



Published in final edited form as:

Int J Cardiol. 2016 January 1; 202: 776–781. doi:10.1016/j.ijcard.2015.09.027.

Neighbourhood socio-economic status and all-cause mortality in adults with atrial fibrillation: a cohort study of patients treated in primary care in Sweden

Per Wändell^{1,2,*}, Axel C Carlsson^{1,3}, Danijela Gasevic⁴, Jan Sundquist^{5,6}, and Kristina Sundquist^{5,6}

¹ Division of Family Medicine, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Huddinge, Sweden

²Academic Primary Healthcare Centre, Stockholm County Council, Huddinge, Sweden

³ Department of Medical Sciences, Molecular Epidemiology and Science for Life Laboratory, Uppsala University, Uppsala, Sweden

⁴Centre for Population Health Sciences, College of Medicine and Veterinary Medicine, University of Edinburgh, Edinburgh, UK

⁵ Center for Primary Health Care Research, Lund University, Malmö, Sweden

⁶ Stanford Prevention Research Center, Stanford University School of Medicine, Palo Alto, California, USA

Abstract

Objective—Our aim was to study potential impact of neighbourhood socio-economic status (SES) on all-cause mortality in atrial fibrillation (AF) patients treated in primary care.

Methods—Study population includes adults (n=12,283) of 45 years and older diagnosed with AF in 75 primary care centres in Sweden. Association between neighbourhood SES and all-cause mortality was explored using Cox regression analysis, with hazard ratios (HRs) and 95% confidence intervals (95% CIs); and by Laplace regression where years to death (95% CI) of the first 10% of the participants were used as an outcome. All models were conducted in both men and women and adjusted for age, educational level, marital status, change of neighborhood status, cardiovascular co-morbidities, anticoagulant treatment and statin treatment. High- and low-neighbourhood SES were compared with middle SES as reference group.

Results—After adjustments for potential confounders, higher relative risk of all-cause mortality (HR 1.49, 95% CI 1.13-1.96) was observed in men living in low SES neighborhoods compared to

*Corresponding author Address: Division of Family Medicine, Dpt NVS, Karolinska Institutet, Alfred Nobels Allé 12, S-141 83 Huddinge, Sweden, Phone: +, Fax: +46-8-52488706, per.wandell@ki.se.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Disclosures

The authors have no conflict of interest to disclose.

those from middle SES neighbourhoods. The results were confirmed using Laplace regression; the time until the first 10% of the men in low SES neighbourhoods died was 1.45 (95% CI 0.48-2.42) years shorter than for the men in middle SES neighbourhoods.

Conclusions—Increased rates of heart disease and subsequent mortality among adults in deprived neighbourhoods raises important clinical and public health concerns. These findings could serve as an aid to policy-makers when allocating resources in primary health care settings as well as to clinicians who encounter patients in deprived neighbourhoods.

Keywords

Neighbourhood; atrial fibrillation; mortality; gender; follow-up; co-morbidity; antithrombotic drugs

1. Introduction

Atrial fibrillation (AF) is the most common form of arrhythmia in humans, and, if left untreated, it is associated with significant morbidity, especially from stroke [1, 2]. The prevalence of atrial fibrillation is about 2% in the Swedish population [3]. The lifetime risk to develop atrial fibrillation from 40 years of age and older, around one out of four, is similar for men and women [4]. However, men have a 1.5-fold higher risk of developing atrial fibrillation compared to women, when adjusted for age and predisposing conditions [5]. Adjusting for age is important, since men develop atrial fibrillation around five years earlier than women do [6].

Patients with atrial fibrillation are found to have an excess mortality compared to individuals without atrial fibrillation [7]. The excess mortality is 50% higher in men and 100% higher in women [8]. The higher mortality risk in women may partly be explained by a higher risk for stroke than in men [7].

Many atrial fibrillation patients in Sweden receive medical care at primary health care centres, and in Stockholm County, 64% of the atrial fibrillation patients had an AF diagnosis registered in primary care [3]. We have previously investigated mortality among Swedish men and women with atrial fibrillation in primary care, and observed a decreased mortality related to treatment with certain cardio-vascular drugs, especially anticoagulants [9]. Among medications, anticoagulant treatment plays a significant role [10], not only in stroke-prevention but also in preventing myocardial infarction [11], and decreasing mortality [12].

