

THE LANCET Neurology

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Al-Shahi Salman R, Minks DP, Mitra D, et al. Effects of antiplatelet therapy on stroke risk by brain imaging features of intracerebral haemorrhage and cerebral small vessel diseases: subgroup analyses of the RESTART randomised, open-label trial. *Lancet Neurol* 2019; published online May 22. [http://dx.doi.org/10.1016/S1474-4422\(19\)30184-X](http://dx.doi.org/10.1016/S1474-4422(19)30184-X).

- 1 **Effects of antiplatelet therapy on stroke risk by brain imaging features of intracerebral haemorrhage and**
- 2 **cerebral small vessel diseases: subgroup analyses of the RESTART randomised, open-label trial**
- 3 Online appendix

4 **Appendix of collaborators on delegation logs at hospital sites that recruited at least one participant to RESTART**

5 Sites are listed in descending order of cumulative recruitment (quantified in square brackets), indicating which people
6 took the role of principal investigator (PI).

7

8 **Edinburgh Royal Infirmary, Edinburgh [39]** (Prof. R Al-Shahi Salman (PI), Prof. G Mead, S Burgess, C Lerpiniere, R
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24 Muddegowda (PI), R Sanyal (PI), S Stevens, A Butler, R Varquez, A Remegoso, N Abano, F Alipio, H Denic, R Carpio,

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36 Kingwell, C Roughan, A Hemsley, J Sword, K Miller, A Goff, K Gupwell, K Thorpe); **Royal Preston Hospital, Preston**
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43 Procter, S Buckle, J Whiteman, C Triscott, R Mardania, R Wallace, J Gray); **Calderdale Royal Hospital, Halifax [7]** (A
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48 Caine (PI), M Osborn, E Dodd, P Murphy, N Devitt, P Baker, A Steele, L Guthrie, S Clarke); **Gloucestershire Royal**
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51 Dixon, K Chapman, A Young, A Bergin, A Sigsworth); **Kings Mill Hospital, Mansfield [6]** (M Cooper (PI), M Nasar, I
52 Wynter, A Rajapakse); **Leeds General Infirmary, Leeds [6]** (A Hassan (PI), M Kambafwile, L Makawa, D Waugh, E
53 Veraque, M Randall, V Papavasileiou); **Royal Liverpool and Broadgreen University Hospital, Liverpool [6]** (A
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60 David, E Rogers, C Ovington, J Bell, B Longland, G Hann); **University Hospital Aintree, Liverpool [6]** (C Cullen (PI),
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70 Stewart); **John Radcliffe Hospital, Oxford [5]** (U Schulz (PI), R Teal, P Mathieson, I Reckless, J Kennedy, Prof. G
71 Ford, G Lenti, G Harston); **Nevill Hall Hospital, Abergavenny [5]** (B Richard (PI), S Buckle, S Procter, S Moseley, C
72 Nott, J Whiteman, C Triscott, R Wallace, M Edwards, H Lawson, M Tayler); **The Royal London Hospital, London [5]**
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76 Naeem, V Baliga); **University Hospital of Wales, Cardiff [5]** (T Hughes (PI), B Morse, S White, S Schwarz, E
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79 Henry); **Charing Cross Hospital, London [4]** (M Venter (PI), A Kar (PI), S Mashate, K Harvey, L Gardener, V
80 Nguyen, B Hazel, O Geraghty, O Halse, P Wilding, V Tilley); **Derby Royal Hospital, Derby [4]** (Prof. T England (PI),
81 A Hedstrom, M Maddula, Prof. R Donnelly); **Heartlands Hospital, Birmingham [4]** (R Yadava (PI), K Azhar (PI), M
82 Sangombe, J Reddan, S Stafford); **New Cross Hospital, Wolverhampton [4]** (K Fotherby (PI), D Morgan, F Baig, K
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86 McClelland, M Bokhari); **Raigmore Hospital, Inverness [4]** (P Findlay (PI), A Macaden, I Shread, C Barr); **Royal
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89 Gallagher); **William Harvey Hospital, Ashford [4]** (T Webb (PI), L Cowie, A Thomson, H Rudenko, A Verrion, E
90 Beranova, T Cosier, S Walker, S McDonald, N Schumacher); **Derriford Hospital, Plymouth [3]** (A Mohd Nor (PI), C
91 Eglinton, N Persad, C Brown, M Weinling, A Shah, J Baker, B Hyams); **Forth Valley Royal Hospital, Larbert [3]** (A
92 Byrne (PI), C McGhee, A Smart, C Copeland); **Hull Royal Infirmary, Hull [3]** (R Rayessa (PI), L Wilson, C Naylor, A
93 Rodgers, S Wilson, E Clarkson); **Pinderfields Hospital, Wakefield [3]** (M Carpenter (PI), M Walker, R Davey, A

