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ORIGINAL ARTICLE

Frequency of Cardiac Rhythm Abnormalities in a Half Million Adults

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BACKGROUND: The frequency of cardiac rhythm abnormalities and their risk factors in community-dwelling adults are not well characterized.

METHODS: We determined the frequency of rhythm abnormalities in the UK Biobank, a national prospective cohort. We tested associations between risk factors and incident rhythm abnormalities using multivariable proportional hazards regression.

RESULTS: Of 502 627 adults (median age, 58 years [interquartile range, 13]; 54.4% women), 2.35% had a baseline rhythm abnormality. The prevalence increased with age with 4.84% of individuals aged 65 to 73 years affected. During 3 368 332 person-years of follow-up, 15 906 new rhythm abnormalities were detected (4.72 per 1000 person-years; 95% confidence interval [CI]: 4.65–4.80). Atrial fibrillation (3.11 per 1000 person-years; 95% CI: 3.05–3.17), bradyarrhythmias (0.89 per 1000 person-years; 95% CI: 0.86–0.92), and conduction system diseases (1.06 per 1000 person-years; 95% CI: 1.02–1.09) were more common than supraventricular (0.51 per 1000 person-years; 95% CI: 0.48–0.53) and ventricular arrhythmias (0.57 per 1000 person-years; 95% CI: 0.55–0.60). Older age (hazard ratio [HR]: 2.35 per 10-year increase; 95% CI: 2.29–2.41; $P<0.01$), male sex (HR: 1.83; 95% CI: 1.76–1.89; $P<0.01$), hypertension (HR: 1.49; 95% CI: 1.44–1.54; $P<0.01$), chronic kidney disease (HR: 1.95; 95% CI: 1.67–2.27; $P<0.01$), and heart failure (HR: 1.99; 95% CI: 1.76–2.26; $P<0.01$) were associated with new rhythm abnormalities.

CONCLUSIONS: The frequency of rhythm abnormalities in middle-aged to older community-dwelling adults is substantial. Atrial fibrillation, bradyarrhythmias, and conduction system diseases account for most rhythm conditions.

VISUAL OVERVIEW: An online visual overview is available for this article.

Key Words: atrial fibrillation ■ bradycardia ■ heart failure ■ tachycardia, supraventricular ■ tachycardia, ventricular

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WHAT IS KNOWN?

- Abnormalities of cardiac rhythm are associated with substantial morbidity and economic costs.

WHAT THE STUDY ADDS?

- Abnormalities of cardiac rhythm are prevalent in community-dwelling adults, affecting >2% of individuals.
- Incident cardiac rhythm abnormalities occur at a rate of 0.5% per year, similar to rates of stroke, myocardial infarction, and heart failure.
- Risk of incident rhythm abnormalities is increased in the setting of older age, male sex, traditional cardiac risk factors, chronic kidney disease, and heart failure.

Abnormalities of cardiac rhythm are associated with substantial morbidity and economic costs. Atrial fibrillation affects at least 2.3 million people in the United States alone and is associated with increased risks of stroke and mortality.[1–5] About 90 000 cases of supraventricular tachycardia are detected annually in the United States,[6] and ≈25% of all emergency department visits for supraventricular tachycardia result in hospitalization.[7] Bradyarrhythmias and other forms of conduction disease may cause syncope, fatigue from chronotropic incompetence, or sudden death from asystole or ventricular tachycardia.[8] Ventricular arrhythmias are thought to cause 75% to 80% of cases of sudden cardiac death, which are estimated to result in 184 000 to 450 000 lives lost in the United States per year.[9,10]

Although previous studies have characterized the prevalence and incidence of selected rhythm abnormalities, including atrial fibrillation, supraventricular arrhythmias, and ventricular arrhythmias, a robust description of the overall rhythm condition profile encountered among adults is lacking. The UK Biobank is a prospective study of ≈500 000 individuals from the United Kingdom with detailed characterization of medical conditions and risk factors and longitudinal follow-up.[11] With its large size, prospective design, and systematic data ascertainment, the UK Biobank provides an opportunity to examine the contemporary frequency of and risk factors for cardiac rhythm abnormalities in the community.

In this study, we leveraged the UK Biobank to determine the age- and sex-stratified prevalence and incidence of cardiac rhythm abnormalities and provide a benchmark of the contemporary extent of rhythm conditions in the community. We contrasted the frequency of rhythm abnormalities across broad subclasses, including atrial fibrillation, bradyarrhythmias, conduction system diseases, supraventricular arrhythmias, and ventricular arrhythmias. We then assessed associations between selected clinical factors and incident rhythm abnormalities.

