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Association between systolic blood pressure and cardiovascular inpatient cost moderated by peer-support intervention among type 2 diabetes: two cohorts study

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TITLE PAGE**TITLE: Association between systolic blood pressure and cardiovascular inpatient cost moderated by peer-support intervention among type 2 diabetes: two cohorts study**

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KEY MESSAGE

- It's unclear whether there is SBP threshold impacting on CVD inpatient costs and could be altered by peer-support in people with diabetes
- Association between SBP and CVD inpatient payment was a 'hockey-stick' shape with a threshold at 133-141 mmHg
- A novel two-part model revealed the combined peer-support intervention altered the above association

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Author Disclosures

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1 **TITLE: Association between systolic blood pressure and cardiovascular inpatient cost**
2 **moderated by peer-support intervention among type 2 diabetes: two cohorts study**

3 **ABSTRACT**

4
5 **Objective**

6 People with type 2 diabetes and increased systolic blood pressure (SBP) are at high risk of
7 cardiovascular diseases (CVD). We aimed to investigate the association between CVD
8 related hospital payments and SBP and test whether it is influenced by diabetes peer-
9 support.

10
11 **Methods**

12 Two cohorts comprising people with type 2 diabetes were included. The first cohort includes
13 4,704 patients with type 2 diabetes assessed between 2008-2009 from 18 general practices
14 in Cambridgeshire and followed up to 2009-2011. The second cohort comprises 1,121
15 patients with type 2 diabetes from post-trial follow-up data, recruited between 2011-2012 and
16 followed up to 2015. The SBP was measured at baseline. Inpatient payments for CVD
17 hospitalization within 2 years since baseline was the main outcome. The impact of 1:1, group
18 or combined diabetes peer support and usual care were investigated in the second cohort.
19 Adjusted mean CVD inpatient payments per person were estimated using a two-part model
20 after adjusting for baseline characteristics.

21
22 **Results**

23 A 'hockey-stick' relationship between baseline SBP and estimated CVD inpatient payment
24 was identified in both two cohorts, with a threshold at 133-141 mmHg, suggesting increased
25 payments for patients with SBP below and above the threshold. The combined peer-support
26 intervention altered the above association, with no increased payment with SBP above the
27 threshold, and payment slightly decreased with SBP beyond the threshold.

28
29 **Conclusion**

30 SBP maintained between 133-141 mmHg is associated with the lowest CVD disease
31 management costs for patients with Type 2 diabetes. Combined peer-support intervention
32 could significantly decrease CVD related hospital payments.

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35
36 **INTRODUCTION**

37 The rapid increase in prevalence and health costs associated with type 2 diabetes has been
38 observed worldwide ¹. It has been estimated that the risk of hospitalisation is two-fold higher
39 in people with diabetes compared to those without diabetes, and the proportion with diabetes
40 is >10% in those admitted to hospital at any one time ². Among some specific age-strata, the
41 proportion is over 20% ³. The associated costs of excess admissions, as well as increased
42 costs per admission, are significant contributors to the financial burden borne by healthcare
43 systems from diabetes and often reflect preventable morbidity suffered by patients ⁴.

44 Systolic blood pressure (SBP), as the most common modifiable risk factor, has been found
45 to be associated both with cardiovascular diseases (CVD) mortality and CVD hospitalisation
46 among people with type 2 diabetes ^{5,6}. However, no established association between SBP
47 and inpatient cost due to CVD hospitalisation has been shown among people with type 2
48 diabetes. Although a target SBP has been agreed to lower the risk of eg CVD mortality and
49 CVD hospitalisation, it is unclear whether this threshold will potential impact on inpatient
50 costs due to CVD mortality.

51 Diabetes peer support involves people with diabetes assisting each other to improve their
52 social, mental and physical wellbeing. Peer support can be provided through individual or
53 group approaches and either face-to-face, telephone or online contact. It is generally seen
54 as a low-cost intervention has been suggested to reduce health-care costs ⁷. Some studies
55 have reported that peer support can reduce health-care costs among people with type 2
56 diabetes ^{8,9}. The RANdomised controlled trial of Peer Support In type 2 Diabetes (RAPSID)
57 was the largest randomised controlled trial (RCT) of type 2 diabetes peer support to date ¹⁰.

58 The intervention was recently shown to be cost-effective during the trial based on self-
59 reported costs ¹¹ and also from prospective hospital costs [12]. In RAPSID, group peer
60 support was associated with 2-3 mm Hg lower SBP, however, it was unclear whether this
61 was a mediator in the reduction in inpatient costs, and whether this was through an effect on
62 CVD hospitalisation specifically.