94 Needle, R Fathima, G Bateman, A Stanners, P Datta, L Jackson, J Ball); **Royal Victoria Infirmary, Newcastle upon**
95 **Tyne [3]** (M Davis (PI), H Guy, N Atkinson, M Fawcett, T Thompson, C Hays, S Woodward, V Hogg); **Salisbury**
96 **District Hospital, Salisbury [3]** (T Black (PI), A Anthony, S Miriam, C Clarke, D Mead, M Tribbeck, J Cronin, R
97 Fennelly); **St Mary's Hospital, Newport Isle of Wight [3]** (M Haque (PI), E Hakim (PI), S Symonds, M Maanoosi, J
98 Herman); **St Richards Hospital, Chichester [3]** (S Ivatts (PI), Y Baird, M Sally, I Amey, L Clayton- Evans, S Newton, I
99 Chadbourn); **Victoria Hospital, Blackpool [3]** (J McIlmoyle (PI), C Jeffs, C Dickinson, J Howard, S Anwar, S Dhar, K
100 Jones, M Siddiq, C Clay); **Arrowe Park Hospital, Wirral [2]** (R Davies (PI), P Owings, G Sangster, V Gott, V Little, P
101 Weir, S Cherian, D Jose, H Moroney, S Downham, A Dodd, L Codd, V Vettimootal Johnson, N Robinson); **Barnsley**
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103 Cunningham); **Countess of Chester NHS Foundation Trust, Chester [2]** (T Webster (PI), K Chatterjee, A Nallasivan,
104 S Haider, S Leason, C Perkins, S Seagrave); **Hereford County Hospital, Hereford [2]** (C Jenkins (PI), F Price, C
105 Hughes, L Mercer); **Leicester Royal Infirmary, Leicester [2]** (D Eveson (PI), A Mistri, L Manning, C Patel, M
106 Moqsith, S Khan, C Stephens, S Sattar, M Lam, K Musarrat); **Leighton Hospital, Crewe [2]** (L Kalathil (PI), R Miller,
107 M Salehin, N Gautam, D Bailey, K Amor, J Meir); **Luton & Dunstable NHSFT University Hospital, Luton [2]** (L
108 Sekaran (PI), F Justin, M Tate, K Bharaj, R Simon, N Mohammed, S Sethuraman, D Phiri, M Chauhan); **Musgrove**
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111 (K Metcalf (PI), J Jagger, S McDonald, K Waterfield, P Sutton, J Saada, A Wiltshire, R Perfitt, R Greenwood, N Shinh,
112 A Anversha, G Ravenhill); **Pilgrim Hospital, Boston [2]** (D Mangion (PI), S Markova, A Hardwick, T Lawrence, J
113 Fletcher, C Constantin, K Pettitt, I Thomas); **Queens Hospital, Romford [2]** (S Andole (PI), N Gadapa, K Dunne, M
114 Krommyda, E Bursens, C Plewa, S King); **Royal Hampshire County Hospital, Winchester [2]** (N Smyth (PI), J
115 Wilson, E Giallombardo, C Eglinton, L Sykes); **Royal Lancaster Infirmary, Lancaster [2]** (P Kumar (PI), P Thomas, I
116 Dunn, C Culmsee, I Huggett, J Barker); **Royal Victoria Hospital, Belfast [2]** (I Wiggam (PI), A Wallace, E Kerr, A
117 Fulton, A Hunter, S Tauro, S Cuddy); **Solihull Hospital, Solihull [2]** (K Elfandi (PI), U Khan, S Stafford, J Reddan);
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121 (E Orugun (PI), U Poultney, H Crowther, R Glover, S Thornthwaite); **West Suffolk Hospital, Bury St Edmunds [2]** (A
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124 **Hospital NHS Foundation Trust, Dorchester [1]** (H Proeschel (PI), S Sharpe, S Horton, S Jones, E Beaves); **Epsom**
125 **General Hospital, Epsom [1]** (J Putterill (PI), R Jha, R Gallifent, P Kakar); **Hairmyres Hospital, East Kilbride [1]** (B
126 Yip (PI), M Bell, B MacInnes, L MacLiver, D Esson); **Lister Hospital, Stevenage [1]** (A Pusalkar (PI), K Chan, P
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128 Owusu-Agyei (PI), N Temple, N Butterworth-Cowin); **Poole Hospital, Poole [1]** (S Ragab (PI), K Knops, E Jinks, C
129 Dickson, L Gleave, J Leggett, J Dube, T Garcia); **Prince Charles Hospital, Merthyr Tydfil [1]** (R Dewar (PI), K
130 Thomas, J White); **Queen Elizabeth Hospital, Birmingham [1]** (D Sims (PI), J Hurley, M Willmot, C Sutton, E
131 Littleton, S Maiden, J Cunningham, R Jones, C Green, M Bates); **Queen Elizabeth Hospital, Kings Lynn [1]** (R
132 Shekhar (PI), R Crown, E Gilham, T Fuller, I Ahmed, K Waterfield); **Royal Blackburn Hospital, Blackburn [1]** (N
133 Goorah (PI), A Bell, C Kelly, A Singh, J Walford, S Duberley, B Tomlinson, F Patel); **Royal Sussex County Hospital,**
134 **Brighton [1]** (I Kane (PI), N Gainsborough, J Gaylard, J Breeds, Prof. C Rajkumar, S Hervey, A Pitt-Ford, L Latter, E
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136 Hayes); **South West Acute Hospital, Enniskillen [1]** (B Keegan (PI), M Doherty, J Kelly, C Blair); **Stepping Hill**
137 **Hospital, Stockport [1]** (S Krishnamoorthy (PI), J Vassallo, D Walter, H Cochrane); **The Princess Royal Hospital,**
138 **Telford [1]** (M Srinivasan (PI), F Hurford, D Donaldson, R Campbell, N Motherwell, I Mukherjee); **University**
139 **Hospitals Coventry and Warwickshire, Coventry [1]** (A Kenton (PI), S Nyabadza, I Martin, B Hunt, H Hassan, B
140 Dallol, S O'Toole).
141