METHODS

Individual level data from individuals described in this analysis are available to approved investigators by application to the UK Biobank (www.ukbiobank.ac.uk).

Study Population

The UK Biobank is a publicly available population-based prospective cohort of 502 627 participants recruited between 2006 and 2010 in the United Kingdom primarily established to investigate the genetic and lifestyle determinants of a wide range of diseases of middle and later life.[12,13] Approximately 9.2 million individuals aged 40 to 69 years who lived within 25 miles of the 22 assessment centers in England, Wales, and Scotland were invited, and 5.4% participated in the baseline assessment. Individuals who were invited but elected not to participate tended to be younger, men, more socioeconomically deprived, and with fewer self-reported health outcomes.[14] Extensive questionnaire data, physical measures, and biological samples were collected at recruitment, with ongoing enhanced data collection in large subsets of the cohort, including repeated assessments, genotyping, biochemical assays, web-based questionnaires, physical activity monitoring, and multimodal imaging. All participants are followed up for health outcomes through linkage to national electronic health-related data sets. Participants provided written informed consent to participate in research as previously described.[12] The UK Biobank was approved by the UK Biobank Research Ethics Committee (reference number 11/NW/0382). Use of UK Biobank data was approved by the local Partners Healthcare Institutional Review Board.

Baseline Clinical Characteristics

Baseline age, sex, race (white or nonwhite), and body mass index were obtained from the initial assessment visit. Potential clinical factors for rhythm abnormalities were chosen a priori and included hypertension, hyperlipidemia, diabetes mellitus, chronic kidney disease, obstructive sleep apnea, asthma, chronic obstructive pulmonary disease, hyperthyroidism, hypothyroidism, depression, venous thromboembolism, peripheral arterial disease, stroke, coronary artery disease, and heart failure. Each clinical factor was defined by either self-reported questionnaire at the initial assessment visit or at least 1 *International Statistical Classification of Diseases, Ninth or Tenth Revision* (*ICD-9 or ICD-10*) code for the condition as a primary diagnosis, secondary diagnosis, or cause of death in a linked medical encounter.

The presence of tobacco use was ascertained using self-reported questionnaires at the initial assessment visit, with smoking status classified categorically as current, previous, or never. Participants with at least 1 *ICD-9* or *ICD-10* code indicating active tobacco use during a linked medical encounter (eg, toxic effect of tobacco and nicotine) were classified as current smokers. Alcohol use frequency was ascertained using self-reported questionnaires at the initial assessment visit, which we further classified categorically as frequent (corresponding to daily or almost daily drinking), occasional (corresponding to drinking 1×–4× per week), or infrequent (corresponding to drinking 1×–3× per month or fewer). We

also classified participants with at least 1 *ICD-9* or *ICD-10* code indicating active alcohol use during a linked medical encounter (eg, delirium tremens) as frequent alcohol users. A complete list of clinical factor definitions can be found in Table I in the Data Supplement.

Rhythm Abnormality Definitions

We defined 6 classes of rhythm abnormalities a priori for the purposes of our analysis: atrial fibrillation (or flutter), bradyarrhythmias, conduction system diseases, supraventricular arrhythmias, ventricular arrhythmias, and any rhythm abnormality (defined as at least one of the aforementioned rhythm abnormalities). Prevalent rhythm abnormalities were based on self-report on the initial assessment visit questionnaire, at least 1 *ICD-9* or *ICD-10* code for the condition listed as either a primary diagnosis, secondary diagnosis, or cause of death for a linked medical encounter, or occurrence of a relevant procedure for a particular rhythm abnormality (eg, pacemaker insertion for bradyarrhythmias, cardioversion or catheter ablation for atrial fibrillation, accessory pathway ablation for supraventricular arrhythmia). Abnormalities in rate or rhythm resulting in pathologically slow ventricular response were classified as bradyarrhythmias while isolated conduction abnormalities without derangements of rate or rhythm were classified as conduction system diseases. The supraventricular arrhythmia definition included all individuals with atrioventricular preexcitation (n=107), or Wolff-Parkinson-White pattern, given the clinical importance of risk stratifying such individuals, and because >80% also had a concominant code for supraventricular arrhythmia or preexcitation syndrome.[15] A complete list of rhythm abnormality definitions can be found in Table II in the Data Supplement.