63 In this study, we aimed to investigate the association between SBP measured in primary
64 care settings and inpatient cost for CVD hospitalisation over the next 2 years accounting for
65 the risk of hospitalisation among people with type 2 diabetes, using data from two cohorts.
66 We have then examined the impact of peer support on this association.

67 **MATERIAL AND METHODS**

68 **Data source and study population**

69 We followed the methods of Dahai Yu et al. 2018 for the data and data collection ¹². Briefly
70 we utilised two cohorts from Cambridgeshire, England: one (main cohort) based on the
71 electronic health record data from primary care settings to develop our CVD hospitalisation
72 and re-hospitalisation risk scores and another (replication cohort) based on post-trial cohort
73 data for external validation.

74 **Main cohort**

75 Patient lists from 18 general practices across Cambridgeshire, England, in 2008/2009 were
76 collated and linked with hospital admissions (Secondary Uses Service) data as part of an
77 evaluation of diabetes care across the county by the local health board, National Health
78 Service (NHS) Cambridgeshire. This cohort was limited to volunteer practices using the
79 Egton Medical Information Systems general practitioner software system, from which a
80 predefined set of data could be extracted. There was no systematic selection process for
81 these surgeries, and data extracted were for their entire diabetes population. All patients with
82 diabetes had follow-up hospitalisation data to 2010–2011. Hospital admissions to NHS and
83 private hospitals within and outside Cambridgeshire were followed-up. No personal
84 identifiers were released to researchers, and all subsequent analyses were conducted on
85 anonymised datasets. Baseline blood pressure and clinical measurements were recorded as
86 part of clinical practice in primary care settings⁶.

87
88

89 Replication cohort

90 The design and methods of the RAPSID trial have been published previously ¹⁰, as have its
91 Consolidated Standards of Reporting Trials diagram and the results of its primary outcomes
92 ¹⁰. Briefly, RAPSID was a 2x2 factorial cluster RCT comparing 4 groups: Controls, 1:1
93 (individual) peer support, group peer support, and combined 1:1 and group peer support
94 among patients with type 2 diabetes. Participants had their diabetes for at least 12 months
95 and those with dementia or psychotic illness were excluded. Participants were recruited from
96 communities across Cambridgeshire and neighbouring areas of Essex and Hertfordshire.
97 Follow up data were only available for participants in Cambridgeshire and neighbouring
98 areas of Hertfordshire that are served by the Cambridgeshire and Peterborough Clinical
99 Commissioning Group (CCG). Clusters were defined by local government ('parish council')
100 boundaries. The intervention was developed following a pilot, using a framework defined by
101 Peers for Progress ¹¹. Peers facilitating peer support were termed peer support facilitators
102 and their selection, training, support and the overall programme are described elsewhere ¹⁰.
103 The intervention lasted 8-12 months and was commenced and concluded, cluster by cluster,
104 between 02/06/11 to 12/04/12. Ethics approval was received from the Cambridgeshire
105 REC2 Committee (10/H0308/72), and signed consent included agreement for access to
106 hospital data.

107 Demographic data, blood pressure, and HbA1c and lipid profiles information were collected
108 at baseline. Blood pressure were measured using the Omron 705IT Electronic BP Monitor ¹³.
109 Each participant was followed up until June 2015 (0.91-4.07 years' follow-up from
110 beginning/entry into the trial). Hospitalisation (NHS hospitals & private hospitals), Accident &
111 Emergency and outpatient visits within/outside Cambridgeshire and the included areas of
112 Hertfordshire were collected through Cambridgeshire and Peterborough Clinical CCG ¹⁴ as
113 well as elective/non-elective status, and International Classification of Diseases (ICD-10)
114 codes¹⁵.

115 Ethical approval

116 Ethics approval was received from the Cambridgeshire REC2 Committee (10/H0308/72),
117 and signed consent included agreement for access to hospital data.

118 **Defining CVD hospitalisation**

119 The primary outcome of the study was having at least one hospitalisation with CVD as the
120 primary diagnosis (ICD-10: I20–I25, I60–I69 and I73 in the first ICD field) over the 2-year
121 follow-up.