142 **Literature search strategies used to put the research in context**

143

144 **MEDLINE search strategy**

- 145 1. exp Cerebral Hemorrhage/
146 2. ((brain\$ or cerebr\$ or cerebell\$ or intracerebral or intracran\$ or parenchymal or intraparenchymal or
147 intraventricular or infratentorial or supratentorial or basal gangli\$ or putaminal or putamen or posterior fossa or
148 hemisphere\$) adj5 (h?emorrhag\$ or h?ematoma\$ or bleed\$)).tw.
149 3. ((h?emorrhag\$ or bleed\$) adj5 (stroke or apoplex\$)).tw.
150 4. (ICH or ICHs).tw.
151 5. 1 or 2 or 3 or 4
152 6. Randomized Controlled Trials/
153 7. random allocation/
154 8. Controlled Clinical Trial/
155 9. control groups/
156 10. clinical trials/ or clinical trials, phase i/ or clinical trials, phase ii/ or clinical trials, phase iii/ or clinical trials,
157 phase iv/
158 11. double-blind method/
159 12. single-blind method/
160 13. Placebos/
161 14. placebo effect/
162 15. randomi\$ed controlled trial.mp.
163 16. controlled clinical trial.pt.
164 17. (clinical trial or clinical trial phase i or clinical trial phase ii or clinical trial phase iii or clinical trial phase iv).pt.
165 18. (random\$ or RCT or RCTs).tw.
166 19. (controlled adj5 (trial\$ or stud\$)).tw.
167 20. (clinical\$ adj5 trial\$).tw.
168 21. ((control or treatment or experiment\$ or intervention) adj5 (group\$ or subject\$ or patient\$)).tw.
169 22. (quasi-random\$ or quasi random\$ or pseudo-random\$ or pseudo random\$).tw.
170 23. ((singl\$ or doubl\$ or tripl\$ or trebl\$) adj5 (blind\$ or mask\$)).tw.
171 24. (placebo\$ or sham).tw.

172 25. ((control or experiment\$ or conservative) adj5 (treatment or therapy or procedure or manage\$)).tw.
173 26. trial.ti.
174 27. (assign\$ or allocat\$).tw.
175 28. or/6-27
176 29. exp amyloid/
177 30. exp Cerebral Amyloid Angiopathy/
178 31. exp Amyloid beta-Peptides/
179 32. cerebral amyloid angiopathy.mp.
180 33. CAA.mp.
181 34. white matter lesion\$.mp.
182 35. WML.mp.
183 36. white matter disease\$.mp.
184 37. white matter hyperintensit\$.mp.
185 38. WMH.mp.
186 39. leu?oaraiosis.mp.
187 40. exp Microcirculation/
188 41. lacun\$.mp.
189 42. lacunar infarct\$.mp.
190 43. exp Stroke, Lacunar/
191 44. small vessel\$.mp.
192 45. small infarct\$.mp.
193 46. microinfarct\$.mp.
194 47. subcortical lesion\$.mp.
195 48. subcortical infarct\$.mp.
196 49. microvascular\$.mp.
197 50. microbleed\$.mp.
198 51. micro-bleed\$.mp.
199 52. microh?emorrhage\$.mp.
200 53. micro-h?emorrhage\$.mp.
201 54. perivascular space\$.mp.

