**Supplementary Material**

Temporal trends and patterns in cause-specific mortality and hospitalisations after diagnosis of atrial fibrillation

Prof Jianhua Wu, PhD; Ramesh Nadarajah, MA; Yoko M Nakao, MD; Kazuhiro Nakao, MD; Chris Wilkinson, MD; J Campbell Cowan, DPhil; Prof A John Camm, MD; Prof Chris P Gale PhD

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## Supplement. Baseline Variables

For patients with incident AF, we extracted their most recent measurement of baseline characteristics recorded in patients’ primary care record within 1 year of a diagnosis of AF, including systolic and diastolic blood pressure, smoking status and body mass index (BMI).

We also extracted information about comorbidities, socioeconomic status and ethnicity. To describe comorbidities, we selected 18 common chronic conditions *a priori* that impact on quality and quantity of life: anaemia, cancer, chronic kidney disease, chronic obstructive pulmonary disease, dementia, depression, diabetes, dyslipidaemia, heart failure, hypertension, ischaemic heart disease, obesity, obstructive sleep apnoea, osteoarthritis, peripheral arterial disease, stroke or transient ischaemic attack, thyroid disease, and valvular heart disease.1 For each condition, except obesity, code lists from the CALIBER code repository were used to report prevalence, defined as the percentage of patients with a diagnosis recorded in their primary care or hospital discharge record before their first diagnosis of AF. Obesity was identified by a recorded body mass index (BMI) ≥30 kg/m2.

We used the Index of Multiple Deprivation (IMD) 2015 quintile to describe socioeconomic status, a

composite measure of relative deprivation at a small area level, ranked in ascending order of deprivation score and grouped in equal fifths. Ethnicity is reported as recorded in patient’s electronic health record.

## Supplement. Validity of diagnoses recorded in electronic health record databases, hospital episodes data and cause of death records

Adapted from information provided in *Conrad et al*.2

CPRD

* A systematic review, published in 2010, reports 212 validation studies over a broad range of conditions with an average positive predictive value of 89%.3
* Three studies of other common morbidities in the general population:
  + Heart failure diagnoses showed a positive predictive value of 82%.4
  + Chronic obstructive pulmonary disease diagnoses had an accuracy of 87% compared with specialist assessment.5
  + A specific asthma code diagnosis has a positive predictive value of 86%.6

Hospital episodes data

* A systematic review including 12 studies in England and Wales found that the median coding accuracy rates were 91% for discharge diagnostic codes.7

Causes of death records

* A study performed by the Office of National Statistics (ONS) examined causes of death recorded on death certificates in five pilot areas in the UK, and found that on scrutiny of an independent medical examiner, the broad underlying cause of death (as defined by International Classification of Diseases chapter [ICD]) remained unchanged in 88% of cases.8 In the present study, in line with previous methodology,2 the 22 ICD chapters were grouped into higher-level disease categories (respectively 9 and 11 disease categories for death and hospitalizations).2
* Most deaths (around 80%) have the underlying cause of death coded automatically using coding software, which improves the international and temporal comparability of mortality statistics. The remainder are coded manually by experienced coders.9

## Supplementary Table 1. Diagnostic codes that refer to a new diagnosis of atrial fibrillation

|  |  |
| --- | --- |
| **Code** | **Description** |
| Readcodes | |
| G573200 | Paroxysmal atrial fibrillation |
| G573400 | Permanent atrial fibrillation |
| G573500 | Persistent atrial fibrillation |
| 3272 | ECG: atrial fibrillation |
| G573000 | Atrial fibrillation |
| G573300 | Non-rheumatic atrial fibrillation |
| G573.00 | Atrial fibrillation and flutter |
| G573z00 | Atrial fibrillation and flutter NOS |
| 3273 | ECG: atrial flutter |
| G573100 | Atrial flutter |
| ICD-10 codes | |
| I48 | Atrial fibrillation and flutter |

