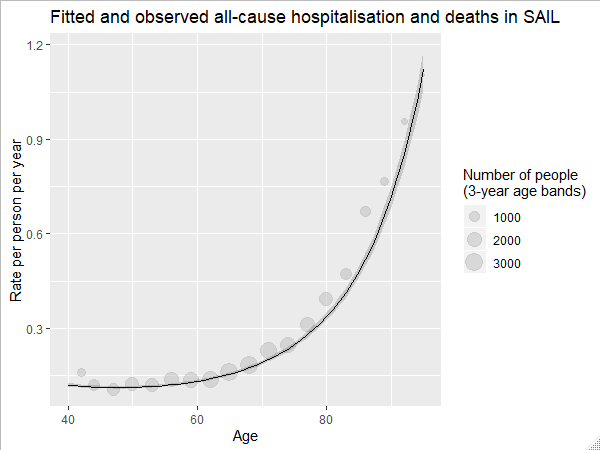
# Model of event rates in SAIL

The plot below shows the model predictions for the rates of all-cause hospitalisation or death among people with hypertension starting RAAS drugs, identified from the SAIL databank. The circles indicate the actual observed event rate (size indicating total number of people in the denominator). Model coefficients, variance covariance matrix, and aggregate data on observed events is also shown below.



|  |  |
| --- | --- |
| Model covariates | Coefficients |
| (Intercept) | -2.81218 |
| I((age/100)^0.5) | -10.1156 |
| I((age/100)^2) | 7.65768 |
| GNDR\_CD | -0.05278 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | (Intercept) | I((age/100)^0.5) | I((age/100)^2) | GNDR\_CD |
| (Intercept) | 0.047022 | -0.07699 | 0.034684 | -0.0004 |
| I((age/100)^0.5) | -0.07699 | 0.128211 | -0.05876 | 0.000211 |
| I((age/100)^2) | 0.034684 | -0.05876 | 0.028355 | -0.00019 |
| GNDR\_CD | -0.0004 | 0.000211 | -0.00019 | 0.000208 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Age | Sex | Number of people | Observation time (days) | Number of events |
| 40 | Men | 120 | 128317 | 40 |
| 40 | Women | 89 | 95670 | 20 |
| 41 | Men | 139 | 148700 | 57 |
| 41 | Women | 113 | 118935 | 48 |
| 42 | Men | 161 | 171325 | 99 |
| 42 | Women | 121 | 129997 | 47 |
| 43 | Men | 178 | 191988 | 72 |
| 43 | Women | 140 | 147073 | 48 |
| 44 | Men | 177 | 189171 | 58 |
| 44 | Women | 162 | 174770 | 53 |
| 45 | Men | 220 | 234766 | 63 |
| 45 | Women | 165 | 174706 | 69 |
| 46 | Men | 235 | 248747 | 55 |
| 46 | Women | 185 | 197986 | 59 |
| 47 | Men | 244 | 257079 | 97 |
| 47 | Women | 200 | 214045 | 64 |
| 48 | Men | 267 | 285851 | 53 |
| 48 | Women | 228 | 246431 | 96 |
| 49 | Men | 259 | 274305 | 75 |
| 49 | Women | 248 | 261026 | 120 |
| 50 | Men | 306 | 323958 | 106 |
| 50 | Women | 263 | 281671 | 75 |
| 51 | Men | 303 | 321003 | 106 |
| 51 | Women | 270 | 284881 | 109 |
| 52 | Men | 288 | 307662 | 89 |
| 52 | Women | 273 | 295761 | 107 |
| 53 | Men | 316 | 333170 | 88 |
| 53 | Women | 277 | 295186 | 122 |
| 54 | Men | 294 | 310504 | 91 |
| 54 | Women | 279 | 300417 | 105 |
| 55 | Men | 300 | 314698 | 113 |
| 55 | Women | 290 | 305513 | 113 |
| 56 | Men | 332 | 349859 | 125 |
| 56 | Women | 298 | 314693 | 103 |
| 57 | Men | 359 | 377819 | 178 |
| 57 | Women | 333 | 355693 | 131 |
| 58 | Men | 359 | 380207 | 136 |
| 58 | Women | 339 | 360585 | 137 |
| 59 | Men | 382 | 407232 | 150 |
| 59 | Women | 337 | 354926 | 102 |
| 60 | Men | 389 | 411155 | 167 |
| 60 | Women | 356 | 376171 | 157 |
| 61 | Men | 452 | 475405 | 167 |
| 61 | Women | 405 | 427818 | 164 |
| 62 | Men | 400 | 422452 | 156 |
| 62 | Women | 403 | 430273 | 150 |
| 63 | Men | 494 | 522990 | 241 |
| 63 | Women | 418 | 437279 | 161 |
| 64 | Men | 494 | 518033 | 214 |
| 64 | Women | 526 | 557523 | 264 |
| 65 | Men | 523 | 555455 | 199 |
| 65 | Women | 515 | 541858 | 235 |
| 66 | Men | 501 | 524599 | 235 |
| 66 | Women | 548 | 582564 | 295 |
| 67 | Men | 485 | 507014 | 294 |
| 67 | Women | 559 | 595451 | 273 |
| 68 | Men | 479 | 500945 | 293 |
| 68 | Women | 572 | 604075 | 248 |
| 69 | Men | 389 | 405405 | 232 |
| 69 | Women | 480 | 504858 | 230 |
| 70 | Men | 418 | 437244 | 254 |
| 70 | Women | 528 | 553794 | 332 |
| 71 | Men | 366 | 382103 | 202 |
| 71 | Women | 454 | 477499 | 248 |
| 72 | Men | 387 | 398883 | 282 |
| 72 | Women | 471 | 490434 | 402 |
| 73 | Men | 329 | 339650 | 237 |
| 73 | Women | 458 | 477991 | 230 |
| 74 | Men | 308 | 316630 | 255 |
| 74 | Women | 460 | 484686 | 289 |
| 75 | Men | 276 | 286518 | 197 |
| 75 | Women | 456 | 474227 | 395 |
| 76 | Men | 302 | 310872 | 261 |
| 76 | Women | 440 | 461783 | 336 |
| 77 | Men | 244 | 246301 | 254 |
| 77 | Women | 361 | 373268 | 282 |
| 78 | Men | 240 | 233251 | 262 |
| 78 | Women | 426 | 429698 | 363 |
| 79 | Men | 230 | 232381 | 262 |
| 79 | Women | 328 | 335518 | 312 |
| 80 | Men | 194 | 190311 | 216 |
| 80 | Women | 310 | 308072 | 302 |
| 81 | Men | 180 | 174649 | 228 |
| 81 | Women | 309 | 305368 | 340 |
| 82 | Men | 168 | 158338 | 214 |
| 82 | Women | 277 | 282629 | 273 |
| 83 | Men | 156 | 146364 | 206 |
| 83 | Women | 282 | 269154 | 330 |
| 84 | Men | 107 | 104541 | 151 |
| 84 | Women | 231 | 219063 | 349 |
| 85 | Men | 107 | 92063 | 167 |
| 85 | Women | 203 | 185406 | 280 |
| 86 | Men | 102 | 90464 | 187 |
| 86 | Women | 183 | 169992 | 324 |
| 87 | Men | 76 | 67520 | 154 |
| 87 | Women | 159 | 143411 | 264 |
| 88 | Men | 76 | 67749 | 137 |
| 88 | Women | 142 | 127758 | 212 |
| 89 | Men | 59 | 49690 | 99 |
| 89 | Women | 132 | 107718 | 260 |
| 90 | Men | 47 | 35279 | 97 |
| 90 | Women | 122 | 96428 | 211 |
| 91 | Men | 27 | 21212 | 41 |
| 91 | Women | 79 | 60978 | 189 |
| 92 | Men | 23 | 17131 | 40 |
| 92 | Women | 76 | 58771 | 143 |
| 93 | Men | 14 | 9541 | 30 |
| 93 | Women | 65 | 48601 | 123 |
| 94 | Men | 19 | 12624 | 56 |
| 94 | Women | 38 | 24898 | 60 |
| 95 | Men | 16 | 12097 | 29 |
| 95 | Women | 39 | 26909 | 64 |