Because some abnormalities included in our rhythm condition definitions may confer limited clinical significance (eg, first-degree atrioventricular block, fascicular block, premature atrial depolarizations, premature ventricular depolarizations, etc), we performed a secondary analysis in which we included only defining features we considered of highest clinical relevance (Table III in the Data Supplement). For the purposes of this analysis, the definitions of atrial fibrillation and bradyarrhythmias were unchanged, and isolated conduction system diseases were excluded.

Because manual validation of the conditions is not possible in the UK Biobank, we performed manual validation of our rhythm abnormality definitions in the Partners HealthCare System Research Patient Data Registry, an independent electronic health record data warehouse spanning ≈7 million individuals and several Partners affiliated hospital systems in the United States.[16,17] We adapted rhythm abnormality definitions used in the UK Biobank for use in the Partners HealthCare sample by mapping procedural codes to corresponding Current Procedural Terminology codes and retaining *ICD-9* and *ICD-10* codes. We did not include any self-reported features in the Partners HealthCare system. We then randomly selected 50 records within each of the 5 main rhythm abnormality subclasses (total n=250 records) from a sample of 66 661 ambulatory adults treated within the Partners HealthCare system between 2013 and 2014 with outpatient visits in both calendar years and manually adjudicated the entire medical record for the presence of the abnormality in question. The positive predictive values of our definitions for atrial fibrillation, bradyarrhythmias, conduction system diseases, supraventricular arrhythmias, and ventricular arrhythmias in the Partners sample were 92%, 80%, 97%, 82%, and 84%, respectively, which we considered sufficient for further analysis.

Follow-Up and Censoring

We classified incident rhythm abnormalities as not having the abnormality at baseline but subsequently meeting the criteria during the study period. For each participant, person-time began at the initial assessment visit and lasted until the last known ascertainment of the earliest of death or last follow-up (ie, February 9, 2016, for participants enrolled in Wales, February 16, 2016, for participants enrolled in England, and October 31, 2015, for participants enrolled in Scotland). Participants were presumed to be alive at last follow-up if there was no preceding report of death in the death register. For analyses of incident rhythm abnormalities, follow-up was censored at the earliest of either last known follow-up or development of the rhythm abnormality in question.

Statistical Analysis

We tabulated the prevalence of rhythm abnormalities by dividing the number of individuals with an event at baseline enrollment by the number of eligible individuals, which we stratified by age (<55, 55–65, >65 years, with cut points chosen to approximate tertiles of the age distribution) and sex. We estimated the incidence rate of rhythm abnormalities by dividing the number of incident events by the total person-time observed within the same age and sex strata. For prevalence and incidence calculations, individuals meeting criteria for multiple rhythm abnormality subclasses were counted within each relevant subclass. Confidence intervals (CIs) were estimated using an exact method. To determine clinical factors associated with the development of incident rhythm abnormalities, we performed multivariable Cox proportional hazards regression in which we regressed the presence of any incident rhythm abnormality, as well as each subclass separately (ie, atrial fibrillation, bradyarrhythmias, conduction system diseases, supraventricular arrhythmias, and ventricular arrhythmias), on potential risk factors. Potential risk factors included age, sex, race, body mass index, tobacco use, alcohol use, hypertension, hyperlipidemia, diabetes mellitus, chronic kidney disease, obstructive sleep apnea, asthma, chronic obstructive pulmonary disease, hyperthyroidism, hypothyroidism, depression, venous thromboembolism, peripheral arterial disease, stroke, coronary artery disease, and heart failure. Models were generated using a complete case analysis approach (see Figure I in the Data Supplement for a CONSORT diagram). For each model, the Cox proportional hazards assumption was assessed by inspecting Schoenfeld residuals. In an exploratory analysis, we repeated the above modeling using obesity as a categorical variable rather than body mass index. In a second exploratory analysis, we regressed the incidence of each rhythm condition subclass on prevalent rhythm abnormalities of a different subclass. We considered associations between potential risk factors and incident rhythm

abnormalities to be significant if the 2-sided *P* value was <0.05. All analyses were performed using R v.3.2.2, including the epitools and survival packages.[18]

RESULTS

Of the 502 627 individuals included in these analyses, the median age was 58 years (interquartile range, 50–63), 94.1% were white, and 54.4% were women. Median follow-up was 7.0 years (interquartile range, 1.4) for the overall sample and was similar within each age stratum (7.1 years [interquartile range, 1.3] for individuals aged <55 years, 7.0 years [interquartile range, 1.4] for individuals aged 55–64 years, and 6.8 years [interquartile range, 1.5] for individuals aged ≥65 years). In total, 14 419 (2.87%) participants died during follow-up after a median of 4.33 years (interquartile range, 3.22). Other baseline clinical characteristics are listed in Table 1.

