gains estimated from the Short Form 12 (SF-12) version 2.<sup>52,53</sup> We calculated individual-level total costs (English pounds sterling, £, 2011–12 prices) 822 823 by attaching unit costs from national sources to individual-level (all-cause) resource use 824 quantities covering a retrospective 6-month period at baseline and 18 months. Use of hospital 825 services was assessed by retrospective review of hospital records. Use of out-of-area hospital 826 services, community-based services, and medications were measured by self-report using a 827 specifically developed proforma. Cost estimates for D6 included the full costs of staff 828 training/supervision/assessment and time spent on delivery to patients. Outcomes and costs at 829 18 months were discounted by 3.5%.

830 Costs and QALY gains at 18 months were compared using non-parametric bootstrap 831 regressions (10000 repetitions) with baseline covariates and adjustment for nurse. We only 832 calculated incremental cost-effectiveness ratios where either group showed statistically 833 greater costs and outcomes. The probability of cost-effectiveness for D6 was assessed by 834 constructing cost-effectiveness acceptability curves (10000 bootstrap repetitions) for 835 threshold ranges of £0-£50,000 per QALY gain/point improvement in HbA1c. Sensitivity 836 analyses explored the impact on cost and/or outcome differences when: (a) missing data due 837 to loss of follow-up were imputed (using multiple imputation in STATA 11.2) rather than 838 excluded, (b) the unit cost of the D6 intervention was lowered by assuming 50% more people 839 received D6, (c) accounting for the inadvertent inclusion of 29 individuals with HbA1c <64 840 mmol/mol by including a binary covariate for this, and (d) accounting for clustering at 841 practice rather than nurse level.

# **4.2 Intervention Costs**

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

| Intervention<br>Component | Description   | Resources         | Resource and cost details   | Total cost | Unit cost per<br>participant (n164) |
|---------------------------|---|-------------------|---|------------|-------------------------------------|
| Training                  | One training session (three hours) per<br>week for 12 weeks, for 11 trainees.<br>Delivered by one clinical psychologist<br>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 $(1 * 4 * 12 * 2 * \pm 60^1) \pm 5,760$  | £20,074    | £122                                |
|                           |   | Trainees' time    | 11 trainees (primary care nurses) for 3 hours for 12 weeks (11 * 3 * 12 * $\pounds 35^2$ ) $\pounds 13,860$ .   |            |                                     |
|                           |   | Capital/materials | Room to train in: 3 hours training for 12 weeks for 2 courses $(3 * 12 * 2 * \pounds 3.10 \text{ per hour}^3) \pounds 223.20$ .<br>Printing of 11 D6 psychology skills handbook: $(11 * \pounds 11.94^4) \pounds 131.34$ .<br>Printing of 10 A4 PowerPoint presentations for 12 session for 11 trainees $(10 * 12 * 11 * \pounds 0.06^5) \pounds 79.20$ .<br>Use of 1 video camera: $\pounds 19.99^6$ |            |                                     |
| Supervision               | 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 $(1 * 3 * 35 * \pounds 60^1)$<br>£6,300.<br>1 band 8a clinical psychologist for 30 minutes for transcription of 131 taped trainee sessions $(0.5 * 131 * \pounds 60^1)$ £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 <sup>7</sup> .  |            |                                     |
|                           |   | Materials         | 1 audio recorder per trainee: (11 * £24.99 <sup>8</sup> ) £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 * $\pounds 60^{9}$ ) $\pounds 330$   | £330       | £2                                  |