In addition to individual factors, such as age, gender and other predisposing conditions for atrial fibrillation, it is also important to consider the potential impact of environmental factors on atrial fibrillation. For example, neighbourhood SES has been found to be associated with overall health [13], cardiovascular health [14, 15], and all-cause mortality [16, 17]. A previous study found an association between neighbourhood SES and hospitalization of atrial fibrillation patients in women that no longer remained significant after adjustment for individual factors [18]. However, no studies to date have described the possible association between neighbourhood SES and mortality in atrial fibrillation patients. Herein, the objective of our study was to explore the potential effect of neighbourhood SES

on all-cause mortality in men and women diagnosed with atrial fibrillation and to evaluate whether this relationship is independent of factors known to influence mortality in atrial fibrillation, such as age, cardiovascular co-morbidities, as well as marital status and educational level. We hypothesize that all-cause mortality among patients with atrial fibrillation is higher in neighbourhoods with lower SES than in neighbourhoods with higher SES and that this is independent of potential confounders.

2. Methods

2.1 Design

This study was performed using individual-level patient data from 75 Swedish primary health care centers (PHCC). The majority was located in Stockholm County (n=48). Men and women visiting any of the participating PHCCs between 2001 and 2007 were included in the study. We used *Extractor* software (http://www.sll.se/SLPOtemplates/SLPOPage1___10400.aspx; accessed September 19, 2010) to collect individual files from the electronic patient records (EPR) at the PHCCs. Individual identification numbers were replaced by serial numbers to ensure anonymity. The EPR files were linked to a database constructed using Swedish national registers.[19] The registers used were: The Total Population register (which contains data on, e.g., age and education for the entire population of Sweden); The Inpatient Register (hospital admissions); and The Cause of Death Register. These registers contain individual-level population data for all residents registered in Sweden. Thus, a new research database was created, containing individual clinical patient data from a total of 1,098,420 subjects registered at these 75 PHCCs, linked to national demographic and socioeconomic data. Follow-up was performed using the Swedish Cause of Death Register, which has been shown to be almost complete, 99.8%, and lacking data only for a few emigrants from Sweden to other countries and thus lost to follow-up [20].

2.2 Study population and co-morbidities

The study included all patients with diagnosed atrial fibrillation, identified by the presence of the ICD-10 code (10th version of the WHO's International Classification of Diseases) for atrial fibrillation (I48) in patients' medical records. The following related cardiovascular disorders were used as covariates: hypertension (I10-15), coronary heart disease (CHD; I20-25), cardiac heart failure (CHF; I50 and I110), non-rheumatic valvular diseases (I34-38), cardiomyopathy (I42), cerebrovascular diseases (CVD; I60-69), including intracranial bleedings (I60-62), and peripheral embolism (I74). In addition, presence of diabetes mellitus (E10-14) was also recorded. In total, 6,646 men and 5,637 women 45 years of age at the time of atrial fibrillation diagnosis who visited any of the 75 participating PHCCs from 1 January 2001 until 31 December 2007 and with data on neighborhood socioeconomic status were included in the study [9].

2.3 Outcome variable

Time to death during the assessment period (from registration of the atrial fibrillation diagnosis to December 31, 2007).

2.4 Demographic and socio-economic variables

Sex: Men and women.

Age was categorized as follows: 45–54, 55–64, 65–74, 75–84 and 85 years. Individuals younger than 45 years were excluded (atrial fibrillation was rare in individuals below 45 years of age and non-representative of atrial fibrillation patients in general).

Educational attainment was categorized as 9 years (partial or complete compulsory schooling), 10–12 years (partial or complete secondary schooling) and >12 years (attendance at college and/or university).

2.5 Neighbourhood socio-economic status

The neighbourhoods were derived from Small Area Market Statistics (SAMS), which were originally created for commercial purposes and pertain to small geographic areas with boundaries defined by homogenous types of buildings. The average population in each SAMS neighbourhood is approximately 2000 people for Stockholm and 1000 people for the rest of Sweden. A summary index was calculated to characterise neighbourhood-level deprivation. The neighbourhood index was based on information about female and male residents aged 20 to 64 years because this age group represents those who are among the most socioeconomically active in the population (i.e., a group that has a stronger impact on the socioeconomic structure in the neighbourhood compared to children, younger women and men, and retirees). The index was based on the following four variables: low educational status (<10 years of formal education); income from all sources, including interest and dividends, that is <50% of the median individual income); unemployment (excluding full-time students, those completing military service, and early retirees); and receipt of social welfare. The index was categorized into three groups: more than one standard deviation (SD) below the mean (high SES or low deprivation level), more than one SD above the mean (low SES or high deprivation level), and within one SD of the mean (middle SES or deprivation level), [15] with neighbourhood status classified as high, middle or low SES, or on low, middle and high deprivation index [18].