Within the overall cohort, 11 805 (2.35%; 95% CI: 2.31–2.39) individuals had a rhythm abnormality at baseline. The baseline prevalence of atrial fibrillation, bradyarrhythmias, conduction system diseases, supraventricular arrhythmias, and ventricular arrhythmias was 1.54% (95% CI: 1.50–1.57), 0.42% (95% CI: 0.40–0.44), 0.28% (95% CI: 0.26–0.29), 0.43% (95% CI: 0.41–0.45), and 0.22% (95% CI: 0.21–0.23), respectively. The age- and sex-stratified prevalence of any rhythm abnormality and the component subclasses is displayed in Table 2 and Figure 1. Overall, rhythm abnormalities were more prevalent at older ages, with 1857 individuals (0.96%; 95% CI: 0.91–1.00) aged <55 years (minimum age, 37 years) and 4652 individuals (4.84%; 95% CI: 4.71–5.00) aged ≥65 years (maximum age, 73 years) affected by a rhythm abnormality.

In secondary analyses restricted to rhythm abnormalities of highest clinical relevance, the prevalence of any rhythm abnormality, bradyarrhythmias, supraventricular arrhythmias, and ventricular arrhythmias was 2.15% (95% CI: 2.11–2.19), 0.42% (95% CI: 0.41–0.44), 0.42% (95% CI: 0.40–0.44), and 0.19% (95% CI: 0.18–0.21). The age- and sex-stratified prevalence of rhythm abnormalities of highest clinical relevance is listed in Table IV in the Data Supplement.

Among the 490 822 participants without a prevalent rhythm abnormality, 15 906 cases of an incident rhythm condition developed over 3 368 332 person-years of follow-up (4.72 cases per 1000 person-years; 95% CI: 4.65–4.80). The specific incidence rates of atrial fibrillation, bradyarrhythmias, conduction system diseases, supraventricular arrhythmias, and ventricular arrhythmias were 3.11 (95% CI: 3.05–3.17), 0.89 (95% CI: 0.86–0.92), 1.06 (95% CI: 1.02–1.09), 0.51 (95% CI: 0.48–0.53), and 0.57 (95% CI: 0.55–0.60) cases per 1000 person-years, respectively. The age- and sex-stratified incidence rates of any rhythm abnormality and the component subclasses are listed in Table 3 and depicted in Figure 1.

In secondary analyses restricted to rhythm abnormalities of highest clinical relevance, the specific incidence rates of any rhythm abnormality, supraventricular arrhythmias, and ventricular arrhythmias were 3.99 (95% CI: 3.93–4.06), 0.48 (95% CI: 0.46–0.51), and 0.49 (95% CI: 0.46–0.51) cases per 1000 person-years, respectively. Overall, these rates were similar to those of the more broadly defined rhythm abnormality definitions. The age- and sex-stratified incidence rates of rhythm abnormalities of highest clinical relevance are listed in Table V in the Data Supplement.

In multivariable-adjusted analyses among individuals without a prevalent rhythm abnormality, many clinical factors were associated with incident rhythm condi-

Table 1. Study Sample Characteristics

Baseline Characteristics (N=502 627)	N or Distribution*	Percentage
Age†	58 (5063)	…
Female sex	273 459	54.4
Race, white	472 811	94.1
Race, Indian	5950	1.18
Race, Caribbean	4519	0.90
Race, African	3396	0.68
Race, other/unknown	15 052	2.99
Body mass index, kg/m²‡	27.4±4.8	…
Obese	122 192	24.5
Tobacco, current	55 931	11.2
Tobacco, former	170 824	34.2
Tobacco, never	273 045	54.6
Alcohol, frequent	106 304	21.2
Alcohol, occasional	242 139	48.3
Alcohol, infrequent	152 796	30.5
Hypertension	142 860	28.4
Hyperlipidemia	70 029	13.9
Diabetes mellitus	27 571	5.5
Chronic kidney disease	1574	0.3
Obstructive sleep apnea	3511	0.7
Asthma	61 080	12.2
Chronic obstructive pulmonary disease	10 956	2.2
Hyperthyroid	4517	0.9
Hypothyroid	23 358	5.0
Depression	30 627	6.1
Venous thromboembolism	12 891	2.6
Peripheral arterial disease	3511	0.7
Stroke	7780	1.6
Coronary artery disease	15 386	3.1
Heart failure	2791	0.6

*Individuals with missing data for each characteristic were removed from the denominator. Details on handling of missing data are provided in Figure I in the Data Supplement.

