Association of household income and adverse outcomes in patients with atrial fibrillation

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ABSTRACT
Background Social determinants of health are relevant to cardiovascular outcomes but have had limited examination in atrial fibrillation (AF).

Objectives The purpose of this study was to examine the association of annual household income and cardiovascular outcomes in individuals with AF.

Methods We analysed administrative claims for individuals with AF from 2009 to 2015 captured by a health claims database. We categorised estimates of annual household income as <$40 000; $40–$59 999; $60–$74 999; $75–$99 999; and ≥$100 000. Covariates included demographics, education, cardiovascular disease risk factors, comorbid conditions and antiagulation. We examined event rates by income category and in multivariable-adjusted models in reference to the highest income category (≥$100 000).

Results Our analysis included 336 736 individuals (age 72.7±11.9 years; 44.5% women; 82.6% white, 8.4% black, 7.0% Hispanic and 2.1% Asian) with AF followed for median (25th and 75th percentile) of 1.5 (95% CI 0.6 to 3.0) years. We observed an inverse association between income and heart failure and myocardial infarction (MI) with evidence of progressive risk across decreased income categories. Individuals with household income <$40 000 had the greatest risk for heart failure (HR 1.17; 95% CI 1.05 to 1.30) and MI (HR 1.18; 95% CI 0.98 to 1.41) compared with those with income ≥$100 000.

Conclusions We identified an association between lower household income and adverse outcomes in a large cohort of individuals with AF. Our findings support consideration of income in the evaluation of cardiovascular risk in individuals with AF.

INTRODUCTION
Atrial fibrillation (AF) is a common, highly morbid cardiac arrhythmia that is associated with multiple cardiovascular and non-cardiovascular complications. AF results in significant social and medical burdens and accounts for $6 billion in annual US healthcare spending. Care for AF is complex and requires adequate social resources and health literacy to monitor for symptoms, navigate and adhere to complicated medication regimens (such as antiagulation) and coordinate primary and specialty care services.

Social determinants of health are relevant to AF given their potential to affect treatment and associated outcomes. To date, the foremost focus of social determinants in AF has been on race. Studies have underscored racial differences in treatment, awareness of the condition and risk for adverse outcomes. In a community-based study, income has likewise been related to increased risk of developing AF. Median neighbourhood income has also been positively associated with access to direct oral antiagulants (as opposed to warfarin).

Additional social determinants of health, such as neighborhood-level and community-level factors and healthcare access, likewise have relevance to health outcomes and may mediate associations between income and health outcomes in AF. Examination of the interaction of race and income in AF remains limited and may demonstrate how interrelated social factors contribute towards adverse outcomes and thereby direct treatment efforts.

We investigated the association of household income and cardiovascular outcomes in individuals with AF. We used a database of deidentified, aggregated commercial and Medicare Advantage health claims, thereby enabling us to conduct our analysis in a large, socially diverse cohort with enhanced generalisability. Our primary hypothesis was that lower income would be associated with increased risks of heart failure, myocardial infarction and stroke in this large cohort of individuals with AF. Our secondary hypothesis was that lower income would be a stronger risk factor for adverse outcomes in racial and ethnic minorities compared with white referents.

METHODS
Cohort selection
We obtained data from Optum Clinformatics Data Mart (Eden Prairie, Minnesota, www.optum.com), a large US database composed of inpatient, outpatient, emergency department, pharmacy and laboratory health claims. Data are deidentified, and informed consent is thereby waived. Medical claims include International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes; Current Procedural Terminology, Version 4 procedure codes; HealthCare Common Procedure Coding System procedure codes; and site of service codes. The database includes commercial and Medicare Advantage enrollees and is geographically diverse across the USA and similar to the insured population. Patients

or the public were not involved in the design, or conduct, or reporting, or dissemination of our research.

We selected individuals having a diagnosis of AF during the period of 1 January 2009–30 September 2015. AF was defined by the presence of at least one inpatient or two outpatient claims for AF (ICD-9-CM 427.31 or 427.32 in any diagnostic position). We required two outpatient claims in order to minimise the impact of rule-out diagnoses and improve the specificity of our definition of AF; this restriction is not applied to inpatient claims, which have greater specificity for the diagnosis of AF. This approach has been validated elsewhere.9 Outpatient AF diagnostic codes were temporally separated by a minimum of 1 week to a maximum of 1 year. Date of diagnosis (first in-patient claim or second out-patient claim) was defined as the date of study entry for time-dependent analyses. We used the second outpatient claim of AF to preclude the immortal time bias inherent to initiating analysis at the first date of AF diagnosis. We identified 727 935 individuals with a diagnosis of AF.