# Sensitivity analysis

|  |  |  |  |
| --- | --- | --- | --- |
|  | Standardised ratio of community rate versus trial rate for older people trials | Standardised ratio of community rate versus trial rate for standard trials | Ratio of standardised ratios (older:standard) |
| Main analysis |  |  |  |
| Unadjusteda | 4.00 (2.17-7.69) | 4.17 (3.45-5.26) | 0.96 (0.49-1.85) |
| Adjustedb | 4.78 (2.22-11.10) | 4.55 (2.86-7.69) | 1.05 (0.53-2.08) |
|  |  |  |  |
| Sensitivity analysis |  |  |  |
| Unadjusteda | 3.70 (1.96-6.67) | 3.70 (3.12-4.55) | 0.98 (0.51-1.89) |
| Adjustedb | 4.35 (2.00-10.00) | 4.17 (2.63-6.67) | 1.09 (0.53-2.22) |
| a offset by estimated follow-up time  b additionally adjusted for direct renin inhibitor trial (yes/no), comparison type (placebo, different ATC class to 3-character, different ATC class to 5-character), phase (3 or 4) and outcome type (hard or soft). | | | |

The analysis presented in the main text compared SAE rates in RAAS trials for hypertension to rates of all-cause hospitalisation and death in people with hypertension in the community starting RAAS drugs, after excluding people with recent stroke or myocardial infarction. This sensitivity analysis repeats this same comparison after also excluding people with heart failure, diabetes mellitus, or chronic kidney disease from the community comparison.

|  |
| --- |
| Observed and expected event rates: sensitivity analysis |
|  |

|  |
| --- |
| Ratio of observed to expected: sensitivity analysis |
|  |