122 **Statistical Analysis**

124 A large proportion of the population do not attend hospital as an inpatient or outpatient in
125 any given year and therefore health care payment data demonstrate a skewed
126 utilisation/payment pattern¹⁶. To take into account the problem of ‘zero mass’ and skewed
127 outcomes, the demand functions were modelled using a two-part model¹⁷. In this two-part
128 model, a probit model was estimated for the probability of observing “zero” versus positive
129 medical expenditure. Positive medical expenditure is defined as any healthcare expenditure
130 greater than zero. A generalized linear model (GLM) was estimated, conditional on having
131 healthcare expenditure. GLM was used, instead of log ordinary least squares regression,
132 since it relaxes the normality and homoscedasticity assumption, and avoids bias associated
133 with re-transforming to the raw scale¹⁸. The results of the modified Park test verified that the
134 use of a gamma distribution, with a log link, was the best fitted GLM for consistent estimation
135 of coefficients¹⁹. The variance inflation factor (VIF) for all predictors used in the two-part
136 model indicated no-existence of multi-collinearity²⁰. The F-test for the two-part regression
137 models was found to be significant, which indicated the overall significance of the regression
138 model. Predicted inpatient cost was estimated in the two-part model by the level of baseline
139 SBP with adjustment of other co-variables. Confidence intervals (95% CI) for estimated
140 payments were estimated by a bootstrap process with 1000 samples. Analysis restricted
141 analyses in each financial year were carried out as sensitivity analyses. All analyses were
142 performed with STATA (STATA/SE 14.0 StataCorp Texas).

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145
146

RESULTS

147 In our main cohort, we analysed information on 4,704 type 2 diabetes patients with 588 CVD
148 hospitalisations within 2 years. Our replication cohort had information on 1,121 type 2
149 diabetes patients with 183 CVD hospitalisations. **Table-1** summarises the basic
150 characteristics and clinical measurements of the study population. Patients with type 2
151 diabetes in both cohorts had similar age, gender, blood pressure and total cholesterol.
152 Patients in the main cohort had a higher level of high density lipoprotein, low density
153 lipoprotein, and HbA1c. Compared with the main cohort, those in the replication cohort were
154 more likely to be prescribed lowering lipid medicine. Baseline data for the 4 groups of the
155 replication cohort were well matched (**Table-1**). The sample size of the cohort and
156 intervention groups, characteristics of participants and median cost by baseline systolic
157 blood pressure categories: <120, 120-129, 130-139, 140-149, 150-159, and >160 mmHg are
158 presented in **Table-2**.

159 As shown in Supplemental **Table-1**, inpatient cost data from CVD hospitalisation were
160 typically skewed due to the mass of 'zero' payments and a relatively small proportion of
161 patients incurring extremely high expenditure. 87.5% and 83.7% of participants in the main
162 and replication cohort were not hospitalised due to CVD diseases over the two year of
163 follow-up. Within the replication cohort, 79.7% of controls and 82.8%, 85.4% and 86.8% of
164 patients in the 1:1 group, and combined intervention groups respectively were not
165 hospitalised due to CVD disease. Among patients hospitalised due to CVD diseases, median
166 inpatient costs were £4348.35 (IQR: 1623.50 to 8766.75) and £2430.72 (IQR: 793.06 to
167 4026.20) for the main and replication cohort, respectively. With the replication cohort,
168 median inpatient costs were £2419.60 (1006.91 to 4387.66), £2489.40 (770.69 to 4387.66),
169 £1963.56 (714.93 to 4032.55) and £2436.00 (885.19 to 3473.12) for control, 1:1, group and
170 combined intervention groups, respectively. Compared with patients with no inpatient costs
171 due to cardiovascular diseases hospitalization, patients with such costs were more likely to

172 be older, male, have higher systolic blood pressure, body mass index, and HbA1c, with a
173 lower proportion were prescribed lipid lowering treatment (**Supplemental Table-2**).

174

175 **Results from two-part model**

176 Dose-response relationship curves between SBP and predicted inpatient cost for CVD
177 hospitalisation derived from the two-part models after accounting for the risk of CVD
178 hospitalisation with adjustment of co-variables in **Table-1** are presented in **Figure-1** for the
179 main cohort and the replication cohort. SBP was non-linearly associated with adjusted
180 predicted inpatient cost for CVD hospitalisation (linearity test: all $P < 0.00001$) both in the
181 main and replication cohort. The threshold was estimated at 137 (133-141) mmHg for SBP
182 both in the main sample and replication sample, with consistent stable adjusted predicted
183 inpatient cost for CVD hospitalisation below the threshold and increased predicted inpatient
184 cost above the threshold.