202 55. PVS.mp.
203 56. enlarged perivascular space\$.mp.
204 57. EPVS.mp.
205 58. virchow-Robin space\$.mp.
206 59. VRS.mp.
207 60. small vessel disease\$.mp.
208 61. SVD.mp.
209 62. exp arteriolosclerosis/
210 63. exp Arteriosclerosis/
211 64. (atherosclerosis adj3 small).mp.
212 65. fibrinoid necrosis.mp.
213 66. lipohyalinosis.mp.
214 67. microatheroma.mp.
215 68. microaneurysm\$.mp.
216 69. venous collagenosis.mp.
217 70. cerebral vascu\$.mp.
218 71. cerebrovasc\$.mp.
219 72. exp Cerebrovascular Circulation/
220 73. exp Cerebrovascular Disorders/
221 74. microscopic bleed\$.mp.
222 75. microscopic hemorrhag\$.mp.
223 76. microscopic haemorrhag\$.mp.
224 77. dot like h?emosiderin spot.mp.
225 78. Dot-like h?emosiderin spot.mp.
226 79. Multifocal signal loss.mp.
227 80. Hypointense lesion.mp.
228 81. Hypointense foci.mp.
229 82. Lacunar hemorrhag\$.mp.
230 83. Lacunar haemorrhag\$.mp.
231 84. minute hemorrhag\$.mp.

232 85. minute haemorrhag\$.mp.

233 86. superficial siderosis.mp.

234 87. cSS.mp.

235 88. exp Brain/

236 89. cranial.mp.

237 90. cerebr\$.mp.

238 91. cerebell\$.mp.

239 92. brain\$.mp.

240 93. intracerebral.mp.

241 94. intracranial.mp.

242 95. hemispher\$.mp.

243 96. infratentorial.mp.

244 97. supratentorial.mp.

245 98. or/88-97

246 99. or/29-87

247 100. 98 and 99

248 101. exp anticoagulants/

249 102. exp Vitamin K/ai or thrombin/ai or factor Xa/ai or exp Blood coagulation factors/ai

250 103. exp antithrombins/ or hirudin therapy/

251 104. (anticoagul\$ or antithromb\$).tw.

252 105. (Vitamin K antagonist\$ or VKA or VKAs).tw.

253 106. (direct\$ adj3 thrombin adj3 inhib\$).tw.

254 107. DTIS1.tw.

255 108. ((factor Xa or factor 10a or fXa or autoprothrombin c or thrombokinese) adj3 inhib\$).tw.

256 109. (activated adj3 (factor X or factor 10) adj3 inhib\$).tw.

257 110. (acenocoumarol\$ or dicoumarol\$ or ethyl biscoumacetate\$ or phenprocoumon\$ or warfarin\$ or ancrod\$ or citric

258 acid\$ or coumarin\$ or chromonar\$ or coumestro\$ or esculi\$ or ochratoxin\$ or umbelliferone\$ or dermatan

259 sulfate\$ or dextran\$ or edetic acid\$ or enoxaparin\$ or gabexate\$ or heparin\$ or lmwh\$ or nadroparin\$ or pentosan

260 sulfuric polyester\$ or phenindione\$ or protein c or protein s or tedelparin\$).tw,nm.