Household income
Household income was derived by AmeriLINK Consumer Marketing Database, which provides estimates of annual household income. Income data are collected by monthly survey from a representative cross section of the US population of >30 000 households and are informed by 130 variables that encompass ZIP +4 (a highly specific geographic locator), Internal Revenue Service data, address-level home value, aggregated credit and short-term loans. Derived estimates of household income are validated by comparison to self-reported income collected by household surveys.10 The claims database divides household income into six categories: <$40 000, $40–$49 999, $50–$59 999, $60–$74 999, $75–$99 999 and ≥$100 000. For this analysis, we categorised income as <$40 000; $40–$49 999; $50–$59 999; $60–$74 999; $75–$99 999; and ≥$100 000. We combined the analysis, we categorised income as <$40 000; $40–$49 999; $50–$59 999; $60–$74 999; $75–$99 999; and ≥$100 000. We combined the income ≥$100 000 as the highest income category for those endpoints in which we found associations. The E-Commerce Marketing Database, which provides estimates of annual household income. We then examined associations of income with myocardial infarction, heart failure and ischaemic stroke in individuals with AF. Date of AF diagnosis was defined as time 0, and time of study entry for each individual was included in our cohort. We calculated the rates of incident events during follow-up through database disenrolment or 30 September 2015, whichever came first. We then examined associations of income with myocardial infarction, heart failure and ischaemic stroke in multivariable-adjusted Cox proportional hazards models that compared risk by income category using income ≥$100 000 as the referent. For each outcome assessed, we excluded the respective prevalent disease. We then examined for interactions by race and ethnicity as well as for income and education. All analyses were adjusted initially for age, sex and race (model 1); then for age, sex, race, education, hypertension, diabetes, ischaemic stroke, coronary heart disease and heart failure (model 2); and then adjusted for all covariates including age, sex, race, education, hypertension, diabetes, ischaemic stroke, coronary heart disease, heart failure, chronic obstructive pulmonary disease and chronic kidney disease as well as oral anticoagulant use (model 3). We stratified individuals by race and ethnicity to assess for differences in risk by income level to investigate differences by race and ethnicity strata.

We verified the assumption of proportional hazards with Schoenfeld residuals. All statistical analyses were performed using SAS V.9.4. Given the potential for residual confounding in our analysis, we conducted a bias analysis using the methods articulated by VanderWeele and Ding.17 Specifically, we calculated the E-value for the HRs obtained comparing the lowest to the highest income category for those endpoints in which we found associations. The E-value can be interpreted as the minimum strength of association that an unmeasured confounder would need to have with both the exposure and the outcome, after adjusting for the measured covariates, to explain away an observed association.17

RESULTS
After excluding individuals with <180 days of enrolment before a diagnosis of AF (n = 3 12 958), and those missing income (n = 66

Person-centred long-term care
822), race or ethnicity (n=11 130), or education (n=289), there were 336 736 individuals included in the analysis (mean age 72.7±11.9 years; 44.5% women), as summarised in Table 1.

The majority were white race (82.6%) with 28 286 (8.4%) black, 23 510 (7.0%) Hispanic and 6976 (2.1%) Asian. Education was likewise distributed by income category. With increasing income category, event rates decreased with respect to myocardial infarction, heart failure and stroke.

Table 1 summarises the HRs with p values for the trend of the associations of income with each of the cardiovascular outcomes, while figure 1 presents them graphically. We observed a graded, inverse association between income and the risks for heart failure and myocardial infarction. Individuals in the lowest income category had the greatest risk for heart failure with a HR of 1.17 (95% CI 1.05 to 1.30) and myocardial infarction with an HR of 1.18 (95% CI 1.08 to 1.41) relative to the highest income category. The association between income and heart failure remained significant in the lowest income category after multivariable adjustment with the clinical covariates, oral anticoagulant use and education. We did not observe an association between income and ischaemic stroke.

Interactions for race/ethnicity and income and for income and education were not statistically significant in multivariable-adjusted models. The results of analyses stratified by race and ethnicity are presented in online supplementary table 2A and 2D. Our bias assessment identified an E-value of 2.17 (CI, lower limit, 1.88) for the association between extreme income categories.

Table 3 presents them graphically.