185 Within the replication cohort, dose-response relationship curves between SBP and adjusted
186 predicted inpatient cost for CVD hospitalisation in each group is presented in **Figure-2**. A
187 non-linear association between SBP and adjusted predicted inpatient cost was found in
188 control, 1:1 and group intervention groups (linearity test: all $P < 0.00001$). The threshold at
189 137 (133-141) mmHg for SBP was consistently found in each group, with consistent stable
190 adjusted predicted inpatient cost for CVD hospitalisation below the threshold and increased
191 predicted inpatient cost above the threshold. In the combined intervention group, the
192 adjusted predicted inpatient cost was linearly stable as SBP increased (linearity test:
193 $P=0.05263$). Associations between baseline systolic blood pressure and predicted inpatient
194 cost due to cardiovascular diseases hospitalisation in those receiving 1:1 peer support and
195 among the rest within the replication cohort are presented in **Supplemental Figure 1**. In
196 each baseline systolic blood pressure level, patients who received the 1:1 peer support

197 intervention (as 1:1 alone or as the combined intervention) were more likely to have lower
198 inpatient costs due to cardiovascular diseases hospitalisation.

199 200 **DISCUSSION**

201
202 In this study, using two prospective cohorts, we found a non-linear association between SBP
203 measured in UK populations with type 2 diabetes and the adjusted predicted inpatient cost
204 for CVD hospitalization over 2 years of follow-up, after accounting for the risk of CVD
205 hospitalisation both in the main and replication cohort. Further investigation revealed: SBP
206 below 137 mmHg was associated with stable lowest inpatient cost; inpatient cost increased
207 with an increase in SBP above 137 mmHg. The peer support intervention, especially group
208 intervention combined with 1:1 support had a significant impact on the association between
209 inpatient cost for CVD hospitalisation and SBP.

210 211 **Comparison with previous studies**

212 It is well established that SBP is the major determinant of CVD risk in the population who are
213 aged over 50²¹. In patients with type 2 diabetes, previous studies have revealed a J-shape
214 relationship between SBP and CVD event risk, for example, the United Kingdom Prospective
215 Diabetes Study²² showed a lowered CVD event rate with an attained lower BP goal of
216 144/82 mm Hg. The International Verapamil SR—Trandolapril²³ and the Avoiding CVD
217 Events in Combination Therapy in Patients Living with Systolic Hypertension²⁴ trials also
218 failed to demonstrate a CVD outcome benefit at a blood pressure below 130/80 mm Hg. We
219 have previously shown that an SBP between 133-141 mmHg was associated with the lowest
220 risk of CVD hospitalisation among patients with type 2 diabetes⁶. However, it was not clear
221 whether this J-shape relationship exists between SBP and inpatient costs for CVD
222 hospitalisation as most studies analysed health cost/payments which had a skewed
223 distribution Ours is the first study among patients with T2DM, following adjustment for the
224 individual probability of being hospitalised, and we now show that there is a 'hockey-stick'
225 shape relationship between SBP and CVD inpatient payment. This finding suggests that

226 CVD inpatient payments are stable for SBP below 133-141 mmHg and linearly increase
227 above this range. This in turn supports a SBP target between 133-141 mmHg to minimise
228 future risks of CVD hospitalisation and associated inpatient payments.

229 Although we have shown that CVD hospital payments increase with a baseline SBP above
230 133-144 mm Hg, this was not found to occur in the 2-year post-trial period of RAPSID
231 intervention participants. In RAPSID, group peer support was associated with a significant
232 reduction in SBP after 8-12 month follow-up from baseline and we speculate that it was this
233 lower SBP that was responsible for this finding. Hospitalisation was shown to be reduced in
234 Hong Kong with peer support among those who had high diabetes distress²⁵. We have not
235 been able to elucidate the mechanism behind the lower SBP in RAPSID and have excluded
236 a greater effect among those with high diabetes distress and medication adherence. There
237 was also no evidence of changes in lifestyle as measured by questionnaires, or crudely by
238 body weight (a small reduction in waist circumference was found in the per protocol
239 analyses). The current finding of reduced CVD hospitalisation costs does provide some
240 validity that the lower SBP described was not simply due to chance.