2.6 Statistical analysis

Baseline subject characteristics across neighbourhood SES were presented as mean (SD) if continuous and as frequencies if categorical, and differences were calculated by ANOVA or chi-square test. Test for trends was performed by Cuzick's non-parametric test. The potential effects of neighbourhood SES on mortality in adults diagnosed with atrial fibrillation were evaluated using Cox-proportional hazards modelling. Before running the regression models, variables were tested for interactions. The only significant one was between age and diabetes in men ($p=0.041$), which we added to the models. The following four models were created: 1) Model A: neighbourhood SES (high, middle or low) and age group; 2) Model B: Model A and educational attainment (compulsory school, secondary school or college/university) and marital status (married, unmarried, divorced or widowed); 3) Model C: Model B and change of residence according to neighbourhood status (higher to lower, lower to higher, or no change of neighbourhood SES level), as well as comorbidities (hypertension, coronary heart disease, heart failure, cerebrovascular disease and diabetes)

and possible interaction terms (only age group x diabetes for men); and 4) Model D: Model C and prescribed anticoagulant treatment and statins. The effects of neighbourhood SES on mortality were also assessed by Laplace regression by applying the same models as described above. Laplace regression was used to calculate the difference in years until death of the first 10% of the participants in the different socio-economic neighborhood groups, using the middle group as reference.[21, 22] Since different distributions and mathematical calculations are used to obtain results in Cox and Laplace regression, respectively, putting emphasis on findings significant with both methods may reduce the risk of chance findings. [23] Analyses were performed separately for men and women. *P*-values of <0.05 were considered statistically significant. The study was approved by the regional ethics boards at Karolinska Institutet and Lund University.

3. Results

The mean follow-up time was 3.5 years (standard deviation 2.1) and the median follow-up time 3.5 years (95% CI 3.5-3.5; interquartile range 1.5-5.5). The calculated hazard ratios were based on a total of 42,907 person-years at risk, 23,234 person-years among men and 19,673 among women. A total of 701 men and 744 women died during follow-up, 10.5% vs. 13.2% ($p < 0.001$). Many men and women changed their place of residence during the follow-up. Some moved from neighbourhoods of higher to those of lower SES (men 1,861 (28.0%) and women 1,564 (27.8%)); and others moved from lower SES neighbourhoods to higher SES neighbourhoods (men 712 (10.7%) and women 625 (11.1%)). The remaining 4,073 (61.3%) men and 3,448 (61.2%) women did not change their place of residence during the study.

Table 1 presents the characteristics of the 6,646 men and 5,637 women included in the study. In men and women, percent of individuals being married, and those with higher levels of formal education increased when neighbourhood SES increased. Furthermore, rates of unmarried and divorced men decreased when neighbourhood SES increased. In contrast, the prevalence of comorbidities including hypertension, coronary heart disease, heart failure and diabetes decreased when neighbourhood SES increased.

The potential effects of neighbourhood SES on all-cause mortality are presented in Table 2 (Cox proportional-hazards regression models), and Table 3 (Laplace regression models). After adjustment for age group, educational level, marital status, change of neighborhood status, and cardiovascular co-morbidity, a higher relative risk of all-cause mortality (HR 1.49, 95% CI 1.13-1.96) was observed in men living in low SES neighborhoods compared to those from middle SES neighbourhoods (Table 2). The potential effects of neighbourhood deprivation on all-cause mortality was slightly attenuated after adjustment for prescription of anticoagulants and statins, but remained statistically significant (HR 1.39, 95% CI 1.05-1.83). The higher mortality in low SES neighborhoods was confirmed using Laplace regression; the time until the first 10% of the men in low SES neighbourhoods died was 1.45 (95% CI 0.48-2.42) years shorter than for the men in middle SES neighbourhoods (Table 3). Among women, Cox regression was significant in Model D when adjusting for all potential confounders (including prescription of anticoagulants and statins) with an OR of 1.25 (95% CI 1.01-1.56) for high SES neighbourhoods, but not in the Laplace regression models.

