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## Research Article

# Can Cardiovascular Risk Management be improved by Shared Care with General Practice to Prevent Cognitive Decline Following Stroke/TIA? A feasibility randomised controlled Trial (SERVED Memory)

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24

## 25 **Abstract**

26

### 27 Background

28 Cognitive impairment and dementia following cerebrovascular disease are increasingly  
29 common in the UK. One potential strategy to prevent post-stroke cognitive decline is  
30 multimodal vascular risk factor management. However, its efficacy remains uncertain and its  
31 application in vulnerable patients with incident cerebrovascular disease and early cognitive  
32 impairment has not been assessed.

33 The primary aim of this study was to assess the feasibility of recruitment and retention of  
34 patients with early cognitive impairment post-stroke or transient ischaemic attack (TIA) to a  
35 trial of enhanced vascular risk factor management combining primary and secondary care.

### 36 Methods

37 In this single centre, open label trial adults with a recent stroke or TIA and mild cognitive  
38 impairment (MCI) were randomised 1:1 to a three-monthly multimodal vascular risk factor  
39 intervention jointly delivered by the trial team and General Practitioner (GP), or control  
40 (defined as usual care from the GP). Chosen risk factors were blood pressure (BP), total  
41 cholesterol, blood glucose (HbA1C) in those with diabetes, and heart rate and adequacy of  
42 anticoagulation in those with atrial fibrillation (AF). Similar patients with normal cognition

43 were enrolled in an embedded observational cohort and also received usual care from the  
44 GP. All participants underwent repeat cognitive screening after 12 months.

#### 45 Results

46 Seventy three participants were recruited to the randomised trial and 94 to the  
47 observational cohort (21.8% of those screened). From the randomised trial 35/73 (47.9%)  
48 dropped out before final follow-up. In all groups guideline based rates of risk factor control  
49 were mostly poor at baseline and did not significantly improve. The observational cohort  
50 demonstrated greater decline in cognitive test scores at 12 months, with no difference  
51 between the randomised groups.

#### 52 Conclusions

53 Recruitment to such a study was feasible, but retention of participants was difficult and rates  
54 of risk factor control did not improve with the intervention. Consequently, successful scaling  
55 up of the trial would require protocol changes to improve participant retention, perhaps  
56 with less reliance on primary care services. Any future trial should include participants with  
57 normal cognition post-stroke as they may be at greatest risk of cognitive decline.

#### 58 Trial Registration

59 ISRCTN, ISRCTN42688361. Registered 16 April 2015, <https://www.isrctn.com/ISRCTN42688361>

60

61 **Keywords:** cognitive impairment, dementia after stroke, vascular dementia, stroke, cerebrovascular  
62 disease.

63

#### 64 Background

65 Dementia is a significant and increasing health problem in the UK, yet disease modifying  
66 treatments are lacking [1], therefore strategies to prevent cognitive decline are desirable.  
67 Given that cognitive impairment may affect up to 40% of patients following stroke and TIA  
68 [2-4], such strategies may be particularly valuable in this patient group. One potential  
69 strategy is multimodal vascular risk factor control as these risk factors contribute to  
70 recurrent stroke as well as both vascular dementia (VaD) and Alzheimer’s disease [5-7], and  
71 their presence also increases the risk of early cognitive decline progressing to dementia [8].  
72 Evidence supports the value of good BP control for reducing the risk of subsequent severe  
73 cognitive impairment post-stroke, yet there remains uncertainty about the value of targeting  
74 other vascular risk factors that are relevant to secondary stroke recurrence, especially as  
75 part of a multimodal risk factor approach [5, 9, 10]. Furthermore, whether targeting such a  
76 strategy at patients who already have MCI post-stroke in order to prevent further cognitive  
77 deterioration has not been studied [11-13].

78 SERVED Memory (Screening and Enhanced Risk factor management to prevent Vascular  
79 Event related Decline in Memory) was developed to investigate the feasibility of recruiting  
80 patients with MCI post-stroke or TIA to a pragmatic intervention trial of enhanced vascular  
81 risk factor management. It was hypothesised that enhanced risk factor management with a  
82 “treat to target” approach, delivered by a combination of the patient’s GP and a trial team,  
83 would be safe and effective, potentially reducing the risk of progression of MCI compared to  
84 standard GP management alone. The trial also incorporated an embedded non-randomised  
85 observational cohort with the aim of providing epidemiological data regarding the natural  
86 history of cognitive impairment post-stroke or TIA.