241

242 This suggests that the peer support intervention was associated with a reduced inpatient
243 payment, however in the 2-year post-trial follow-up, among patients in the combined
244 intervention group, CVD inpatient payment did not increase along with the increase of SBP,
245 especially beyond 133-141 mmHg, the slightly reduction in the CVD inpatient payment,
246 suggesting that patients whose SBP beyond 133-141 mmHg were less likely to trigger the
247 CVD hospitalisation that primarily due to the combined peer-support intervention. The
248 potential mechanism could be that patients in the combined intervention might stick to the
249 healthy lifestyle in the post-trial follow-up, which might have an impact on patients' obesity
250 status and then SBP as observed in the trial follow-up. However, there was no post-trial
251 measurements on obesity measurements to prove this hypothesis. Although in the trial
252 follow-up the SBP reduction could not be explained by increased medication adherence as

253 this as previously found to be unchanged [27,28], it was unclear whether anti-hypertensive
254 treatments adherence pattern was modified in the post-trial follow-up restricted by the post-
255 trial information on the medication adherence.

256
257 **Strength and limitation**

258 Strengths of the analysis include that the association between SBP and CVD inpatient
259 payment was examined in two independent cohorts. A further strength is the minimal
260 information bias, with the outcome used, recorded inpatient payments, having been fully
261 recorded by the CCG ²⁶. In particular, as these are payment details, both NHS hospitals and
262 private hospital admissions were able to be included. There would have been some loss for
263 patients where no component of care was paid for by the CCG.

264 Some limitations have to be considered in the interpretation of our findings. Unlike
265 pharmaceutical interventions, where adherence can be assessed using pill counters, it is
266 difficult to evaluate the magnitude of peer-support intervention on an individual level, and
267 although we did record attendance and telephone calls, we did not assess engagement.
268 The payment/savings from similar peer-support interventions should be further investigated
269 in other post-trial observation studies. Another limitation in this study is the inconsistent
270 blood pressure measuring methods between primary care recorded blood pressure
271 measurements (main cohort) and the blood pressure measurement in the trial (replication
272 cohort), in terms of attended or unattended, standardized protocol vs usual measurement,
273 automated vs mercury sphygmomanometer. A further limitation of our study is that we have
274 not been able to describe the activities of participants after the trial was completed. All
275 participants were sent the results, and we are aware that some intervention (e.g. peer
276 support groups) continued including with support from the Diabetes UK "Type 2 Together"
277 programme ¹¹.

278
279 **CONCLUSION**

280 As far as we are aware, our study is the first study to examine the prospective association
281 between SBP and 2-year estimated CVD inpatient payment. A 'hockey-stick' relationship
282 between SBP and 2-year estimated CVD inpatient payment was identified in two
283 independent cohorts, with a consistent threshold at 133-141 mmHg and a linearly increased
284 payment beyond the threshold. Alteration in this relationship following a combined peer-
285 support intervention (group and 1:1 interventions) is suggested by their lack of an increase in
286 estimated CVD payment. Our findings suggest that among people with type 2 diabetes,
287 blood pressure management should target a SBP of 133-141 mmHg. Integration of this
288 threshold into clinical practice guidance, could lower both individual risk of, and associated
289 payments for, CVD hospitalisation.

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300 **Funding statement**

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317 **Author Disclosures**

318 Conflicts of interest: None.

319 **Author Contributions**

320 D.Y., Y.C., Z.Z., and D.S. contributed to the conception and design of this work and to the
321 interpretation of the data. D.Y. performed the data cleaning and analysis and drafted the
322 initial manuscript. D.Y., Y.C., Z.Z., D.H., J.G., and D.S. reviewed and revised the paper and
323 approved the final manuscript.

324 **REFERENCES**

- 325 1. American Diabetes Association. Executive summary: Standards of medical care in
326 diabetes--2012, *Diabetes Care* 2012;35 Suppl 1:S4-S10.
- 327 2. Sampson MJ, Dozio N, Ferguson B, Dhatariya K. Total and excess bed occupancy by age,
328 specialty and insulin use for nearly one million diabetes patients discharged from all English
329 Acute Hospitals, *Diabetes Res Clin Pract* 2007;77:92-98.
- 330 3. Simmons D, English P, Robins P, Craig A, Addicott R. Should diabetes be commissioned
331 through multidisciplinary networks, rather than Practice Based Commissioning? *Prim Care*
332 *Diabetes* 2011;5:39-44.
- 333 4. Vamos EP, Millett C, Parsons C, Aylin P, Majeed A, Bottle A. Nationwide study on trends
334 in hospital admissions for major cardiovascular events and procedures among people with
335 and without diabetes in England, 2004-2009, *Diabetes Care* 2012;35:265-272.
- 336 5. Yamout H, Bakris GL. In search for the 'sweet spot' for blood pressure level in diabetes,
337 *Heart* 2014;100:1404-1405.