4. Discussion

This study explored the potential effects of neighbourhood SES on all-cause mortality in patients with atrial fibrillation. The results of the study indicate higher all-cause mortality in men living in low SES neighbourhoods compared to their counterparts from middle SES neighbourhoods. This was independent of individual socio-demographic characteristics, presence of comorbidities, change of place of residence over the time of the study and antithrombotic and statin treatment. The relationship between neighbourhood SES and all-cause mortality was statistically significant among women only in the Cox regression model when adjusting for all confounders, including prescription of anticoagulants and statins, with higher all-cause mortality in high SES neighbourhoods, however, not confirmed in the Laplace regression model.

Low neighbourhood SES is shown to predict all-cause mortality [16, 17, 24], mortality after myocardial infarction [25], and the risk of mortality among adults with cancers [26]. The results of our study extend the above-mentioned findings by reporting the effects of neighbourhood deprivation on all-cause mortality among patients with atrial fibrillation. The findings of the study indicate that the potential effects of neighbourhood SES are independent of socio-demographic characteristics, comorbidities and anticoagulant therapy, and suggest that there potentially are some other mechanisms by which neighbourhood SES drives mortality among men with AF. It has been suggested that the relationship between neighbourhood SES and all-cause mortality may be influenced by the regional context; however, the results of a recent Scottish study indicate no spatial heterogeneity in the relationship between neighbourhood deprivation and mortality [27]. Living in low SES neighbourhoods has been shown to be associated with an increased morbidity risk [28, 29], such as that of hypertension [30], CHD [15], CHF [31], and diabetes [32]. In our study, we observed that rates of these comorbidities increased with a decrease of neighbourhood SES. Differences in healthy lifestyles are important factors to consider behind the increased risk of morbidity and mortality, and attitudes and beliefs about these differ across SES levels [33]. Individuals living in low SES neighbourhoods are shown to have significantly lower health knowledge and a lower probability of positive behaviour changes than individuals in middle SES neighbourhoods [34]. Besides, living in a low SES neighbourhood is also associated with an earlier onset of multi-morbidity [35]. Furthermore, the individuals residing in a low SES neighborhood are also shown to experience feelings of inferiority and self-doubt as a consequence of the lower social status [36-38]. Another factor is the financial stress [39], as residents in these neighborhoods have less money to spend, as a part of the general psychosocial stress [40]. Allostatic load is a concept related to stress, with allostasis being the physiological stress response to acute stress [41-43]. The allostatic load is connected with the development of cardiovascular risk factors [44], such as increased level of catecholamines and non-normal cortisol levels, connected to increase of blood pressure and blood lipids, as well as poor glycemic control and increase in abdominal obesity [45, 46]. Furthermore, high allostatic load is also related to lower self-rated health [46].

We have good explanations to the different patterns found among men and women, with a higher mortality and lower survival among men with AF living in low SES neighbourhoods, which contrast an increased mortality among women with AF living in high SES

neighbourhoods. However, as a higher mortality among women living in high SES neighbourhoods was found in the Cox regression, but not in the Laplace regression, the results should be interpreted with some caution. We have earlier found more favourable patterns for prescription of warfarin and statins among men and women in high SES neighbourhoods, and less favourable among men and women in low SES neighbourhoods [47]. There may be other differences of importance among men and women with AF why the observed gender differences warrant further investigation.

Another explanation to the present findings is a lower availability of recommended pharmacotherapies; using the same data in the present study, we recently showed that individuals in high SES neighbourhoods receive warfarin according to guidelines to a higher extent than individuals in low and middle SES neighbourhoods [47]. This was also shown in an Italian study, with both lower prescription rates and lower patient adherence in low SES neighbourhoods [48]. Moreover, statins were more frequently prescribed to AF patients in high SES neighbourhoods than in middle and low SES neighbourhoods [47], which may be of importance since both statins and warfarin have been previously shown to be associated with lower mortality [9, 49, 50]. The findings of these previous studies together with the findings of the present study illuminate the need of improving health in low resource settings, which is underway in Europe [51].

It is important to note that a significant number of individuals changed their place of residence, and neighborhood SES, during the follow-up. Many of them were elderly, and it was to expect that some of them would downsize by moving from their larger house to an apartment, such as in the case of being widowed. We adjusted our analyses for the move of participants to a neighbourhood of differing SES, and the relationship between neighbourhood SES and all-cause mortality remained significant among men.