## Supplementary Table 2. Definition of disease categories for causes of deaths and hospitalisations

|  |  |
| --- | --- |
| **Causes of death** | **Causes of hospitalisation** |
| **Cardiovascular disorders**: ICD chapter  ‘Diseases of the circulatory system’ (code range:  I00–I99), excluding codes relating to infections or cerebrovascular disease. | **Heart failure:** ICD codes: I50 ‘Heart failure’ (incl.  I50.0, I50.1, I50.9), I42.0 ‘Dilated cardiomyopathy’,  I42.9 ‘Cardiomyopathy, unspecified’, I11.0  ‘Hypertensive heart disease with (congestive) heart  failure’, I25.5 ‘Ischemic cardiomyopathy’, I13.0  ‘Hypertensive heart and renal disease with  (congestive) heart failure’, I13.2 ‘Hypertensive heart  and renal disease with both (congestive) heart  failure and renal failure’. |
|  | **Other cardiovascular disorders**: ICD chapter  ‘Diseases of the circulatory system’ (code range:  I00–I99), excluding codes relating to heart failure or  infections or cerebrovascular disorders |
| **Cerebrovascular disorders:** ICD chapter ‘Diseases of the circulatory system’ **(**I60-I69) | |
| **Neoplasms**: ICD chapter ‘Neoplasms’ (C00–D48). | |
| **Infections**: infectious and parasitic diseases, respiratory infections, urinary tract infections, and  cellulitis, as defined by individual codes as Conrad et al. | |
| **Chronic respiratory diseases**: individual codes Conrad et al. | |
| **Digestive diseases**: ICD chapter: ‘Diseases of the digestive system’ (K00–K93), excepting selected  codes categorized as infections. | |
| **Mental and neurological disorders:** ICD chapter ‘Mental and behavioral disorders’ (F00–F99) and  ICD chapter ‘Diseases of the nervous system’ (G00–G99) | |
| **-** | **Musculoskeletal disorders**: ICD chapter  ‘Diseases of the musculoskeletal system and  connective tissue’ (M00-M99). |
| **Injuries**: ICD chapters ‘Injury, poisoning and certain other consequences of external causes’ (S00–T98)  and ‘External causes of morbidity and mortality’ (V01–Y98) | |
| **Kidney diseases** ICD sub-chapters ‘Renal failure’ (N17-N19), ‘Glomerular diseases’ (N00-N08), ‘Renal  tubulo-interstitial diseases’ (N10-N16), ‘Other disorders of kidney and ureter’ (N25-N29). | |
| **Other**: any code not falling into any of the above  categories. | **Other**: ICD chapter ‘Symptoms, signs and  abnormal clinical and laboratory findings, not  elsewhere classified’ (R00-R99) as well as any  code not falling into any of the above categories. |

In sub-group analyses, categories were grouped into cardiovascular causes, cerebrovascular causes, and non-cardiovascular or cerebrovascular causes (all other categories).

To categorise cause of death or hospitalisation as infections or chronic respiratory diseases we used the same codelists as Conrad N, Judge A, Canoy D, et al. Temporal trends and patterns in mortality after incident heart failure: a longitudinal analysis of 86 000 individuals. *JAMA cardiology* 2019;4(11):1102-11

## Supplementary Table 3. Characteristics of patients at time of diagnosis with atrial fibrillation by sex and socioeconomic status