- 338 6. Yu D, Simmons D. Association between blood pressure and risk of cardiovascular hospital
339 admissions among people with type 2 diabetes, *Heart* 2014;100:1444-1449.
- 340 7. Dale JR, Williams SM, Bowyer V. What is the effect of peer support on diabetes outcomes
341 in adults? A systematic review, *Diabet Med* 2012;29:1361-1377.
- 342 8. Johansson T, Keller S, Sonnichsen AC, Weitgasser R. Cost analysis of a peer support
343 programme for patients with type 2 diabetes: a secondary analysis of a controlled trial, *Eur J*
344 *Public Health* 2017;27:256-261.
- 345 9. Burton J, Eggleston B, Brenner J, Truchil A, Zulkiewicz BA, Lewis MA. Community-Based
346 Health Education Programs Designed to Improve Clinical Measures Are Unlikely to Reduce
347 Short-Term Costs or Utilization Without Additional Features Targeting These Outcomes,
348 *Popul Health Manag* 2017;20:93-98.
- 349 10. Simmons D, Prevost AT, Bunn C, et al. Impact of community based peer support in type
350 2 diabetes: a cluster randomised controlled trial of individual and/or group approaches, *PLoS*
351 *One* 2015;10:e0120277.
- 352 11. Simmons D, Cohn S, Bunn C, et al. Testing a peer support intervention for people with
353 type 2 diabetes: a pilot for a randomised controlled trial, *BMC Fam Pract* 2013;14:5-2296-14-
354 5.
- 355 12. Yu D, Cai Y, Graffy J, Holman D, Zhao Z, Simmons D. Development and External
356 Validation of Risk Scores for Cardiovascular Hospitalization and Rehospitalization in
357 Patients With Diabetes, *J Clin Endocrinol Metab* 2018;103:1122-1129.
- 358 13. . [https://www.nice.org.uk/guidance/cg127/resources/hypertension-in-adults-diagnosis-
and-management-pdf-35109454941637](https://www.nice.org.uk/guidance/cg127/resources/hypertension-in-adults-diagnosis-
359 and-management-pdf-35109454941637).

- 360 14. Simmons D, Yu D, Wenzel H. Changes in hospital admissions and inpatient tariff
361 associated with a Diabetes Integrated Care Initiative: preliminary findings, *J Diabetes*
362 2014;6:81-89.
- 363 15. Yu D, Simmons D. Association between blood pressure and risk of cardiovascular
364 hospital admissions among people with type 2 diabetes, *Heart* 2014;100:1444-1449.
- 365 16. Andrade LF, Rapp T, Sevilla-Dedieu C. Exploring the determinants of endocrinologist
366 visits by patients with diabetes, *Eur J Health Econ* 2016;17:1173-1184.
- 367 17. Egede LE, Walker RJ, Bishu K, Dismuke CE. Trends in Costs of Depression in Adults
368 with Diabetes in the United States: Medical Expenditure Panel Survey, 2004-2011, *J Gen*
369 *Intern Med* 2016;31:615-622.
- 370 18. Bruno G, Picariello R, Petrelli A, et al. Direct costs in diabetic and non diabetic people:
371 the population-based Turin study, Italy, *Nutr Metab Cardiovasc Dis* 2012;22:684-690.
- 372 19. Smith VA, Preisser JS, Neelon B, Maciejewski ML. A marginalized two-part model for
373 semicontinuous data, *Stat Med* 2014;33:4891-4903.
- 374 20. Rudisill C, Charlton J, Booth HP, Gulliford MC. Are healthcare costs from obesity
375 associated with body mass index, comorbidity or depression? Cohort study using electronic
376 health records, *Clin Obes* 2016;6:225-231.
- 377 21. Bangalore S, Messerli FH, Wun CC, et al. J-curve revisited: An analysis of blood
378 pressure and cardiovascular events in the Treating to New Targets (TNT) Trial, *Eur Heart J*
379 2010;31:2897-2908.
- 380 22. Bloch MJ, Basile JN. Analysis of recent papers in hypertension. Lack of legacy effect
381 with more intensive blood pressure control in the long-term follow-up of the United Kingdom
382 Prospective Diabetes Study, *J Clin Hypertens (Greenwich)* 2009;11:46-49.