†Presented as median (quartile 1, quartile 3).

‡Presented as mean±SD.

Table 2. Age- and Sex-Stratified Prevalence of Rhythm Abnormalities

	<55 y* (N=194 253)	55 to 64 y (N=212 346)	≥65 y† (N=96 028)
Males (N=229 078)			
Any rhythm abnormality	1104 (1.28%)	3456 (3.62%)	3112 (6.56%)
Atrial fibrillation	649 (0.75%)	2415 (2.53%)	2299 (4.85%)
Bradyarrhythmias	188 (0.22%)	618 (0.65%)	599 (1.26%)
Conduction system diseases	134 (0.16%)	405 (0.42%)	370 (0.78%)
Supraventricular arrhythmias	241 (0.28%)	491 (0.51%)	350 (0.74%)
Ventricular arrhythmias	138 (0.16%)	351 (0.37%)	279 (0.59%)
Females (N=273 549)			
Any rhythm abnormality	753 (0.70%)	1840 (1.57%)	1540 (3.17%)
Atrial fibrillation	297 (0.28%)	1035 (0.89%)	1027 (2.11%)
Bradyarrhythmias	130 (0.12%)	320 (0.27%)	268 (0.55%)
Conduction system diseases	86 (0.08%)	222 (0.19%)	167 (0.34%)
Supraventricular arrhythmias	320 (0.30%)	495 (0.42%)	258 (0.53%)
Ventricular arrhythmias	93 (0.09%)	149 (0.13%)	99 (0.20%)

*Minimum age=37 years.
†Maximum age=73 years.

tions including older age (hazard ratio [HR]: 2.35 per 10-year increase; 95% CI: 2.29–2.41; *P*<0.01), male sex (HR: 1.83; 95% CI: 1.76–1.89; *P*<0.01), white race (HR: 1.24; 95% CI: 1.14–1.35; *P*<0.01), hypertension (HR: 1.49; 95% CI: 1.44–1.54; *P*<0.01), chronic kidney disease (HR: 1.95; 95% CI: 1.67–2.27; *P*<0.01), sleep apnea (HR: 1.32; 95% CI: 1.16–1.50; *P*<0.01), and heart failure (HR: 1.99; 95% CI: 1.76–2.26; *P*<0.01). In models in which we examined associations with specific rhythm condition subclasses, the risk factor profiles were qualitatively similar among the different subclasses although some notable differences in risk factor profiles were observed. For example, male sex was strongly associated with atrial fibrillation, bradyarrhythmias, conduction system diseases, and ventricular arrhythmias, but only marginally with supraventricular arrhythmias. The complete results of multivariable Cox proportional hazards modeling for each subclass of rhythm abnormality are listed in online Table VI in the Data Supplement and depicted in Figure 2. The results of an exploratory analysis using obesity rather than body mass index are presented in Table VII in the Data Supplement.

The results of a second exploratory analysis examining the association between prevalent and incident rhythm abnormalities of different subclasses are presented in online Table VIII in the Data Supplement and Figure II in the Data Supplement.

DISCUSSION

In a contemporary prospective cohort of >500 000 community-dwelling middle-aged to older adults with >3 million person-years of follow-up, we observed that 1% of participants <55 years had a prevalent rhythm abnormality, with ≈5% aged 65 to 73 years of age affected. Among individuals without a baseline rhythm abnormality, ≈16 000 incident abnormalities developed during follow-up, corresponding to a rate of ≈5 events per 1000 person-years. The majority of new rhythm abnormalities comprised atrial fibrillation, bradyarrhythmias, and conduction system diseases. Risk factors for rhythm abnormalities included older age, male sex, white race, and multiple cardiovascular comorbidities, with largely similar profiles among rhythm condition subtypes.