87

## 88 **Methods**

89 SERVED Memory was a single-centre, open-label parallel group randomised controlled  
90 feasibility trial, with embedded non-randomised observational cohort. The trial was granted  
91 ethical approval and was prospectively registered (ISRCTN 42688361). The full trial protocol  
92 has previously been published [14].

93 In brief, participants were recruited from stroke services at the Norfolk and Norwich  
94 University Hospital (NNUH). Adults with a mild stroke or TIA within the last eight weeks and  
95 Montreal Cognitive Assessment (MoCA) score  $\geq 26$  were eligible for the observational cohort,  
96 and those with a MoCA score consistent with MCI (i.e. 20-25 [11, 12]) were eligible for the  
97 randomised controlled trial (RCT). Patients with life expectancy  $< 1$  year, diagnosed  
98 depression, or MoCA score  $< 20$  were excluded. The MoCA has been validated as a screening  
99 tool and for assessing change in cognition over time in patients with stroke, and has been  
100 shown to be more sensitive than other brief cognitive tests (e.g. Mini Mental State  
101 Examination) in assessing MCI [13, 15, 16]. All participants provided written informed  
102 consent. RCT participants were randomised 1:1 by computer generated randomisation table,  
103 with block size of four, to an intervention or control group. Baseline recording of  
104 demographic data, medication use and compliance, and vascular risk factors was completed.  
105 Measured risk factors were clinic BP, total cholesterol, blood glucose HbA1c in those with  
106 diabetes, and heart rate and anticoagulation adequacy for those with AF. Targets were ideal  
107 BP  $< 130/80$ mmHg and standard  $< 140/90$ mmHg [17, 18]; total cholesterol  $< 4.0$ mmol/L  
108 (non-fasting); HbA1C 48-53mmol/mol; heart rate 60-80 beats per minute for those in AF.  
109 Adequate anticoagulation was defined as taking warfarin with INR 2.5-3.0, or a direct oral  
110 anticoagulant, unless contraindicated. Observation and control participants received usual

111 care from their GP only. Intervention participants were seen in hospital by the trial team at  
112 three, six, and nine months post-randomisation for risk factor assessment. Results were  
113 passed immediately to the GP for action by phone and letter with the trial team only making  
114 treatment alterations when necessary for patient safety. All participants were followed up at  
115 12 months for assessment of risk factors, medication adherence, adverse events and repeat  
116 MoCA. Baseline frailty was retrospectively assessed from clinical notes using the Rockwood  
117 Frailty Score by a stroke physician blinded to group allocation.

118 The primary outcome was the assessment of rates of recruitment and retention at 12  
119 months from screening and management logs. Secondary outcomes were (i) rates of risk  
120 factor control to the specified targets in each group (ii) differences in the change in MoCA  
121 score between the intervention and control groups, (iii) change in MoCA score in the  
122 observational arm, and (iv) rates of adverse events (including recurrent stroke) in each  
123 group.

124 A convenience sample size was based on estimates of the prevalence of cognitive  
125 impairment in patients with incident stroke/TIA [4], the incidence of dementia post-stroke  
126 [19], and estimated cognitive screening rates at NNUH [4]. Based on these estimates target  
127 numbers were 100 in the RCT (50 per group) and 100 in the observational cohort.

128

## 129 **Statistical Analysis**

130 Data were analysed using SPSS (version 25.0) with descriptive statistics only unless specified.  
131 Baseline demographics between the randomised groups were compared using independent  
132 samples t test (for normally distributed continuous variables), independent samples median  
133 test (for non-normally distributed continuous variables), or Chi-square test (for categorical