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Table 2 Age-standardised, sex-standardised and race-standardised incidence rates and 95% CIs (per 1000 person-years) of cardiovascular disease (heart failure, myocardial infarction and ischaemic stroke) by income categories

<table>
<thead>
<tr>
<th>Income</th>
<th>&lt;$40 000</th>
<th>$40–$59 000</th>
<th>$60–$74 000</th>
<th>$75–$99 000</th>
<th>≥$100 000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure*</td>
<td>5.4 (4.2 to 6.6)</td>
<td>4.1 (3.5 to 4.6)</td>
<td>3.4 (2.7 to 4.0)</td>
<td>3.1 (2.7 to 3.6)</td>
<td>3.0 (2.4 to 3.5)</td>
</tr>
<tr>
<td>Myocardial infarction†</td>
<td>2.1 (1.6 to 2.7)</td>
<td>1.9 (1.5 to 2.4)</td>
<td>1.4 (1.0 to 1.9)</td>
<td>1.4 (1.0 to 1.7)</td>
<td>1.6 (1.0 to 1.5)</td>
</tr>
<tr>
<td>Stroke‡</td>
<td>3.2 (2.2 to 4.2)</td>
<td>2.5 (2.0 to 3.0)</td>
<td>2.3 (1.9 to 2.7)</td>
<td>2.1 (1.8 to 2.4)</td>
<td>2.3 (2.0 to 2.6)</td>
</tr>
</tbody>
</table>

*Prevalent heart failure was excluded from model 3 when calculating incident heart failure.
†Prevalent coronary heart disease was excluded from model 3 when calculating incident myocardial infarction.
‡Prevalent ischaemic stroke was excluded from model 3 when calculating incident ischaemic stroke.
and heart failure in model 1, and an E-value of 2.04 (CI, lower limit, 1.54) for the association between extreme income categories and myocardial infarction in Model 1. We concluded from these calculations that potential unmeasured confounders, such as neighbourhood SES or racial segregation, have weaker associations with the endpoints of interest and therefore are unlikely to be responsible for the observed associations.18 19

**DISCUSSION**

In a large, geographically diverse health claims database, we observed associations between annual income and increased risk of heart failure and myocardial infarction in individuals with incident AF. Specifically, we observed progressively increased risk for these adverse cardiovascular outcomes, such that individuals with income categorised as < $40 000/year had the greatest risk. The association of lower household income and the increased risk of heart failure remained significant even after multivariable adjustment. These findings were observed over a relatively limited follow-up duration (median 1.5 years).

There was no association between income and risk of ischaemic stroke in the cohort as a whole. Lack of an association may be due to the relatively limited follow-up duration in this study and/or the similar prevalence of anticoagulant prescriptions across income categories.

**Prior study of income in relation to AF and cardiovascular disease**

The examination of income and AF has had limited study with one community-based study identifying a graded, inverse, dose-response association between total family income and risk of incident AF.20 In contrast, the association of income with cardiovascular outcomes and mortality has been well established. Total family income has been inversely associated with cardiovascular disease and cardiovascular death in multiple studies and was deemed a ‘neglected’ metric for cardiovascular disease.21–22 An analysis of the National Longitudinal Mortality Study identified a strong association between income and mortality that was most pronounced at incomes below $22 500.23 Income has further relevance to longevity. Robust data indicate a strong linear association between income and length of life in US adults.24 The aforementioned studies indicate the relevance of income to health outcomes including cardiovascular disease and mortality. Our study now contributes further data on the importance of income, specifically towards the associations of income and health outcomes directly relevant to the increasing number of people with AF.

**Rationale for the association of income and health outcomes**

Multiple potential pathways have been proposed to relate income and health. The sociocological theory asserts that health is shaped by multiple factors: social, family and community networks; living and working conditions; and broad social, economic, cultural and environmental conditions and policies.25 Low income as determined by socioeconomic status has been associated in general with diminished access to preventative care,26 specialty care27 and poorer clinical outcomes.28 Low socioeconomic status yields decreased access to prescription medications29 and may contribute towards competing priorities for using health services, medications and diverse other needs. Low income may complicate adherence to medications or appointments, as individuals struggle to choose between material necessities and medical care. Furthermore, limited health literacy is more prevalent in lower income individuals and likewise may add to the heterogeneous contributions of social determinants on complicated chronic disease such as AF.2 This study demonstrates an important association between income and cardiovascular disease in AF and we recognise that further research is needed to understand the complex pathways by which patients with low income and AF develop adverse outcomes.