Whereas most other large observational studies have primarily focused on a specific common arrhythmia such as atrial fibrillation,[2,19] our study provides a comprehensive assessment of the spectrum of rhythm abnormalities in the community. We observed that rhythm abnormalities are common and that the incidence rises substantially with age. Over a median of 7 years of follow-up, rhythm abnormalities developed at a rate of ≈0.5% per year. The frequencies we observed support the growing recognition of rhythm abnormalities as a major public health problem[19,20] and are comparable to rates of other important cardiovascular diseases, including stroke, nonischemic cardiomyopathy, and acute myocardial infarction.[1]

The prospective and community-based nature of the UK Biobank enabled us to contrast the relative frequency of cardiac rhythm condition subclasses and illustrated that atrial fibrillation, bradyarrhythmias, and conduction system diseases are the most common rhythm abnormalities in the community. The rate of atrial fibrillation of 3.11 cases per 1000 person-years we observed is comparable to that reported by Miyasaka et al,[21] who reported an age- and sex-adjusted incidence of atrial

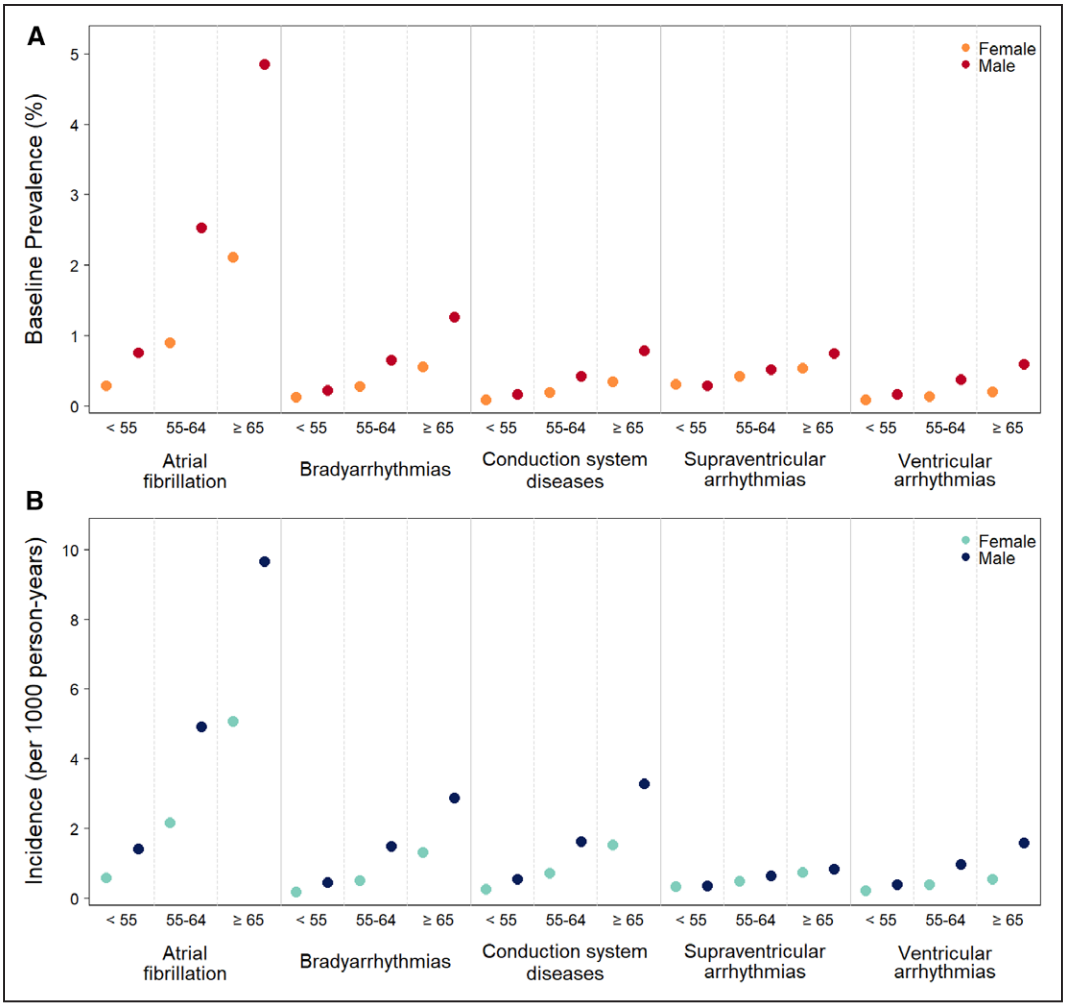

Figure 1. Frequency of cardiac rhythm abnormalities stratified by age and sex.
Plot depicting (**A**) age- and sex-stratified baseline prevalence, and (**B**) age- and sex-stratified incidence rates of rhythm abnormalities during the study period. The minimum age in the age <55 y stratum was 37 y, and the maximum age in the ≥65 y stratum was 73 y.