134 variables). Screening logs were assessed to determine the proportion of eligible participants  
135 who consented to participate in the trial, including the proportion that would have been  
136 eligible for the RCT. Management logs were assessed for retention rates in each trial arm  
137 and, where possible, reasons for attrition were identified. Proportions of participants with  
138 controlled risk factors in each group were calculated at baseline and follow-up along with  
139 the frequency of medication changes that occurred during the trial. Changes in MoCA score  
140 from baseline to follow-up for each arm were assessed using a paired samples t test, with  
141 further testing of any difference between the intervention and control arms. A general linear  
142 model, with a normal error term, was used to estimate the effect of the intervention, with a  
143 95% confidence interval, on the 12 month MoCA values. The model included randomisation  
144 group (intervention or control), sex, diagnosis (stroke or TIA) and baseline MoCA value.  
145 Differences in rates of vascular risk factor control between randomised groups at 12 months  
146 were assessed with a Chi-square test. Post-hoc analysis of the difference in baseline frailty  
147 score in retained vs. not retained participants was assessed with a Mann-Whitney U test.

148

## 149 **Results**

150 Trial recruitment ran from November 2015 to July 2017, with final follow-up completed 12  
151 months later. Seven hundred and sixty-seven patients were screened, with 167 (21.8%)  
152 providing consent to participate (**Figure 1**). Ninety-four participants were included in the  
153 observational cohort and 73 were allocated to the RCT, 37 being randomised to intervention  
154 and 36 to control. Of the remainder screened 362 (47.2%) patients were ineligible and 238  
155 (31.0%) were eligible but declined to participate. Of those declining to participate 18/238  
156 (7.6%) had a MoCA score  $\geq 26$ , 50/238 (21.0%) had a MoCA score between 20-25, and

157 170/238 (71.4%) had not completed cognitive testing at the time of screening. Demographic  
158 details are presented in **Table 1**. There were no significant differences between the  
159 randomised groups.

160 Over the course of the trial 35/73 (47.9%) randomised participants did not complete follow-  
161 up, 14/36 (38.9%) from the control group and 21/37 (56.8%) from the intervention group.

162 Withdrawals accounted for 25/35 (71.4%) of participants not completing the trial and 10/35  
163 (28.6%) were lost to follow-up (i.e. did not respond to telephone calls or written requests to  
164 arrange follow-up visits). The trial team took the decision to withdraw six participants before  
165 completion (three died and three were hospitalised for significant health issues). The other  
166 19 participants withdrew of their own volition. Participants were not required to provide a  
167 reason for dropping out, and 7/19 (36.8%) did not wish to further explain their decision.  
168 However, 6/19 (31.6%) reported that their health had deteriorated such that they no longer  
169 wanted to volunteer their time and 6/19 (31.6%) withdrew because they did not wish to  
170 travel to the hospital for follow-up visits (despite the offer of reimbursement for costs or taxi  
171 services).

172 Average MoCA scores declined significantly in the observation cohort (-1.7 points [95%CI -  
173 2.3 to -1.1,  $p < 0.0001$ ]), but not in the intervention (-0.6 points [95%CI -2.3 to 1.1,  $p = 0.45$ ]) or  
174 control groups (-0.5 points [95%CI -2.1 to 1.1,  $p = 0.45$ ]). From the general linear model to  
175 estimate the effect of the intervention the mean 12 month MoCA for the Intervention group  
176 was 0.664 units lower than for Control, with 95% confidence interval for the difference  
177 (intervention minus control) being -2.69 to 1.37. Baseline rates of control for all risk factors  
178 were low across all trial groups, irrespective of BP threshold value (**Tables 2 and 3**). There  
179 were improvements in the rates of control for cholesterol and adequate anticoagulation in



180 all trial groups at 12 months, however, BP control rates had declined and no changes were  
181 seen in relation to heart rate and HbA1C (**Table 4**). The proportions of participants on  
182 treatment for the selected risk factors were largely unaltered after 12 months, with the  
183 exception of increases in statin use and the prescription of anticoagulants. Rates of adverse  
184 events and recurrent stroke were similar between the randomised groups (**Table 5**). Median  
185 baseline frailty scores were lower in those who completed the trial compared to those who  
186 did not (median 4.0 [IQR 3.0, 6.0] and 5.0 [IQR 4.0, 6.0] respectively,  $p=0.05$ ).