383 23. Bangalore S, Gong Y, Cooper-DeHoff RM, Pepine CJ, Messerli FH. 2014 Eighth Joint
384 National Committee panel recommendation for blood pressure targets revisited: results from
385 the INVEST study, *J Am Coll Cardiol* 2014;64:784-793.

386 24. Bakris G, Hester A, Weber M, et al. The diabetes subgroup baseline characteristics of
387 the Avoiding Cardiovascular Events Through Combination Therapy in Patients Living With
388 Systolic Hypertension (ACCOMPLISH) trial, *J Cardiometab Syndr* 2008;3:229-233.

389 25. Chan JC, Sui Y, Oldenburg B, et al. Effects of telephone-based peer support in patients
390 with type 2 diabetes mellitus receiving integrated care: a randomized clinical trial, *JAMA*
391 *Intern Med* 2014;174:972-981.

392 26. Simmons D, Yu D, Wenzel H. Changes in hospital admissions and inpatient tariff
393 associated with a Diabetes Integrated Care Initiative: preliminary findings, *J Diabetes*
394 2014;6:81-89.

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401 **TABLES AND FIGURE LEGENDS**

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403 **Table-1.** Baseline Characteristics of study cohorts

	Main cohort	Replication cohort				
		All	Control	1:1	Group	Combined
N	4,702	1,121	291	261	288	281
Cardiovascular diseases hospitalisation, n (%)	588 (12.5)	183 (16.3)	59 (20.3)	45 (17.2)	42 (14.6)	37 (13.2)
Age, years	65.0±16.3	65.5±11.4	65.9±12.8	65.3±9.8	65.8±11.9	65.0±10.4
Female, n (%)	1,919 (40.8)	444 (39.6)	122 (41.9)	109 (41.8)	101 (35.1)	112 (39.9)
Systolic blood pressure, mmHg	134.5±16.0	139.7±20.2	140.0±20.6	140.4±20.6	140.8±19.5	137.9±20.3
Diastolic blood pressure, mmHg	76.3±10.0	75.5±11.5	75.0±11.6	75.8±10.9	75.1±11.3	75.6±11.9
Total cholesterol, mmol/L	4.3±1.2	4.2±1.7	4.3±1.5	4.3±1.3	4.1±2.0	4.3±1.7

High density lipoprotein, mmol/L	1.3±0.6	1.1±1.2	1.2±0.9	1.2±1.0	1.0±1.5	1.1±1.1
Low density lipoprotein, mmol/L	2.5±1.4	1.4±3.0	1.3±3.2	1.5±2.8	1.5±2.8	1.5±3.0
Body mass index, kg/m ²	30.8±6.9	32.2±6.0	32.3±6.0	32.6±6.5	32.0±5.9	32.2±5.9
HbA1c, mmol/mol	61.5±17.2	56.2±15.1	55.6±16.2	56.5±15.0	57.3±14.7	55.3±13.8
Lipid Lowering treatment, n (%)	3,342 (71.4)	731 (65.2)	180 (61.9)	173 (66.3)	191 (66.3)	187 (66.6)

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Table-2. Distribution of baseline characteristics and inpatient cost due to cardiovascular diseases hospitalization in study cohorts

	Category of systolic blood pressure, mmHg					
	<120 mmHg	120-129 mmHg	130-139 mmHg	140-149 mmHg	150-159 mmHg	≥160 mmHg
Main Cohort	564	795	1204	1059	324	756
Replication cohort, overall	134 (12.0)	174 (15.5)	244 (21.8)	255 (22.8)	167 (14.9)	147 (13.1)
Replication cohort, control	35 (11.9)	46 (15.8)	64 (22.1)	68 (23.5)	46 (15.8)	32 (10.9)
Replication cohort, group	33 (12.5)	35 (13.6)	50 (19.1)	66 (25.4)	35 (13.6)	41 (15.8)
Replication cohort, 1:1	30 (10.5)	43 (15.0)	67 (23.3)	62 (21.6)	43 (15.0)	42 (14.6)
Replication cohort, combined	37 (13.0)	50 (17.7)	63 (22.4)	58 (20.6)	43 (15.2)	31 (11.2)
Age, years	59.9±18.0	62.7±15.8	65.1±14.0	67.7±12.9	68.6±13.2	65.7±19.2
Female, n (%)	244 (35.0)	382 (39.4)	611 (42.2)	572 (43.5)	208 (42.3)	347 (38.4)
Systolic blood pressure, mmHg	110.3±8.3	123.8±3.1	133.7±3.1	143.0±3.0	153.4±3.1	169.4±10.9
Diastolic blood pressure, mmHg	68.0±9.2	73.4±8.4	76.0±8.3	78.5±8.7	81.2±9.5	85.0±11.3
Total cholesterol, mmol/L	4.2±1.2	4.2±1.1	4.3±1.1	4.3±1.2	4.5±1.2	4.6±1.3
High density lipoprotein, mmol/L	1.3±0.5	1.2±0.4	1.3±0.5	1.3±0.5	1.3±0.5	1.3±0.5
Low density lipoprotein, mmol/L	2.4±1.0	2.4±1.0	2.5±1.0	2.5±1.0	2.5±1.0	2.6±1.0
Body mass index, kg/m ²	29.8±6.3	30.5±6.7	31.5±6.9	31.5±6.6	31.7±6.4	30.4±7.3
HbA1c, mmol/mol	61.5±19.5	60.2±16.9	60.9±15.6	60.5±16.0	61.0±15.8	62.4±16.7
Lipid Lowering treatment, n (%)	459 (65.8)	688 (71.0)	1066 (73.6)	1010 (76.9)	364 (74.2)	484 (53.6)