fibrillation of 3.68 per 1000 person-years. The prevalence of atrial fibrillation we observed is also consistent with the prevalence reported in a recent study using the UK Biobank although this study did not report the incidence of new atrial fibrillation.[22] We also observed that the incidence of bradyarrhythmias was substantial, with 0.89 cases per 1000 person-years overall and 2.86 cases per 1000 person-years among men aged 65 to 73 years. The incidence of bradyarrhythmias we observed is consistent with recent data demonstrating that sick sinus syndrome (which was included in the bradyarrhythmia subtype in our study) occurred with an incidence of ≈1 case per 1000 person-years.[20] Consistent with previous findings,[6] supraventricular and ventricular arrhythmias were less common.

Our findings highlight the importance of selected clinical factors in the development of cardiac rhythm abnormalities. Consistent with previous findings, age and sex emerged as important risk factors for incident rhythm conditions.[19,21] Prevalent heart failure conferred the greatest magnitude of risk for rhythm abnormalities, which may reflect the known relationship between rhythm abnormalities and worsening structural heart disease.[10] Similarly, hypertension and coronary artery disease, both known factors in the development of cardiac remodeling, were associated with incident rhythm abnormalities.[23] The association between both chronic obstructive pulmonary disease and sleep apnea with rhythm abnormalities highlights the important interplay between cardiac and pulmonary physiology in the development of rhythm conditions. Chronic kidney disease also was prominently associated with incident rhythm abnormalities, which may be related to increased risk of electrolyte derangements, or perhaps secondarily with renal dysfunction affecting blood pressure and cardiac remodeling.[24]

By comparing across rhythm condition subtypes, our analyses enabled comparisons of the relative importance of risk factors for each subclass of rhythm abnormality. Overall, risk factors for atrial fibrillation, bradyarrhythmias, conduction system diseases, and ventricular arrhythmias were similar, with age, male sex,

Table 3. Age- and Sex-Stratified Incidence of Rhythm Abnormalities (Cases per 1000 Person-Years)

	<55 y		55 to 64 y		≥65 y	
	Events (n) / Person-Time (y)	Incidence, per 1000 Person-Years (95% CI)	Events (n) / Person-Time (y)	Incidence, per 1000 Person-Years (95% CI)	Events (n)/ Person-Time (y)	Incidence, per 1000 Person-Years (95% CI)
Males						
Any rhythm abnormality	1444/594 720	2.42 (2.30–2.56)	4604/623 076	7.39 (7.18–7.61)	3952/288 704	13.69 (13.27–14.12)
Atrial fibrillation	836/599 744	1.39 (1.30–1.49)	3115/634 606	4.91 (4.74–5.08)	2866/297 140	9.65 (9.30–10.00)
Bradyarrhythmias	259/604 813	0.43 (0.38–0.48)	967/653 532	1.48 (1.39–1.58)	899/314 366	2.86 (2.68–3.05)
Conduction system diseases	326/604 913	0.54 (0.48–0.60)	1062/654 705	1.62 (1.53–1.72)	1029/315 593	3.26 (3.06–3.47)
Supraventricular arrhythmias	202/604 699	0.33 (0.29–0.38)	431/656 454	0.63 (0.60–0.72)	260/318 106	0.82 (0.72–0.92)
Ventricular arrhythmias	227/604 101	0.38 (0.33–0.43)	612/654 393	0.96 (0.89–1.04)	489/316 353	1.57 (1.44–1.72)
Females						
Any rhythm abnormality	882/751 220	1.17 (1.10–1.25)	2711/793 439	3.42 (3.29–3.55)	2313/317 153	7.29 (7.00–7.60)
Atrial fibrillations	436/755 816	0.58 (0.52–0.63)	1729/802 058	2.16 (2.06–2.26)	1637/322 852	5.07 (4.83–5.32)
Bradyarrhythmias	119/758 041	0.16 (0.13–0.19)	402/811 266	0.50 (0.45–0.55)	435/331 810	1.31 (1.19–1.44)
Conduction system diseases	187/758 159	0.25 (0.21–0.28)	565/811 413	0.70 (0.64–0.76)	502/332 227	1.51 (1.38–1.65)
Supraventricular arrhythmias	234/756 442	0.31 (0.27–0.35)	391/810 122	0.48 (0.44–0.53)	241/332 415	0.72 (0.64–0.82)
Ventricular arrhythmias	145/75 6403	0.20 (0.17–0.23)	296/810 065	0.38 (0.34–0.42)	177/332 339	0.53 (0.46–0.61)