187

## 188 **Discussion**

189 At present it is unclear whether control of multiple vascular risk factors can prevent further  
190 cognitive decline in vulnerable patients with a recent cerebrovascular event [5, 9, 20]. Firstly,  
191 trials of antihypertensive therapy to prevent cognitive decline have been inconsistent,  
192 possibly limited by high rates of treatment in placebo groups, poor participant retention, and  
193 short follow-up [5]. However, a large trial in patients with stroke suggested a benefit to  
194 treatment, with this finding corroborated by subsequent meta-analysis [5, 9, 10]. Secondly,  
195 two randomised controlled trials have assessed the use of statins and found no benefit on  
196 cognition despite reduction in cholesterol levels [21]. Thirdly, in the ADVANCE study  
197 intensive blood glucose control in type 2 diabetics successfully reduced microvascular  
198 complications, but did not reduce rates of dementia [5]. However, given that recurrent  
199 stroke is an important factor in the development of post-stroke dementia [2], it remains  
200 plausible that multimodal vascular risk factor intervention in this patient group is valuable,  
201 with a recent review concluding that such interventions are effective at preventing dementia  
202 in the general population [22].

203 SERVED Memory aimed to test the feasibility of conducting such multimodal, guideline  
204 based, risk factor management in a pragmatic trial combining primary and secondary care  
205 input. We demonstrated a recruitment rate of >20% of patients screened, suggesting that  
206 recruitment of patients with MCI associated with cerebrovascular disease to such a trial is  
207 possible. Although short of the recruitment target, the numbers entering the trial support its  
208 feasibility, especially given the proportion of patients with a MoCA score 20-25, or unknown  
209 at the point of screening, who declined to participate. However, nearly half of participants in  
210 the RCT arms did not complete follow-up, with this retention difficulty being partly related  
211 to frailty status. Alterations to the protocol may alleviate these difficulties, for example  
212 carrying out trial visits in the patients' homes, using online assessments, or treatment  
213 changes being made directly by the trial team rather than relaying information to the GP.  
214 Such supported self-management strategies are deliverable in this patient population as  
215 evidenced by the TEST-BP trial [23], but these changes would inevitably increase the  
216 complexity and cost of conducting the trial. With regard to reducing the intervention's  
217 reliance on primary care, the data suggests that the increased risk factor monitoring  
218 provided by the intervention may not have translated into enhancements in treatment. This  
219 may be due to a degree of treatment inertia, but may also relate to additional factors not  
220 captured by our data, for example patient choice, treatment side effects, or a more  
221 pragmatic approach to treatment in individuals with frailty. Although this trial was supported  
222 by a GP applicant, more involvement of primary care in future trial design would be valuable  
223 to explore how the intervention as envisaged could be improved.

224 In terms of the secondary objective of assessing the effect of the intervention we did not  
225 show a between-group difference in change in MoCA score over 12 months. Interestingly a  
226 greater decline in cognitive scores was seen in the observational cohort. These findings are

227 in keeping with the results of two similar trials in patients with recent stroke but no evidence  
228 of early cognitive decline or MCI. Firstly, Ihle-Hansen et al. (N=195) demonstrated no  
229 difference in incident cognitive impairment or dementia at 12 months with a multimodal  
230 intervention (including treatment of BP, cholesterol, AF, and diabetes, and cardiovascular  
231 lifestyle advice) delivered at three and six months post-randomisation compared to usual GP  
232 care [24]. Secondly, Matz et al. (N=202) reported no significant difference in cognitive test  
233 scores at 24 months between those treated with a multimodal vascular risk factor  
234 intervention (including BP treatment, cardiovascular lifestyle advice, and cognitive training)  
235 and usual care [25]. Conversely, the FINGER trial recruited a population of older adults with  
236 cardiovascular risk factors (but only 5% with prior stroke) and randomised them to a  
237 multimodal intervention (including vascular risk factor monitoring similar to this trial) or  
238 usual care. Over a two year follow-up period there was significantly less cognitive decline in  
239 the intervention group [26, 27]. Similarly, another primary care based trial of a multimodal  
240 intervention aimed at treating cardiovascular risk factors, compared to usual care,  
241 demonstrated both improvements in treatment of the relevant risk factors and a reduction  
242 in the need for long-term institutional care with the intervention [28]. Given these positive  
243 trials, and the small sample sizes and short follow-up duration of existing studies of  
244 multimodal vascular risk factor intervention in stroke patients, further trials may be  
245 warranted.