261 111. (tinzaparin or parnaparin or dalteparin or reviparin or danaparoid or lomoparan or org 10172 or mesoglycan or
262 polysaccharide sulphate\$ or sp54 or sp-54 or md805 or md-805 or cy222 or cy-222 or cy216 or cy-216).tw,nm.
263 112. (Marevan or Fraximin\$ or Fraxiparin\$ or Klexane).tw,nm.
264 113. (argatroban or MD805 or MD-805 or dabigatran or ximelagatran or melagatran or efegatran or flovagatran or
265 inogatran or napsagatran or bivalirudin or lepirudin or hirudin\$ or desirudin or desulfatohirudin or hirugen or
266 hirulog or AZD0837 or bothrojaracin or odiparcil).tw,nm.
267 114. (xabans or antistasin or apixaban or betrixaban or du 176b or eribaxaban or fondaparinux or idraparinux or
268 otamixaban or razaxaban or rivaroxaban or edoxaban or yagin or ym 150 or ym150 or LY517717).tw,nm.
269 115. exp platelet aggregation inhibitors/ or exp platelet glycoprotein gpiib-iiia complex/ai
270 116. (antiplatelet\$ or anti-platelet\$ or antiaggreg\$ or anti-aggreg\$ or (platelet\$ adj3 inhibit\$) or (thrombocyt\$ adj3
271 inhibit\$)).tw.
272 117. (alprostadil\$ or aspirin\$ or acetylsalicylic acid or acetyl salicylic acid\$ or acetyl?salicylic acid or epoprostenol\$ or
273 ketanserin\$ or ketorolac tromethamine\$ or milrinone\$ or mopidamol\$ or procainamide\$ or thiophen\$ or trapidil\$
274 or picotamide\$ or ligustrazine\$ or levamisol\$ or suloctidil\$ or ozagrel\$ or oky046 or oky-046 or defibrotide\$ or
275 cilostazol or satigrel or sarpolgrelate or kbt3022 or kbt-3022 or isbogrel or cv4151 or cv-4151 or ((glycoprotein
276 iib\$ or gp iib\$) adj5 (antagonist\$ or inhibitor\$)) or GR144053 or GR-144053 or triflusal).tw,nm.
277 118. (Beraprost or Cicaprost or Cilostazol or Clopidogrel or Dipyridamole or Iloprost or Indobufen or Lepirudin or
278 Pentosan Polysulfate or Pentoxifylline or Piracetam or Prostacyclin or Sulfinpyrazone or Sulphinpyrazone or
279 Ticlopidine or Triflusal or Abciximab or Disintegrin or Echistatin or Eptifibatide or Lamifiban or Orbofiban or
280 Roxifiban or Sibrafiban or Tirofiban or Xemilofiban or terutroban or picotamide or prasugrel).tw,nm.
281 119. (Dispril or Albyl\$ or Ticlid\$ or Persantin\$ or Plavix or ReoPro or Integrilin\$ or Aggrastat).tw,nm.
282 120. or/101-119
283 121. exp Tomography, X-Ray Computed/
284 122. exp Magnetic Resonance Imaging/
285 123. 121 or 122
286 124. 5 and 28 and 100 and 120 and 123
287 125. exp animals/ not humans/
288 126. 124 not 125
289
290

- 291 **EMBASE (Ovid) search strategy**
- 292 1. exp amyloid/
293 2. exp vascular amyloidosis/
294 3. exp amyloid protein/
295 4. exp amyloid beta protein/
296 5. cerebral amyloid angiopathy.mp.
297 6. CAA.mp.
298 7. exp leukoaraiosis/
299 8. exp white matter lesion/
300 9. WML.mp.
301 10. white matter disease\$.mp.
302 11. white matter hyperintensit\$.mp.
303 12. WMH.mp.
304 13. exp brain microcirculation/
305 14. lacun\$.mp.
306 15. lacunar infarct\$.mp.
307 16. small vessel\$.mp.
308 17. small infarct\$.mp.
309 18. microinfarct\$.mp.
310 19. subcortical lesion\$.mp.
311 20. subcortical infarct\$.mp.
312 21. microvascular\$.mp.
313 22. microbleed\$.mp.
314 23. micro-bleed\$.mp.
315 24. microh?emorrhage\$.mp.
316 25. micro-h?emorrhage\$.mp.
317 26. perivascular space\$.mp.
318 27. PVS.mp.
319 28. enlarged perivascular space\$.mp.
320 29. EPVS.mp.

321 30. virchow-Robin space\$.mp.
322 31. VRS.mp.
323 32. small vessel disease\$.mp.
324 33. SVD.mp.
325 34. exp arteriolosclerosis/
326 35. exp microaneurysm/
327 36. (atherosclerosis adj3 small).mp.
328 37. fibrinoid necrosis.mp.
329 38. lipohyalinosis.mp.
330 39. microatheroma.mp.
331 40. venous collagenosis.mp.
332 41. microscopic bleed\$.mp.
333 42. microscopic hemorrhag\$.mp.
334 43. microscopic haemorrhag\$.mp.
335 44. dot like h?emosiderin spot.mp.
336 45. Dot-like h?emosiderin spot.mp.
337 46. Multifocal signal loss.mp.
338 47. Hypointense lesion.mp.
339 48. Hypointense foci.mp.
340 49. Lacunar hemorrhag\$.mp.
341 50. Lacunar haemorrhag\$.mp.
342 51. minute hemorrhag\$.mp.
343 52. minute haemorrhag\$.mp.
344 53. superficial siderosis.mp.
345 54. cSS.mp.
346 55. exp Brain/
347 56. cranial.mp.
348 57. cerebr\$.mp.
349 58. cerebell\$.mp.
350 59. brain\$.mp.

351 60. intracerebral.mp.

352 61. intracranial.mp.

353 62. hemispher\$.mp.

354 63. infratentorial.mp.

355 64. supratentorial.mp.

356 65. or/55-64

357 66. or/1-54

358 67. 65 and 66

359 68. *basal ganglion hemorrhage/ or *brain hemorrhage/ or *brain ventricle hemorrhage/ or *cerebellum hemorrhage/

360 69. ((brain\$ or cerebr\$ or cerebell\$ or intracerebral or intracran\$ or parenchymal or intraparenchymal or

361 intraventricular or infratentorial or supratentorial or basal gangli\$ or putaminal or putamen or posterior fossa or

362 hemispher\$ or stroke or apoplex\$) adj5 (h?emorrhag\$ or h?ematoma\$ or bleed\$)).ti.