CI indicates confidence interval.

and factors related to structural heart disease, including hypertension, coronary artery disease, and heart failure predominating. Chronic obstructive pulmonary disease also appeared to be associated with increased risk of rhythm abnormalities in general, whereas sleep apnea appeared to be most significantly related to atrial fibrillation and supraventricular arrhythmias.[25] Consistent with other studies, white race was associated with atrial fibrillation.[26] Our risk factor analysis also suggests that supraventricular arrhythmias may have a distinct risk factor profile and may be less influenced by sex, hypertension, or coronary artery disease.[27]

Our results also implicate an important role for lifestyle factors in the development of rhythm abnormalities. For example, frequent alcohol consumption (generally defined as daily or almost daily drinking) was associated with increased risk of atrial fibrillation but was not associated with other rhythm condition subtypes.[28] Our findings highlight an association between current smoking and ventricular arrhythmias. Some data suggest that tobacco use may result directly in abnormal repolarization and arrhythmogenesis.[29] Further studies investigating the role of other lifestyle variables, including diet and exercise, may further clarify the relationships between modifiable risk factors and abnormalities of cardiac rhythm.

Our study should be interpreted in the context of the study design. First, although our study was based on a large and prospective cohort, the findings may not be generalizable to all populations owing to methods of enrollment and geographic specificity. The UK Biobank excluded younger adults and children and included healthier and less socioeconomically deprived individuals who were predominantly white and living in the United Kingdom.[13,14] Nevertheless, the frequencies of rhythm abnormalities we observed were consistent with previous findings.[6,20,21] Second, although our phenotype definitions were similar to those used in other large cohort studies,[30] the partial reliance on hospital diagnosis codes for ascertainment of exposures and outcomes introduces some inherent misclassification into our analysis and limits our ability to verify the clinical significance of the conditions. Manual adjudication of charts in an independent ambulatory sample using our rhythm abnormality definitions revealed high positive predictive values despite the facts that the samples are from different continents and healthcare systems, and traditional cardiac risk factors were more prevalent in the validation set. Third, follow-up in the cohort is currently limited, precluding our ability to estimate long-term risks of rhythm abnormalities. Fourth, some rhythm abnormalities included in our study may confer limited clinical significance. However, a sensitivity analysis restricted to abnormalities with highest clinical relevance demonstrated similar prevalence and incidence rates. Fifth, lack of granular data on alcohol and tobacco use limits our ability to precisely quantify the effects of these substances on development of rhythm abnormalities. Sixth, our observational study describes factors associated with incident rhythm abnormalities, but we cannot exclude residual confounding and cannot establish causal relations.

Figure 2. Multivariable associations among clinical risk factors and incident rhythm abnormalities.
Plot depicting multivariable associations between baseline clinical factors and incident rhythm abnormalities. Green shades indicate hazard ratios <1 while red shades indicate hazard ratios ≥1. Intensity of shade is proportional to the magnitude of effect. Grayed cells indicate nonsignificant associations. Because of exclusion of participants with missing data, or prevalent rhythm conditions from incident analyses, the number of participants included in each model varied (485 129 for any arrhythmia, 489 194 for atrial fibrillation, 494 652 for bradyarrhythmias, 495 356 for conduction system disease, 494 796 for supraventricular arrhythmias, and 495 620 for ventricular arrhythmias).

In summary, we estimated the frequency of cardiac rhythm abnormalities in a large prospective cohort including >500 000 community-dwelling middle-aged and older adults. The frequency of rhythm abnormalities in the UK population is substantial and comparable to rates of incident stroke, acute myocardial infarction, and heart failure. The majority of rhythm abnormalities are comprised atrial fibrillation, bradyarrhythmias, and conduction system diseases. Future efforts to quantify the aggregate morbidity and economic costs attributable to abnormalities of cardiac rhythm will enable a broader understanding of the total public health burden imposed by these common conditions.

ARTICLE INFORMATION

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