246 The main strength of this trial is the enrolment of patients with early cognitive decline, who  
247 are at increased risk of developing dementia, and in whom this preventive strategy has not  
248 previously been assessed. A further strength is the use of a pragmatic real-world design,  
249 although this also served to highlight challenges in the optimisation of care for secondary  
250 stroke prevention that would need addressing in any future trial. An important limitation is

251 that we did not consult GP's directly as to why treatment targets were not being met, but it  
252 may reflect ongoing debate about the most appropriate risk factor targets (especially in  
253 older patients) [6, 7, 29], or excessive demands from the existing primary care workload. It is  
254 therefore difficult to know whether the lack of impact of the intervention on vascular risk  
255 factor control was related to deficiencies in the intervention itself, or was related to other  
256 important trial limitations such as small sample size, short duration of follow-up, or the high  
257 dropout rate. This is potentially a missed opportunity to glean information that could have  
258 helped to improve the intervention in any future trial. The assessment of the secondary trial  
259 objectives was also limited by the small sample size and participant dropout. Furthermore,  
260 due to the lack of ethnic diversity in the trial population any findings may lack  
261 generalisability.

262

## 263 **Conclusions**

264 Although the current protocol would not be feasible to deliver a definitive multi-centre trial  
265 due to difficulties with participant retention and application of the intervention, a successful  
266 further trial may be possible with protocol alterations as discussed. In addition, the findings  
267 of the epidemiological observation cohort suggest that such a trial should include patients  
268 with normal cognition and MCI following their cerebrovascular event, as all are at risk of  
269 further cognitive decline.

270

## 271 **List of Abbreviations**

272 TIA                      Transient ischaemic attack

273	MCI	Mild cognitive impairment
274	GP	General Practitioner
275	BP	Blood pressure
276	AF	Atrial fibrillation
277	VaD	Vascular dementia
278	NNUH	Norfolk and Norwich University Hospital
279	MoCA	Montreal Cognitive Assessment
280	RCT	Randomised controlled trial

281

282 **Declarations**

283 **Statement of ethics:** This study was conducted in accordance with the Declaration of  
 284 Helsinki ethical principles for medical research involving human subjects. Ethical approval for  
 285 the trial was granted by the East of England Cambridge East Research Ethics Committee (ref:  
 286 15/EE/0061). All participants provided written informed consent for their involvement.

287 **Consent for publication:** Not applicable.

288 **Availability of data and materials:** The datasets used and/or analysed during the current  
 289 study are available from the corresponding author on reasonable request.

290 **Competing interests:** The authors declare that they have no competing interests.

291 **Funding Sources:** This work was supported by the National Institute for Health Research  
 292 (NIHR) under its Research for Patient Benefit Programme [DRF-2013-06-115]. The views

293 expressed here are those of the author(s) and not necessarily those of the NHS, the NIHR or  
294 the Department of Health.

295 **Author Contributions:** PKM, JFP, YKL, CF, DT and LS were involved in the original conception  
296 and design of the study. Data acquisition was conducted by GR and WJD under the oversight  
297 of PKM and JFP. WJD and LS conducted the statistical analysis for the study. WJD drafted the  
298 initial manuscript which has been revised with input from all other listed authors. The final  
299 manuscript has been reviewed by all authors and approved for submission/publication.

300 **Acknowledgements:** We thank the participants of the trial for their time. We also thank our  
301 research trial nurses Maggie Langley and Laura Ford along with our lay steering committee  
302 members for their significant contributions to the completion of the trial. Additional thanks  
303 are extended to Professor Gordon Wilcock for his advice in developing the study protocol.

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380

381 **Figures and Tables**

382 **Figure 1:** CONSORT flow diagram

383 **Table 1:** Demographic data for each group at baseline.