| Total for training |   |  |   | £43,853          | £267                |  |  |  |  |  |
|--------------------|---|--|---|------------------|---------------------|--|--|--|--|--|
| Intervention       | Participants offered 12 sessions over twelve months.                              | ed 12 sessions over Trainees' time Individually calculated for each case based on number of sessions attended (assume 30 minute session): (30 minutes * £0.75 per minute <sup>10</sup> ) £22.50 per session. |   | Cost per patient | Mean £301           |  |  |  |  |  |
| Sources and de     | Sources and details (all pounds sterling (£), 2011/12 prices):                    |  |   |                  |                     |  |  |  |  |  |
| 1. Curtis L. 201   | 2. Unit Costs of Health and Social Car  | e 2012. Personal Social  | Services Research Unit: University of Kent. Based on £60 per h    | our, band 8a cl  | linical             |  |  |  |  |  |
| psychologist.      | 2 Unit Costs of Hoalth and Social Cos   | a 2012 Demonal Social  | Somioos Descorch Unit: University of Vant Desed on £25 per h      | our avaluding    | qualifications      |  |  |  |  |  |
| 3 Hurley MV        | 2. Onit Costs of Health and Social Car<br>Walsh NE, Mitchell HL, Pimm I, Will     | iamson E Jones RH Re   | eves BC Dieppe PA Patel A Economic evaluation of a rehabil        | itation program  | qualifications.     |  |  |  |  |  |
| exercise, self-m   | anagement, and active coping strategi   | es for chronic knee pain.  | Arthritis & Rheumatism (Arthritis Care & Research) 2007; 57 (     | (7): 1220-122.   | Obtained further    |  |  |  |  |  |
| details via corre  | espondence with the authors. Based on   | capital costs of a gym (#  | £5.10 per hour, 2003/4 prices), halved to give more appropriate s | sized room (£2   | .55), inflated to   |  |  |  |  |  |
| 2011/12 prices     | $(\pounds 3.10)$ , (inflation source: Curtis L. 20                                | 12. Unit Costs of Health   | and Social Care 2012. Personal Social Services Research Unit:     | University of I  | Kent, The           |  |  |  |  |  |
| Hospital & Con     | from the clinical team: f11.94 each   | x – annual percentage pi   | rices increase).  |                  |                     |  |  |  |  |  |
| 5. Rymans phot     | cocopying. Available at: http://www.ry  | man.co.uk/photocopving   | g [accessed: 13/02/2015]: £0.06 per copy for 100+ pages           |                  |                     |  |  |  |  |  |
| 6. Argos camco     | rder. Available at: http://www.argos.c  | o.uk/static/Product/partN  | Number/2268077.htm [accessed: 13/02/2015]: £19.99 for the low     | vest priced cam  | ncorder.            |  |  |  |  |  |
| 7. Transcript D    | ivas Transcription Services. Available  | at: http://transcriptdivas   | .co.uk/ [accessed: 13/02/15] Based on £0.80 per minute of record  | ding data.       |                     |  |  |  |  |  |
| 8. Argos voice     | recorder. Available at: <u>http://www.arg</u>                                     | os.co.uk/static/Product/p  | artNumber/3071452.htm [accessed: 13/02/2015]: £24.99 for the      | lowest priced    | voice recorder.     |  |  |  |  |  |
| 9. Curtis L. 201   | 2. Unit Costs of Health and Social Car<br>and Sa purse, with proportions of a bas | e 2012. Personal Social  | Services Research Unit: University of Kent. Based on £46,600 i    | median full-tim  | ie equivalent total |  |  |  |  |  |
| 10. Curtis L. 20   | 12. Unit Costs of Health and Social C   | are 2012. Personal Socia   | I Services Research Unit: University of Kent. Based on £45 per    | hour of face-to  | -face contact       |  |  |  |  |  |
| excluding quali    | fications.  |  |   |                  |                     |  |  |  |  |  |
|                    |   |  |   |                  |                     |  |  |  |  |  |