363 70. 68 or 69

364 71. (ICH or ICHs).ti.

365 72. 70 or 71

366 73. randomized controlled trial/ or "randomized controlled trial (topic)"/

367 74. Randomization/

368 75. Controlled Study/

369 76. control group/

370 77. clinical trial/ or phase 1 clinical trial/ or phase 2 clinical trial/ or phase 3 clinical trial/ or phase 4 clinical trial/ or

371 controlled clinical trial/

372 78. Double Blind Procedure/

373 79. Single Blind Procedure/ or triple blind procedure/

374 80. placebo/

375 81. drug comparison/ or drug dose comparison/

376 82. random\$.tw.

377 83. (controlled adj5 (trial\$ or stud\$)).tw.

378 84. (clinical\$ adj5 trial\$).tw.

379 85. ((control or treatment or experiment\$ or intervention or surgical) adj5 (group\$ or subject\$ or patient\$)).tw.

380 86. ((singl\$ or doubl\$ or tripl\$ or trebl\$) adj5 (blind\$ or mask\$)).tw.

381 87. or/73-86

382 88. anticoagulant agent/ or antivitamin k/ or exp blood clotting inhibitor/ or exp coumarin anticoagulant/ or

383 defibrotide/ or dextran sulfate/ or fluidione/ or glycosaminoglycan polysulfate/ or exp heparin derivative/ or

384 lupus anticoagulant/ or phenindione/

385 89. (anticoagul\$ or antithromb\$).tw.

386 90. (Vitamin K antagonist\$ or VKA or VKAs).tw.

387 91. (direct\$ adj5 thrombin adj5 inhib\$).tw.

388 92. DTI\$1.tw.

389 93. ((factor Xa or factor 10a or fXa or autoprotease or thrombin\$ or thrombinase) adj5 inhib\$).tw.

390 94. (activated adj5 (factor X or factor 10) adj5 inhib\$).tw.

391 95. (acenocoumarol\$ or dicoumarol\$ or ethyl biscoumatate\$ or phenprocoumon\$ or warfarin\$ or ancrod\$ or citric

392 acid\$ or coumarin\$ or chromonar\$ or coumestrol\$ or esculetin\$ or ochratoxin\$ or umbelliferone\$ or dermatan

393 sulfate\$ or dextran\$ or edetic acid\$ or enoxaparin\$ or gabexate\$ or heparin\$ or lmwh\$ or nadroparin\$ or pentosan

394 sulfuric polyester\$ or phenindione\$ or protein c or protein s or tedelparin\$).tw.

395 96. (tinzaparin or parnaparin or dalteparin or reviparin or danaparoid or lomoparan or org 10172 or mesoglycan or

396 polysaccharide sulphate\$ or sp54 or sp-54 or md805 or md-805 or cy222 or cy-222 or cy216 or cy-216).tw.

397 97. (Marevan or Fragmin\$ or Fraxiparin\$ or Klexane).tw.

398 98. (argatroban or MD805 or MD-805 or dabigatran or ximelagatran or melagatran or efegatran or flovagatran or

399 inogatran or napsagatran or bivalirudin or lepirudin or hirudin\$ or desirudin or desulfatohirudin or hirugen or

400 hirulog or AZD0837 or bothrojaracin or odiparcil).tw.

401 99. (xabans or antistasin or apixaban or betrixaban or du 176b or eribaxaban or fondaparinux or idraparinux or

402 otamixaban or razaxaban or rivaroxaban or yagin or ym 150 or ym150 or LY517717).tw.

403 100. 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99

404 101. exp antithrombocytic agent/

405 102. fibrinogen receptor/dt [Drug Therapy]

406 103. (antiplatelet\$ or anti-platelet\$ or antiaggreg\$ or anti-aggreg\$ or (platelet\$ adj5 inhibit\$) or (thrombocyt\$ adj5

407 inhibit\$)).tw.