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **All patients** | **Sex** | | **Socioeconomic status quintile** | |
|  |  | Women | Men | 1 (least deprived) | 5 (most deprived) |
|  | n = 72 412 | n = 34 903 | n = 37 509 | n = 33 328 | n = 39 084 |
| Age (years) | 75.61 (12.42) | 78.46 (11.62) | 72.95 (12.55) | 74.35 (12.03) | 76.68 (12.64) |
| Men | 37 509 (51.8) | 0 (0.0) | 37509 (100.0) | 17 984 (54.0) | 19 525 (50.0) |
| Ethnicity (White) | 67 299 (94.5) | 32362 (94.0) | 34937 (94.9) | 30 394 (94.5) | 36 905 (94.4) |
| Socioeconomic status quintile |  |  |  |  |  |
| 1 (least deprived) | 15 687 (21.7) | 7246 (20.8) | 8441 (22.5) | 7 929 (23.8) | 7 758 (19.9) |
| 2 | 15 668 (21.6) | 7399 (21.2) | 8269 (22.1) | 7 459 (22.4) | 8 209 (21.0) |
| 3 | 16 421 (22.7) | 7957 (22.8) | 8464 (22.6) | 7 606 (22.8) | 8 815 (22.6) |
| 4 | 13 712 (18.9) | 6896 (19.8) | 6816 (18.2) | 5 965 (17.9) | 7 747 (19.8) |
| 5 (most deprived) | 10 895 (15.1) | 5390 (15.4) | 5505 (14.7) | 4 357 (13.1) | 6 538 (16.7) |
| Ever smoker | 38 473 (53.1) | 14658 (42.0) | 23815 (63.5) | 17 171 (55.1) | 21 302 (58.2) |
| Systolic blood pressure (mm Hg) | 136.58 (16.13) | 138.44 (16.52) | 134.86 (15.55) | 137.43 (15.48) | 135.79 (16.66) |
| Diastolic blood pressure (mm Hg) | 77.26 (8.95) | 77.38 (8.79) | 77.15 (9.10) | 78.56 (8.64) | 76.05 (9.07) |
| Heart rate (bpm) | 77.94 (16.40) | 79.60 (16.29) | 76.46 (16.35) | 78.80 (16.68) | 76.97 (16.02) |
| BMI (kg/m2) | 27.84 (6.29) | 27.63 (6.96) | 28.01 (5.70) | 28.35 (6.25) | 27.33 (6.30) |
| Chronic kidney disease | 13 786 (19.0) | 7493 (21.5) | 6293 (16.8) | 5 483 (16.5) | 8 303 (21.2) |
| Cancer | 15 823 (21.9) | 7308 (20.9) | 8515 (22.7) | 6 365 (19.1) | 9 458 (24.2) |
| Chronic obstructive pulmonary disease | 17 672 (24.4) | 8549 (24.5) | 9123 (24.3) | 7 358 (22.1) | 10 314 (26.4) |
| Diabetes | 12 206 (16.9) | 5309 (15.2) | 6897 (18.4) | 4 946 (14.8) | 7 260 (18.6) |
| Dyslipidaemia | 11 720 (16.2) | 5582 (16.0) | 6138 (16.4) | 5 369 (16.1) | 6 351 (16.2) |
| Heart failure | 13 846 (19.1) | 6770 (19.4) | 7076 (18.9) | 5 549 (16.6) | 8 297 (21.2) |
| Hypertension | 41 326 (57.1) | 21561 (61.8) | 19765 (52.7) | 19 170 (57.5) | 22 156 (56.7) |
| Ischaemic heart disease | 18 364 (25.4) | 7329 (21.0) | 11035 (29.4) | 7 042 (21.1) | 11 322 (29.0) |
| Stroke/TIA | 10 310 (14.2) | 5046 (14.5) | 5264 (14.0) | 4 260 (12.8) | 6 050 (15.5) |
| Osteoarthritis | 26 980 (37.3) | 15089 (43.2) | 11891 (31.7) | 12 057 (36.2) | 14 923 (38.2) |
| Thyroid disease | 7 200 (9.9) | 5513 (15.8) | 1687 (4.5) | 3 165 (9.5) | 4 035 (10.3) |
| Three or more comorbidities | 44 762 (61.8) | 22901 (65.6) | 21861 (58.3) | 8998 (57.4) | 7443 (68.3) |
| CHA2DS2-VASc score | 3.19 (1.66) | 3.90 (1.45) | 2.53 (1.57) | 3.07 (1.65) | 3.26 (1.69) |

Data are mean (SD) or n (%). Socioeconomic status (SES) refers to Index of Multiple Deprivation 2015 quintile, with SES 1 referring to the most affluent and SES 5 to the most deprived socioeconomic quintile. Number of comorbidities refers to any of the 18 conditions investigated. BMI, body-mass index; TIA, transient ischaemic attack. Category percentages refer to complete cases.

## Supplementary Table 4. Characteristics of patients at time of diagnosis with atrial fibrillation across time periods during the study