		<b>Observation</b>	<b>Control</b>	<b>Intervention</b>	<b>P value</b>
<b>N</b>		94	36	37	
<b>Symptom onset to randomisation (days)</b>		25.7 (20.1)	22.6 (20.9)	17.8 (19.7)	0.42
<b>Age (years)</b>		72.1 (10.9)	74.9 (9.2)	75.0 (12.0)	0.97
<b>Gender (male)</b>		59 (62.8%)	23 (63.9%)	27 (73.0%)	0.40
<b>Ethnicity (White British)</b>		94 (100.0%)	36 (100.0%)	37 (100.0%)	-
<b>Smoking status</b>	<b>Non-smoker</b>	38 (40.4%)	17 (47.2%)	26 (70.3%)	0.07
	<b>Ex-smoker</b>	29 (30.9%)	14 (38.9%)	10 (27.0%)	
	<b>Current smoker</b>	6 (6.4%)	5 (13.9%)	1 (2.7%)	
<b>Alcohol (units/wk)</b>		0.0 (0.0, 15.8)	3.0 (0.0, 20.0)	2.0 (0.0, 9.0)	0.73
<b>Diagnosis</b>	<b>TIA</b>	40 (42.6%)	11 (30.6%)	10 (27.0%)	0.74
	<b>Stroke</b>	54 (57.4%)	25 (69.4%)	27 (73.0%)	
<b>OCSF classification</b>	<b>LACS</b>	27 (50.0%)	9 (36.0%)	11 (40.7%)	0.67
	<b>PACS</b>	13 (24.1%)	13 (52.0%)	11 (40.7%)	
	<b>TACS</b>	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	<b>POCS</b>	14 (25.9%)	3 (12.0%)	5 (18.5)	
<b>Past medical history</b>	<b>AF</b>	25 (26.6%)	6 (16.7%)	10 (27.0%)	0.29
	<b>Diabetes</b>	19 (20.2%)	7 (19.4%)	5 (13.5%)	0.49
	<b>IHD</b>	11 (11.7%)	4 (11.1%)	6 (16.2%)	0.53
	<b>Stroke</b>	44 (46.8%)	12 (33.3%)	21 (56.8%)	0.05
	<b>TIA</b>	36 (38.3%)	6 (16.7%)	7 (18.9%)	0.80
	<b>Hypertension</b>	53 (56.4%)	20 (55.6%)	25 (67.6%)	0.29
<b>Rockwood Frailty Score</b>		4.0 (3.0, 6.0)	5.0 (4.0, 6.0)	6.0 (4.5, 6.0)	0.33
<b>MoCA</b>		27.4 (1.4)	23.4 (1.4)	23.2 (1.5)	0.61
<b>Clinic BP</b>	<b>Systolic</b>	147.3 (20.5)	148.1 (21.0)	145.2 (19.5)	0.54



(mmHg)	Diastolic	79.6 (10.5)	78.9 (11.5)	81.8 (12.5)	0.30
Total Cholesterol (mmol/L)		4.9 (1.2)	4.9 (1.2)	4.6 (1.4)	0.34
Heart rate (beats per min) <sup>†</sup>		76.6 (18.9)	75.9 (16.8)	80.4 (10.2)	0.98
On anticoagulation <sup>†</sup>		10/25 (40.0%)	3/6 (50.0%)	3/10 (30.0%)	0.42
HbA1C (mmol/mol) <sup>‡</sup>		52.5 (47.3, 69.5)	49.5 (43.0, 82.3)	73.0 (51.8, 106.3)	0.89

384 Data presented are mean (SD), median (IQR), or frequency (%). P values represent  
385 hypothesis testing for differences between the randomised groups (control vs. intervention).

386 <sup>†</sup>Only those with AF

387 <sup>‡</sup>Only those with diabetes

388

389 **Table 2:** Rates of control for secondary prevention measures by study group.