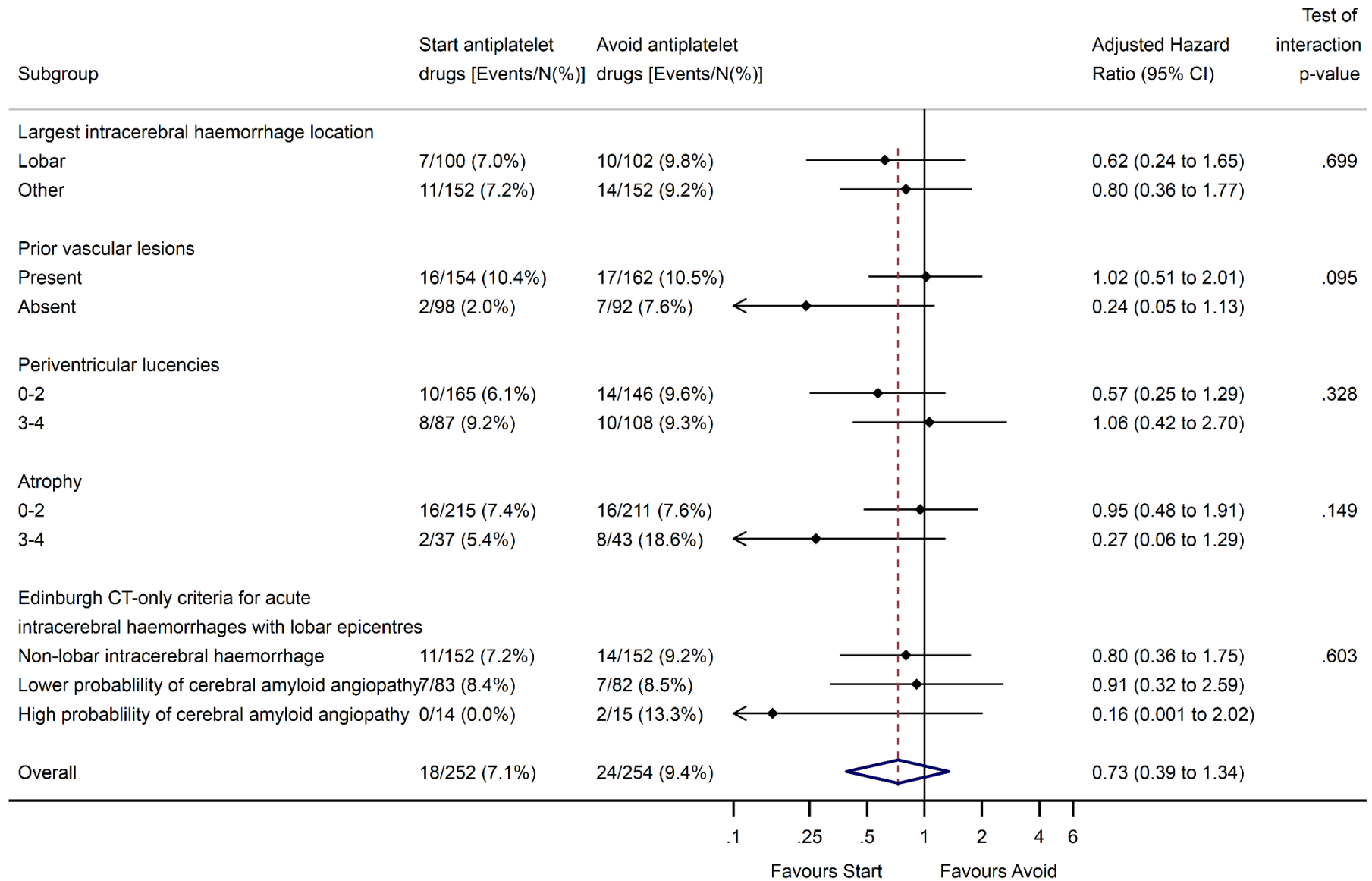
408 104. (alprostadiol\$ or aspirin\$ or acetylsalicylic acid or acetyl salicylic acid\$ or acetyl?salicylic acid or epoprostenol\$ or

409 ketanserine\$ or ketorolac tromethamine\$ or milrinone\$ or mepidamol\$ or procainamide\$ or thiophen\$ or trapidil\$

410 or picotamide\$ or ligustrazine\$ or levamisole\$ or suloctidil\$ or ozagrel\$ or oky046 or oky-046 or defibrotide\$ or

411 cilostazol or satigrel or sarpolgrelate or kbt3022 or kbt-3022 or isbogrel or cv4151 or cv-4151 or ((glycoprotein
412 iib\$ or gp iib\$) adj5 (antagonist\$ or inhibitor\$)) or GR144053 or GR-144053 or triflusal).tw.
413 105. (Argatroban or Beraprost or Cicaprost or Cilostazol or Clopidogrel or Dipyridamole or Iloprost or Indobufen or
414 Lepirudin or Pentosan Polysulfate or Pentoxifylline or Piracetam or Prostacyclin or Sulfinpyrazone or
415 Sulphinpyrazone or Ticlopidine or Triflusal or Abciximab or Disintegrin or Echistatin or Eptifibatide or
416 Lamifiban or Orbofiban or Roxifiban or Sibrafiban or Tirofiban or Xemilofiban or terutroban or picotamide or
417 prasugrel).tw.
418 106. (Dispril or Albyl\$ or Ticlid\$ or Persantin\$ or Plavix or ReoPro or Integrilin\$ or Aggrastat).tw.
419 107. 101 or 102 or 103 or 104 or 105 or 106
420 108. 100 or 107
421 109. exp computer assisted tomography/
422 110. exp nuclear magnetic resonance imaging/
423 111. 109 or 110
424 112. 67 and 72 and 87 and 108 and 111
425 113. exp animals/ not humans/
426 114. 112 not 113