# **4.3 Other Unit Costs**

# 847 Table S2: Unit costs

| Item   | Unit    | Unit     | Sourc | Notes   |
|--|---------|----------|-------|---|
|  | 0       | cost (f) | e     |   |
|  |         | 2011 12  | U     |   |
|  |         | 2011-12  |       |   |
|  |         | prices   |       |   |
| Innationt services                                     |         |          |       |   |
| Nervous System   | bed dav | 368      | 1     | NHS reference cost - Code A   |
| Eves & 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                      | bed day | 452      | 1     | NHS reference cost - Code E   |
| Conditions   |         |          |       |   |
| 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   |
| Eamala Barraduativa System & Assisted                  | bed day | 500      | 1     | NHS reference cost - Code L   |
| Reproduction   | beu uay | 399      | 1     | NHS lefelence cost - Code M   |
| Obstetries   | 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 O   |
| Radiology and Nuclear Medicine                         | bed day | 513      | 1     | NHS reference cost - Code R   |
| Haematology, Chemotherapy, Radiotherapy &              | bed day | 448      | 1     | NHS reference cost - Code S   |
| Specialist Palliative Care                             |         |          |       |   |
| 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<br>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   |
| 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       | I     | Total - OPATT Tab: Direct Access Plain Film -<br>DAPF   |
| Community based professionals                          |         |          |       |   |
| GP at surgery  | contact | 36       | 2     | P183 - PSSRU - per patient contact lasting 11.7<br>minutes - Excludes qualification costs, including<br>direct care staff costs   |
| GP at home   | contact | 92       | 2     | P183 - PSSRU - per patient out of surgery visit<br>lasting 23.4 minutes - Excludes qualification costs,   |
| GP telephone   | contact | 22       | 2     | P183 - PSSRU - per telephone contact lasting 7.2<br>minutes - Excludes qualification costs, including   |
| Diabetes specialist nurse at surgery                   | contact | 11.11    | 2     | unect care start costs.<br>p178 - PSSRU - Nurse specialist - £43 per hour<br>excluding qualifications, assuming 15.5 (specified   |
| Diabetes specialist nurse at home                      | contact | 16.11    | 2     | on p180 for practice nurse) min appointment<br>p178 - PSSRU - Nurse specialist - £43 per hour<br>excluding qualifications, - using per hour of home<br>visiting from community nurse (p175) - £61:£42 = |
| Diabetes specialist nurse telephone                    | contact | 6.78     | 2     | 1.45 SO - 11.11*1.45=16.11<br>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<br>contact excluding qualifications assuming 15.5<br>(specified on p180) min appointment   |
| Practice nurse at home            | contact | 16.166 | 2 | based on practice nurse surgery visit cost above but<br>use the proportion of district nurse home visit hour /<br>clinic hour proportion from PSSRU 2010<br>(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<br>activity - with proportions of home visit from<br>community nurse (p175, PSSRU) - £61:£42 = 1.45<br>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<br>out an NHS sight test by the governments of<br>England, Wales, and Northern Ireland remains at<br>£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<br>proportion of district nurse home visit hour / clinic<br>hour proportion from PSSRU 2010 (68/49=139%)   |
| Optician telephone                | contact | 12.627 | 2 | assume same proportion of costs as a GP telephone<br>call (61% (*0.61))  |
| District nurse at surgery         | contact | 11.347 | 2 | based on district nurse home visit cost above but<br>use the proportion of clinic hour / home visit hour<br>proportion from PSSRU 2010 (49/68=72%)   |
| District nurse at home            | contact | 15.76  | 2 | P175 - PSSRU - Community nurse including<br>district - £61 per hour of home visiting including<br>travel, excluding quals, assume 15.5 (see page 180)<br>min appointment   |
| District nurse telephone          | contact | 9.6136 | 2 | assume same proportion of costs as a GP telephone<br>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<br>proportions of home visit from community nurse<br>(p175, PSSRU) - $\pounds 61: \pounds 42 = 1.45$ SO -<br>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) -<br>N5A1 - Community Physiotherapy Services : Adult<br>- One-to-One Services - £47   |
| Physiotherapist at home           | contact | 70.367 | 1 | TCSCT tab (community based therapy services) -<br>N5A1 - Community Physiotherapy Services : Adult<br>- One-to-One Services - £47 - but with proportions<br>of home visit from community nurse (p175,<br>PSSRI) - f61:f42 = 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 -<br>assume 1 hour meeting, Excludes qualification<br>costs   |
| Occupational therapist at home    | contact | 54.78  | 2 | Cost combines price from 2011/12 (above) but with<br>proportions of client time set down in 2009-10<br>(p152) book (£42 per home visit / £23 per hour =<br>182.61%). £30 per hour (excluding qualifications)<br>multiplied by 182.61%              |
| Occupational therapist telephone  | contact | 18.3   | 2 | assume same proportion of costs as a GP telephone<br>call (61% (*0.61))  |
| Psychiatrist at surgery           | contact | 171.4  | 1 | TMHCSOPFUAF tab (Mental Health Consultant<br>Services (Outpatient Setting) - Follow-up<br>Attendance Face to Face) - MHOPFUA2 (Adult<br>other services)  |
| Psychiatrist at home              | contact | 248.53 | 1 | based on psychiatrist visit cost above but use the<br>proportion of home visiting from community nurse<br>(p175, PSSRU) - £61:£42 = 1.45 SO -<br>166*1.45=240.70   |
| Psychiatrist telephone            | contact | 51.626 | 1 | TMHCSOPFUANF tab (Mental Health Consultant   |