**Relevance of social determinants to clinical care and practice**

Recognising that social determinants are associated with health outcomes, there has been increased focus on their incorporation into routine clinical care. The National Academy of Medicine has recommended inclusion of social and behavioural determinants in electronic health records due to the ‘substantial
Our analysis indicates the substantive contribution of income towards adversity and its prominent role as a social determinant of health. Our study is unable to distinguish the multiple mechanisms and pathways that may relate income and adverse cardiovascular outcomes; however, our findings underscore the importance of further studies to examine the practical implications of using income in routine clinical assessment with the goal of identifying and effectively intervening on high-risk patient populations. Collecting and using income data as one component of a risk stratification tool that incorporates a suite of social determinants of health in the clinical setting may be of interest to clinicians seeking to identify and intervene on vulnerable patients, health systems attempting to improve the outcomes of populations and health plans seeking to provide high value, cost conscious care.

Strengths and limitations

Our analysis had several strengths, most particularly the availability of nationwide health claims data from over 300,000 individuals diagnosed with AF. The generalisability of our analysis to insured persons with AF is strengthened by the utilisation of a database that is geographically diverse and racially representative as well as inclusive of enrollees of both private and Medicare advantage plans.

We would also like to summarise the important limitations of our study. First, inclusion in this cohort required that individuals have health insurance, thereby allowing health claims data to be captured. Consequently, the exclusion of a highly vulnerable patient population may underestimate the effect of income on adverse cardiovascular outcomes in individuals with AF and may not be generalisable to the uninsured population. Second, using claims data selects for individuals with AF who are more often in need of medical care, thereby limiting the generalisability to individuals with AF who do not seek care and do not generate health claims. Third, requiring two outpatient claims for AF was intended to increase specificity of the diagnostic algorithm but excluding individuals with only one outpatient claim may have selected for individuals with more symptomatic AF, again limiting the generalisability of our results to patients with asymptomatic paroxysmal AF. Fourth, we relied exclusively on health claims for ascertainment of AF, covariates and the cardiovascular outcomes; however, our assessment for uncontrolled confounding suggested that only a strong unmeasured confounder associated with AF. However, our assessment for uncontrolled confounding suggested that only a strong unmeasured confounder (E-value >2) would be able to explain the observed associations. Seventh, our follow-up time for this study was limited to a median of 1.5 years. We expect that a longer study interval would have yielded more events to include in the analysis. The limited follow-up time also allows for the potential of reverse causation. Eighth, our analyses do not account for the effect of AF treatment during the observation period. However, we included prescription of oral anticoagulation for stroke prevention as a fundamental metric of routine clinical care for AF. Finally, we recognise our categorisation of income as limited. The measurement of income is complex and may be adjusted for family size, the addition of non-cash benefits such as food stamps or Medicare or broadened to include wealth and assets that are separate from income.


Figure 1: A–C: HRs with 95% CIs of incident heart failure, myocardial infarction and ischaemic stroke by income category and adjusted for covariates in cohort with AF. Figure parts A–C are forest plots of multivariable-adjusted HRs with 95% CIs of incident cardiovascular outcomes heart failure, myocardial infarction and ischaemic stroke by income category. Incident event rates were calculated and related to income in multivariable-adjusted Cox proportional hazard models that compared risk by income category with income >$100,000 as referent. Model 1: adjusted for age, sex and race; model 2: adjusted for age, sex, race, education, hypertension, diabetes, prevalent coronary heart disease and prevalent heart failure; model 3: adjusted for age, sex, race, education, hypertension, diabetes, prevalent coronary heart disease, prevalent heart failure, chronic obstructive pulmonary disease, chronic kidney disease and oral anticoagulant use. (A) Heart failure by income category; (B) myocardial infarction by income category; (C) ischaemic stroke by income category adjusted for the three models. AF, atrial fibrillation.
CONCLUSION

In conclusion, in a retrospective analysis of a large US health-care utilisation database, we observed a significant association between income and risk of cardiovascular outcomes relevant to AF, specifically heart failure and myocardial infarction. Our results are consistent with prior evidence that underscores the relevance of income to increased risk for cardiovascular and health outcomes. Further study must now address how to incorporate data regarding income into the treatment of patients with AF to improve cardiovascular outcomes and mitigate adverse outcomes in vulnerable patient populations.

REFERENCES