	Observation (N=71)		Control (N=22)		Intervention (N=16)		P value
	Baseline	12 months	Baseline	12 months	Baseline	12 months	
Antiplatelet use	50/71 (70.4%)	51/71 (71.8%)	17/22 (77.3%)	15/22 (68.2%)	10/16 (62.5%)	10/16 (62.5%)	0.72
Systolic BP (mmHg)	147.8 (21.2)	152.1 (18.1)	148.3 (20.3)	152.4 (23.3)	143.7 (14.2)	156.1 (19.4)	
Diastolic BP (mmHg)	80.3 (10.4)	84.5 (10.9)	80.2 (10.8)	81.1 (14.3)	82.7 (10.0)	88.9 (12.5)	
BP <130/80mmHg	7/71 (9.9%)	2/71 (2.8%)	2/22 (9.1%)	1/22 (4.5%)	2/16 (12.5%)	0/16 (0.0%)	0.39
BP <140/90mmHg	24/71 (33.8%)	19/71 (26.8%)	7/22 (31.8%)	5/22 (22.7%)	6/16 (37.5%)	2/16 (12.5%)	0.42
Total Cholesterol (mmol/L)	4.9 (1.1)	4.4 (1.0)	4.9 (1.0)	4.3 (1.0)	4.1 (0.8)	3.9 (1.0)	
Total Cholesterol <4.0mmol/L	16/71 (22.5%)	28/71 (39.4%)	4/22 (18.2%)	10/22 (45.5%)	8/16 (50.0%)	10/16 (62.5%)	0.30
Heart rate (beats per min) <sup>1</sup>	75.7 (12.1)	74.5 (12.3)	68.4 (13.8)	72.3 (18.9)	78.3 (5.5)	71.1 (10.5)	
HR 60-80bpm <sup>1</sup>	10/21 (47.6%)	12/23 (52.2%)	2/3 (66.7%)	2/6 (33.3%)	3/5 (60.0%)	5/7 (71.4%)	0.72
Adequate anticoagulation <sup>1,2</sup>	8/21 (38.1%)	18/23 (78.3%)	3/3 (100.0%)	5/6 (83.3%)	1/5 (20.0%)	6/7 (85.7%)	1.00
HbA1C mmol/mol <sup>3</sup>	51.0 (44.3, 64.3)	49.0 (44.0, 69.3)	80.0 (-)	66.0 (-)	53.5 (-)	62.0 (-)	

<b>HbA1C 48-53mmol/mol<sup>3</sup></b>	5/15 (33.3%)	4/17 (23.5%)	0/3 (0.0%)	0/3 (0.0%)	1/2 (50.0%)	1/3 (33.3%)	0.18
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390 Average values and rates of control for secondary vascular prevention measures at baseline  
391 and 12 months by study group (restricted to participants who completed follow-up). Data  
392 presented are mean (SD), median (IQR), or frequency (%). P values represent testing for  
393 differences in rates of control at 12 months between the randomised groups (control vs.  
394 intervention).

395 <sup>1</sup>Only those with AF

396 <sup>2</sup>INR 2.5-3.0 or on a DOAC

397 <sup>3</sup>Only those with diabetes

398

399 **Table 3:** Rates of secondary prevention control at baseline in all participants.

	<b>Observation (N=94)</b>	<b>Control (N=36)</b>	<b>Intervention (N=37)</b>
<b>Antiplatelet use</b>	68/94 (72.3%)	27/36 (75.0%)	24/37 (64.9%)
<b>Systolic BP (mmHg)</b>	147.3 (20.5)	148.1 (21.0)	145.2 (19.5)
<b>Diastolic BP (mmHg)</b>	79.6 (10.5)	78.9 (11.5)	81.8 (12.5)
<b>BP &lt;130/80mmHg</b>	10/94 (10.6%)	6/36 (16.7%)	6/37 (16.2%)
<b>BP &lt;140/90mmHg</b>	35/94 (37.2%)	12/36 (33.3%)	15/37 (40.5%)
<b>Total Cholesterol (mmol/L)</b>	4.9 (1.2)	4.9 (1.2)	4.6 (1.4)
<b>Total Cholesterol &lt;4.0mmol/L</b>	22/94 (23.4%)	7/36 (19.4%)	14/37 (37.8%)
<b>Heart rate (beats per min)<sup>1</sup></b>	76.6 (18.9)	75.9 (16.8)	80.4 (10.2)
<b>HR 60-80bpm<sup>1</sup></b>	11/25 (44.0%)	3/6 (50.0%)	5/10 (50.0%)
<b>Adequate anticoagulation<sup>1,2</sup></b>	10/25 (40.0%)	3/6 (50.0%)	3/10 (30.0%)
<b>HbA1C mmol/mol<sup>3</sup></b>	52.5 (47.3, 69.5)	49.5 (43.0, 82.3)	73.0 (51.8, 106.3)
<b>HbA1C 48- 53mmol/mol<sup>3</sup></b>	6/19 (31.6%)	1/7 (14.3%)	1/5 (20.0%)

400 Average values and rates of control for secondary vascular prevention measures at baseline  
401 by study group (all participants). Data presented are mean (SD), median (IQR), or frequency  
402 (%).