| 1                                 |          |        |        | 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                       |
| Psychologist at home              | contact  | 189.04 | 2      | based on psychologist visit cost above but use the                      |
| r sychologist at nome             | contact  | 107.04 | 2      | 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                       |
|                                   |          | 12.6   | 2      | face to face v non face to face $(30\% (*0.30))$                        |
| Psychotherapist at surgery        | contact  | 136    | 2      | Assume same as a psychologist. "A psychotherapist                       |
|                                   |          |        |        | 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                       |
|                                   |          |        |        | 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  |
| Counsenor at nome                 | contact  | 82.01  | 2      | proportion of district purse 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                        |
| 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                       |
| Home help/ care worker at surgery | contact  | 11.58  | 2      | race to race v non race to race (30% (*0.30))                           |
| Home help/ care worker at surgery | contact  | 11.58  | 2      | P193 PSSRU - Home care worker per hour of face                          |
| <b>r</b>                          |          |        |        | 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                   |
| Home help/ eere worker telephone  | contract | 7 0629 | 2      | so accounting for this $(23.16/2 = \pm 11.58)$                          |
| Home help/ care worker telephone  | contact  | 7.0038 | 2      | 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                               |
|                                   |          | 2.05   | 2      | 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 -                          |
| i namacist for advice at surgery  | contact  | ,      | -      | 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 telephone              | contact  | 22.338 | 4      | 21.02 in $2009/10$ so inflate up to $2011/12$                           |
|                                   | contact  |        |        | m 2003/10 50 minute 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 pump                      | item     | 2375   | 0<br>7 | per 1 pen. p440 - autopen 24  |
| 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   |
|                                   |          |        |        |   |

|      | Sourc | es  |
|------|-------|---|
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# 855 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

857 **costs discounted**)