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Time period** | | | | |
|  | 2003-2005 | 2006-2008 | 2009-2011 | 2012-2015 |
|  | n = 13 389 | n = 14 986 | n = 15 364 | n = 16 600 |
| Age (years) | 75.58 (12.23) | 75.77 (12.35) | 75.58 (12.65) | 75.64 (12.56) |
| Men | 6744 (50.4) | 7725 (51.5) | 8006 (52.1) | 8797 (53.0) |
| Ethnicity (White) | 12207 (92.4) | 14145 (95.5) | 14606 (96.3) | 15615 (95.8) |
| Socioeconomic status quintile |  |  |  |  |
| 1 (least deprived) | 2696 (20.1) | 3172 (21.2) | 3442 (22.4) | 3617 (21.8) |
| 2 | 2887 (21.6) | 3264 (21.8) | 3360 (21.9) | 3591 (21.6) |
| 3 | 3064 (22.9) | 3428 (22.9) | 3452 (22.5) | 3819 (23.0) |
| 4 | 2582 (19.3) | 2833 (18.9) | 2850 (18.6) | 3188 (19.2) |
| 5 (most deprived) | 2151 (16.1) | 2281 (15.2) | 2256 (14.7) | 2383 (14.4) |
| Ever smoker | 5824 (43.5) | 8380 (55.9) | 9059 (59.0) | 10152 (61.2) |
| Systolic blood pressure (mm Hg) | 139.68 (17.55) | 136.68 (15.74) | 135.28 (15.08) | 133.83 (14.39) |
| Diastolic blood pressure (mm Hg) | 78.73 (9.57) | 77.26 (8.72) | 76.73 (8.61) | 75.81 (8.42) |
| Heart rate (bpm) | 80.19 (17.83) | 78.58 (16.87) | 77.58 (16.28) | 76.71 (15.30) |
| BMI (kg/m2) | 27.35 (6.00) | 27.63 (6.14) | 28.02 (6.34) | 28.26 (6.50) |
| Chronic kidney disease | 593 (4.4) | 2913 (19.4) | 4180 (27.2) | 4530 (27.3) |
| Cancer | 2294 (17.1) | 3080 (20.6) | 3632 (23.6) | 4340 (26.1) |
| Chronic obstructive pulmonary disease | 3161 (23.6) | 3597 (24.0) | 3830 (24.9) | 4197 (25.3) |
| Diabetes | 1710 (12.8) | 2284 (15.2) | 2735 (17.8) | 3466 (20.9) |
| Dyslipidaemia | 1458 (10.9) | 2247 (15.0) | 2874 (18.7) | 3469 (20.9) |
| Heart failure | 3129 (23.4) | 2940 (19.6) | 2682 (17.5) | 2501 (15.1) |
| Hypertension | 6862 (51.3) | 8486 (56.6) | 9276 (60.4) | 10417 (62.8) |
| Ischaemic heart disease | 3645 (27.2) | 3920 (26.2) | 3750 (24.4) | 3936 (23.7) |
| Stroke/TIA | 1945 (14.5) | 2168 (14.5) | 2117 (13.8) | 2336 (14.1) |
| Osteoarthritis | 4484 (33.5) | 5534 (36.9) | 6027 (39.2) | 6699 (40.4) |
| Thyroid disease | 1154 (8.6) | 1457 (9.7) | 1648 (10.7) | 1859 (11.2) |
| Three or more comorbidities | 7240 (54.1) | 9187 (61.3) | 10067 (65.5) | 11290 (68.0) |
| CHA2DS2-VASc score | 3.14 (1.65) | 3.17 (1.66) | 3.20 (1.67) | 3.26 (1.67) |

Data are mean (SD) or n (%). Socioeconomic status (SES) refers to Index of Multiple Deprivation 2015 quintile, with SES 1 referring to the most affluent and SES 5 to the most deprived socioeconomic quintile. Number of comorbidities refers to any of the 18 conditions investigated. BMI, body-mass index; TIA, transient ischaemic attack. Category percentages refer to complete cases.