403 <sup>1</sup>Only those with AF

404 <sup>2</sup>INR 2.5-3.0 or on a DOAC

405 <sup>3</sup>Only those with diabetes

406

407 **Table 4:** Rates of vascular risk factor treatment at baseline and 12 months.

		Observation (N=71)		Control (N=22)		Intervention (N=16)	
		Baseline	12 months	Baseline	12 months	Baseline	12 months
Antihypertensive medication (at least one agent)	Proportion treated	46/71 (64.8%)	50/71 (70.4%)	14/22 (63.6%)	16/22 (72.7%)	12/16 (75.0%)	14/16 (87.5%)
	Treatment increased	-	12/71 (16.9%)	-	8/22 (36.4%)	-	6/16 (37.5%)
	Treatment decreased	-	12/71 (16.9%)	-	1/22 (4.5%)	-	2/16 (12.5%)
	Treatment unchanged	-	47/71 (66.2%)	-	13/22 (59.1%)	-	8/16 (50.0%)
Statin or other lipid lowering medication	Proportion treated	52/71 (73.2%)	56/71 (78.9%)	20/22 (90.9%)	20/22 (90.9%)	9/16 (56.3%)	10/16 (62.5%)
	Treatment increased	-	14/71 (19.7%)	-	2/22 (9.1%)	-	3/16 (18.7%)
	Treatment decreased	-	7/71 (9.9%)	-	2/22 (9.1%)	-	4/16 (25.0%)
	Treatment unchanged	-	50/71 (70.4%)	-	18/22 (81.8%)	-	9/16 (56.3%)
Rate lowering medication (e.g. beta blocker)	Proportion treated	10/21 (47.6%)	11/23 (47.8%)	0/3 (0.0%)	4/6 (66.7%)	3/5 (60.0%)	5/7 (71.4%)
	Treatment increased	-	0/23 (0.0%)	-	4/6 (66.6%)	-	3/7 (42.9%)
	Treatment decreased	-	2/23 (8.7%)	-	0/6 (0.0%)	-	0/7 (0.0%)
	Treatment unchanged	-	21/23 (91.3%)	-	2/6 (33.4%)	-	4/7 (57.1%)
Warfarin or direct oral anticoagulant	Proportion treated	13/21 (61.9%)	19/23 (82.6%)	3/3 (100.0%)	5/6 (83.3%)	3/5 (60.0%)	6/7 (85.7%)
	Treatment increased	-	8/23 (34.8%)	-	2/6 (33.4%)	-	3/7 (42.9%)
	Treatment decreased	-	2/23 (8.7%)	-	0/6 (0.0%)	-	1/7 (14.2%)
	Treatment unchanged	-	13/23 (56.5%)	-	4/6 (66.6%)	-	3/7 (42.9%)
Oral diabetic medications or insulin	Proportion treated	8/15 (53.3%)	8/17 (47.1%)	2/3 (66.7%)	2/3 (66.7%)	2/2 (100.0%)	3/3 (100.0%)
	Treatment increased	-	0/17 (0.0%)	-	0/3 (0.0%)	-	1/3 (33.4%)
	Treatment decreased	-	0/17 (0.0%)	-	0/3 (0.0%)	-	0/3 (0.0%)
	Treatment unchanged	-	17/17 (100.0%)	-	3/3 (100.0%)	-	2/3 (66.6%)

408 Rates of vascular risk factor treatment at baseline and 12 months by study group and  
409 changes during the trial (restricted to participants who completed follow-up). Data  
410 presented are frequency (%).

411

412 **Table 5:** Adverse events.

	<b>Observation</b>	<b>Control</b>	<b>Intervention</b>
Serious adverse events	36	25	24
Deaths	3	1	2
Recurrent stroke/TIA events	7	2	5
Withdrawals due to ill health (other than recurrent stroke/TIA)	2	2	0

413 Rates of serious adverse events, including deaths and recurrent stroke events, by study  
414 group.