|                                |         | Control |     |         | Intervention |     | Unadjusted                      | 95% C.I.    | Adjusted                         | 95% C.I. <sup>s</sup> |
|--------------------------------|---------|---------|-----|---------|--------------|-----|---------------------------------|-------------|----------------------------------|-----------------------|
|                                | valid n | Mean £  | SD  | valid n | Mean £       | SD  | mean<br>difference <sup>s</sup> |             | mean<br>difference <sup>ss</sup> |                       |
| Costs at 18 months             |         |         |     |         |              |     |                                 |             |                                  |                       |
| Per protocol                   |         |         |     |         |              |     |                                 |             |                                  |                       |
| Health & social care costs     | 107     | 1025    | 573 | 92      | 1184         | 572 | 159                             | -39 to 357  | 151                              | -32 to 334            |
| including intervention costs   |         |         |     |         |              |     |                                 |             |                                  |                       |
| GP Clustering                  |         |         |     |         |              |     |                                 |             |                                  |                       |
| Health & social care costs     | 107     | 1025    | 573 | 92      | 1184         | 572 | 159                             | -39 to 357  | 150                              | -30 to 329            |
| including intervention costs   |         |         |     |         |              |     |                                 |             |                                  |                       |
| Alternative intervention cost  |         |         |     |         |              |     |                                 |             |                                  |                       |
| Health & social care costs     | 107     | 1025    | 573 | 92      | 1095         | 572 | 70                              | -128 to 268 | 61                               | -123 to 244           |
| including intervention costs   |         |         |     |         |              |     |                                 |             |                                  |                       |
| Intention to treat             | 1 50    | 1053    | 105 | 1.4     | 110/         | 470 |                                 | 10 . 100    | 107                              | 5                     |
| Health & social care costs     | 170     | 1052    | 497 | 164     | 1126         | 473 | 74                              | -42 to 190  | 107                              | 7 to 207*             |
| including intervention costs – |         |         |     |         |              |     |                                 |             |                                  |                       |
| intention to treat             |         |         |     |         |              |     |                                 |             |                                  |                       |

858 <sup>S</sup>Comparisons include clustering for nurse. <sup>SS</sup>Comparisons include clustering for nurse plus covariates for baseline cost, age, gender, marital status, ethnicity, duration of

859 diabetes and baseline utility. \* Statistically significant

# 860

## 861 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 | 95% C.I.                        | Adjusted      | 95% C.I. <sup>s</sup>            |               |
|-----------------------------|---------|-----------|-------|--------------|-----------|------------|---------------------------------|---------------|----------------------------------|---------------|
|                             | valid n | Mean<br>£ | SD    | valid n      | Mean<br>£ | SD         | mean<br>difference <sup>s</sup> |               | mean<br>difference <sup>ss</sup> |               |
| 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 | 48      | 0.36      | 0.06  | 58           | 0.37      | 0.06       | 0.01                            | -0.01 to 0.03 | 0.00                             | -0.01 to 0.02 |
| and interpolated)           |         |           |       |              |           |            |                                 |               |                                  |               |
| 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 | 48      | 0.36      | 0.06  | 58           | 0.37      | 0.06       | 0.01                            | -0.01 to 0.03 | 0.00                             | -0.01 to 0.00 |
| and interpolated)           |         |           |       |              |           |            |                                 |               |                                  |               |
| 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)
<sup>\$</sup>Comparisons include clustering for nurse. <sup>\$\$</sup>Comparisons include clustering for nurse plus covariates for age, gender, marital status, ethnicity, duration of diabetes and 862

863 baseline utility. \* Statistically significant

# 864 4.5 Cost-effectiveness

865 For the economic analysis, 139 (42%) and 85 (25%) participants had the two necessary combinations of cost/HbA1c/covariate and cost/SF-

866 12/covariate data, respectively; characteristics of those with and without data were comparable.

867

Based on QALYs, probabilities of cost-effectiveness for the D6 group at 18 months did not exceed 35% at the examined willingness to pay 868 869 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 870 871 a small improvement is unlikely to be clinically meaningful. Based on QALYs, probabilities of cost-effectiveness for the D6 group at 18 months 872 did not exceed 35% at the examined willingness to pay thresholds. However, based on HbA1c, probabilities of cost-effectiveness were around 873 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 874 for a point improvement in HbA1c is unknown, and such a small improvement is unlikely to be clinically meaningful. 875 876

Figure S1: Cost-effectiveness plane for Figure S2: Cost-effectiveness plane for HbA1c changes at 18 months from a health QALY gains at 18 months from a health & & social care perspective

social care perspective



curve for HbA1c point improvements at 18 curve QALY gains at 18 months from a months from a health & social care health & social care perspective perspective

Figure S3: Cost-effectiveness acceptability Figure S4: Cost-effectiveness acceptability





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