427 Exploratory sub-group analyses of the risk of first ischaemic stroke (the secondary outcome) by CT biomarkers



429 Association between cerebral microbleeds on MRI and first recurrent symptomatic intracerebral haemorrhage
 430 (the primary outcome) in 235 participants who had a brain MRI sequence of sufficient quality to rate cerebral
 431 microbleeds
 432

Cox proportional hazards regression models	Adjusted hazard ratio (95% CI)	Adjusted p-value
Cerebral microbleed presence (2 or more versus 0 or 1)		
Cerebral microbleed presence (2 or more versus 0 or 1)	3.62 (1.34 to 9.79)	0.011
Start versus avoid antiplatelet therapy	0.49 (0.18 to 1.32)	0.16
Lobar versus non-lobar intracerebral haemorrhage location	0.78 (0.30 to 2.02)	0.61
0-30 days versus >30 days since intracerebral haemorrhage onset	1.08 (0.37 to 3.10)	0.89
Intended prescription: aspirin versus other	0.90 (0.34 to 2.33)	0.82
<70 years versus 70 years or more at randomization	0.62 (0.17 to 2.23)	0.47
Predicted probability of a good outcome at six months: <0.15 versus 0.15 or more	2.58 (0.88 to 7.54)	0.084
Cerebral microbleed burden (linear trend of 0 or 1, 2–4, and 5 or more)		
Cerebral microbleed burden (linear trend of 0 or 1, 2–4, and 5 or more)	1.99 (1.20 to 3.31)	0.0077
Start versus avoid antiplatelet therapy	0.53 (0.20 to 1.42)	0.21
Lobar versus non-lobar intracerebral haemorrhage location	0.76 (0.29 to 1.97)	0.57
0-30 days versus >30 days since intracerebral haemorrhage onset	1.11 (0.38 to 3.19)	0.85
Intended prescription: aspirin versus other	0.83 (0.32 to 2.16)	0.70
<70 years versus 70 years or more at randomization	0.69 (0.19 to 2.45)	0.56
Predicted probability of a good outcome at six months: <0.15 versus 0.15 or more	2.80 (0.95 to 8.22)	0.061

433

434 **Association between cerebral microbleeds on MRI and first ischaemic stroke (the secondary outcome) in 235**
 435 **participants who had a brain MRI sequence of sufficient quality to rate cerebral microbleeds**
 436

Cox proportional hazards regression models	Adjusted hazard ratio (95% CI)	Adjusted p-value
Cerebral microbleed presence (2 or more versus 0 or 1)		
Cerebral microbleed presence (2 or more versus 0 or 1)	1.92 (0.83 to 4.46)	0.13
Start versus avoid antiplatelet therapy	0.70 (0.30 to 1.65)	0.42
Lobar versus non-lobar intracerebral haemorrhage location	0.90 (0.38 to 2.13)	0.81
0-30 days versus >30 days since intracerebral haemorrhage onset	1.34 (0.49 to 3.65)	0.57
Intended prescription: aspirin versus other	2.48 (0.91 to 6.81)	0.077
<70 years versus 70 years or more at randomization	1.31 (0.51 to 3.36)	0.57
Predicted probability of a good outcome at six months: <0.15 versus 0.15 or more	0.42 (0.09 to 1.94)	0.26
Cerebral microbleed burden (linear trend of 0 or 1, 2–4, and 5 or more)		
Cerebral microbleed burden (linear trend of 0 or 1, 2–4, and 5 or more)	1.62 (1.03 to 2.55)	0.038
Start versus avoid antiplatelet therapy	0.69 (0.29 to 1.63)	0.40
Lobar versus non-lobar intracerebral haemorrhage location	0.86 (0.36 to 2.04)	0.73
0-30 days versus >30 days since intracerebral haemorrhage onset	1.36 (0.50 to 3.72)	0.55
Intended prescription: aspirin versus other	2.47 (0.90 to 6.78)	0.078
<70 years versus 70 years or more at randomization	1.45 (0.56 to 3.73)	0.44
Predicted probability of a good outcome at six months: <0.15 versus 0.15 or more	0.41 (0.09 to 1.92)	0.26

437

Primary and exploratory sub-group analyses of the risk of first ischaemic stroke (the secondary outcome) by MRI biomarkers