People with zero payment, n(%)	602 (11.9)	865 (29.0)	1263 (25.0)	1109 (22.0)	382 (7.6)	832 (16.5)
Median cost (interquartile of cost), £ among people with non-zero payment	2436.37 (629.40 to 5277.45)	2017.75 (763.53 to 3561.62)	1781.41 (644.42 to 4931.43)	2507.73 (1318.58 to 4786.15)	2801.81 (893.70 to 4008.91)	3485.46 (1362.57 to 4956.08)

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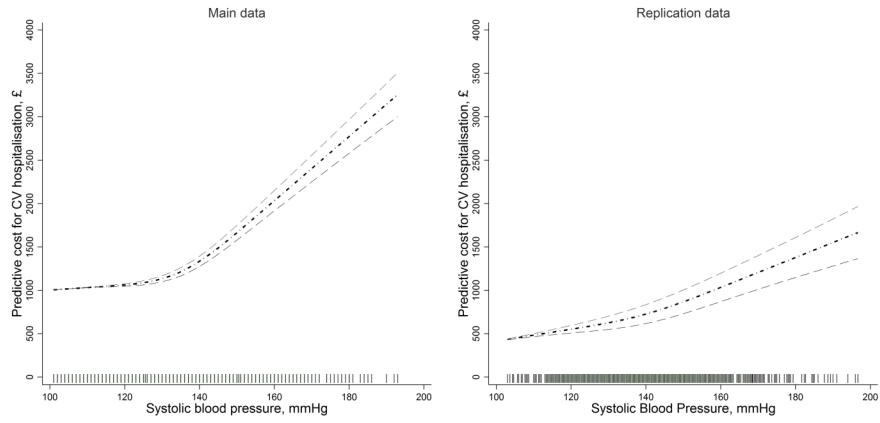
423 **Figure-1.** Adjusted association between baseline systolic blood pressure and predicted
424 inpatient cost due to cardiovascular diseases hospitalisation in main cohort and replication
425 cohort

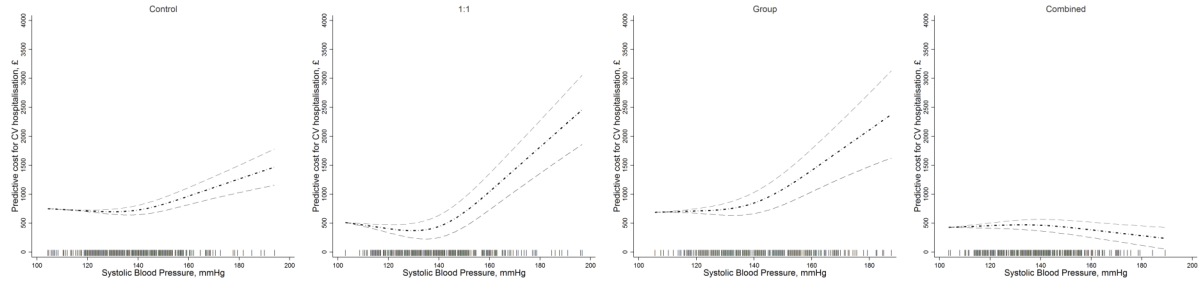
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427 **Figure-2.** Adjusted association between baseline systolic blood pressure and predicted
428 inpatient cost due to cardiovascular diseases hospitalisation in groups of replication cohort

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