## Supplementary Table 5. Number of deaths due to cardiovascular, cerebrovascular, digestive disease, infection, chronic respiratory disease and mental and neurological disease, by disease sub-groups.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | All years | 2001-2002 | 2003-2005 | 2006-2008 | 2009-2011 | 2012-2015 | 2016-2017 | P-value |
|  | 14481 | 1436 | 2860 | 3184 | 3046 | 3125 | 830 |  |
| Cardiovascular disease | 3856 (26.6) | 507 (35.3) | 909 (31.8) | 913 (28.7) | 719 (23.6) | 655 (21.0) | 153 (18.4) | <0.001 |
| Acute myocardial infarction | 763 (19.8) | 114 (22.5) | 197 (21.7) | 168 (18.4) | 135 (18.8) | 121 (18.4) | 28 (18.3) | <0.001 |
| Heart failure | 485 (12.6) | 50 (9.9) | 93 (10.2) | 147 (16.1) | 93 (12.9) | 80 (12.1) | 22 (14.4) | <0.001 |
| Cerebrovascular disease | 1577 (10.9) | 178 (12.4) | 359 (12.6) | 375 (11.8) | 319 (10.5) | 288 (9.2) | 58 (7.0) | <0.001 |
| Acute stroke | 189 (12.0) | 16 (9.0) | 46 (12.8) | 36 (9.6) | 38 (11.9) | 47 (16.3) | 6 (10.3) | 0.267 |
| Acute haemorrhage | 156 (9.9) | 11 (6.2) | 24 (6.7) | 38 (10.1) | 35 (11.0) | 35 (12.2) | 13 (22.4) | 0.381 |
| Digestive disease | 677 (4.7) | 56 (3.9) | 132 (4.6) | 142 (4.5) | 158 (5.2) | 151 (4.8) | 38 (4.6) | 0.511 |
| GI bleeding | 91 (13.4) | 12 (21.4) | 15 (11.4) | 24 (16.9) | 18 (11.4) | 18 (11.9) | 4 (10.5) | 0.735 |
| Infection | 1624 (11.2) | 136 (9.5) | 334 (11.7) | 378 (11.9) | 332 (10.9) | 358 (11.5) | 86 (10.4) | 0.187 |
| Influenza and pneumonia | 1047 (64.5) | 101 (74.3) | 236 (70.7) | 211 (55.8) | 200 (60.2) | 238 (66.4) | 58 (67.4) | 0.107 |
| Urinary tract infections | 196 (12.1) | 13 (9.6) | 36 (10.8) | 59 (15.6) | 46 (13.9) | 37 (10.3) | 5 (8.6) | 0.023 |
| Chronic respiratory disease | 1337 (9.2) | 115 (8.0) | 236 (8.3) | 292 (9.2) | 290 (9.5) | 319 (10.2) | 85 (10.2) | 0.057 |
| COPD | 876 (65.5) | 85 (73.9) | 158 (66.9) | 179 (61.3) | 173 (59.7) | 220 (69.0) | 59 (69.4) | 0.074 |
| Mental and neurological disease | 761 (5.3) | 36 (2.5) | 92 (3.2) | 110 (3.5) | 174 (5.7) | 265 (8.5) | 84 (10.1) | <0.001 |
| Dementia | 500 (65.7) | 19 (52.8) | 39 (42.4) | 60 (54.5) | 120 (69.0) | 195 (73.6) | 67 (79.8) | <0.001 |
| Alzheimer's disease | 77 (10.1) | 5 (13.9) | 12 (13.0) | 19 (17.3) | 8 (4.6) | 25 (9.4) | 8 (9.5) | 0.022 |
| Parkinson’s disease | 82 (11.4) | 8 (22.2) | 18 (19.6) | 10 (9.1) | 20 (11.5) | 21 (7.9) | 5 (6.0) | 0.083 |
| Mental disorders (F04-F99) | 13 (1.7) | 0 (0.0) | 4 (4.3) | 1 (0.9) | 5 (2.9) | 2 (0.8) | 1 (1.2) | 0.358 |
| Injuries | 296 (2.0) | 21 (1.5) | 46 (1.6) | 71 (2.2) | 72 (2.4) | 59 (1.9) | 27 (3.3) | 0.018 |
| Fall | 94 (31.8) | 4 (19.0) | 11 (35.2) | 25 (34.7) | 25 (34.7) | 21 (35.6) | 8 (29.6) | 0.082 |

Data are presented as n (%). Percentages refer to the total number of deaths within each disease category. The difference between time period was tested through Chi-squared test, and p-value was reported. Clinical codes used to identify each disease group are available upon request.

## Supplementary Figure 1. All-cause and cause-specific mortality rates at 1-year following atrial fibrillation diagnosis, by age and sex.

C:\Users\hww459\Downloads\Figure mortality by age and sex (2023).tif

Crude rates of all-cause mortality rates at 1 year following diagnosis of atrial fibrillation, and cause-specific mortality presented as a proportion of patients deceased at 1 year. Adjusted comparison present rate ratios for all-cause mortality at 1 year in women versus men from multivariable Poisson regression models. ‘Other’ refers to any other causes except the predefined 9 disease conditions for cause of death.

## Supplementary Figure 2. Differences in hospitalisation 1 year after atrial fibrillation diagnosis by sex, socioeconomic status and place of diagnosis



Total number of hospitalisation events by each category of sex, socioeconomic status, and diagnostic setting alongside rate ratios (RRs), 95% confidence intervals from multivariable Poisson regression models accounting for year of diagnosis, age (as a continuous variable), sex, socioeconomic status, region, and 18 baseline comorbidities.

## Supplementary Figure 3. Temporal trends in hospitalisation at 1 year following atrial fibrillation diagnosis by age group.

Mean number of hospitalisation events by age-groups alongside rate ratios (RRs), 95% confidence intervals, and interaction P values from multivariable Poisson regression models accounting for year of diagnosis, age (as a continuous variable), sex, socioeconomic status, region, and 18 baseline comorbidities. Interaction P values refer to the interaction between age group (categorized as age <70 years, 70-79 years, or age ≥80 years) and year of diagnosis.



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