This study has certain limitations. Data were extracted from primary health care electronic patient records, and some data may be missing from those records. In addition, listings of diagnoses may be incomplete. However, diagnoses of common diseases such as cardiovascular diseases and diabetes could be expected to be more accurate and complete than many other diagnoses.[52] Furthermore, data on disease severity, e.g. NYHA classification of congestive heart failure, were not available. We had no data available on the type of atrial fibrillation (paroxysmal, persistent, permanent) and rhythm (sinus rhythm, fibrillation). Given that our focus was predominantly on cardiovascular co-morbidity and whether the relationship between neighbourhood SES and all-cause mortality is independent of cardiovascular comorbidity, we did not include other potential diagnoses associated with mortality such as presence of cancers, or other non-cardiovascular prescriptions. We also had no information on catheter ablation procedures or Cox-Maze operations. On the other hand, since the variables available in the present study were obtained from primary health care electronic patient records they may be assumed to mirror the information available for the clinician. In addition, we did not have access to multiple measures of individual SES. However, we adjusted our analyses for level of formal education, which is a commonly used proxy for individual SES [53], and the relationship between neighbourhood SES and mortality remained significant after this adjustment. Another important point to be made is that there may be other factors that can influence the relationship between neighbourhood

SES and mortality (Figure 1). For example, many of the traditional CVD risk factors such as blood pressure, lipids, and obesity may mediate the relationship between neighbourhood SES and mortality; however we did not have access to such measures in order to include them in our models. Furthermore, our database does not contain specifics on the number of people per centre or information on local/regional health care resources.

Despite the limitations, one of the key strengths of this study is the linkage of clinical data from individual patients to national demographic and socioeconomic data with less than 1% missing data. The clinical data were also highly complete; less than 2% of the total number of diagnoses were missing [52]. The comprehensive nature of our data made it possible to analyze men and women from all educational backgrounds and marital statuses. Another strength is the sample size of the study, i.e. 6,646 men and 5,637 women, and almost 43,000 person-years at risk analyzed. We also had access to data on change of place of residence, and consequently neighborhood SES, which is important in this sample out of whom the majority was older, and almost 40 % changed their neighborhood SES. Finally, many previous follow-up studies of atrial fibrillation have used data from hospital samples, which could display higher rates of all-cause morbidity and mortality than are found in primary care.

In conclusion, we found an increased mortality risk among men residing in low SES neighbourhoods, which was independent of individual socio-demographics, cardiovascular co-morbidity and anticoagulant and statin therapy. The increased rates of heart disease and subsequent mortality among adults in deprived neighbourhoods raise important clinical and public health concerns. These findings could serve as an aid to policy-makers when allocating resources in primary health care settings. They are also important for clinicians who encounter patients with atrial fibrillation in deprived neighbourhoods. Clinicians should consider that the cardiovascular risk is higher among patients in low SES neighbourhoods, where multi-morbidity is more common [1]. Awareness of the difficulties that may affect adherence to drug therapy and lifestyle recommendations in patients residing in low SES neighbourhoods may warrant more careful follow-up. It is also important that the prescription of effective medications such as anticoagulant drugs and statins follow guidelines that are tailored to the risk of the patient [1, 2].

Acknowledgments

This work was supported by grants to Kristina Sundquist and Jan Sundquist from the Swedish Research Council as well as ALF funding to Jan Sundquist and Kristina Sundquist from Region Skåne.

Research reported in this publication was also supported by the National Heart, Lung, And Blood Institute of the National Institutes of Health under Award Number R01HL116381 to Kristina Sundquist. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health

References

1. Hobbs FR, Taylor CJ, Jan Geersing G, Rutten FH, Brouwer JR. European Primary Care Cardiovascular Society (EPCCS) consensus guidance on stroke prevention in atrial fibrillation (SPAF) in primary care. *Eur J Prev Cardiol.* 2015
2. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr. et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive

summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. *Circulation*. 2014; 130:2071–2104. [PubMed: 24682348]

3. Forslund T, Wettermark B, Wandell P, von Euler M, Hasselstrom J, Hjemdahl P. Risk scoring and thromboprophylactic treatment of patients with atrial fibrillation with and without access to primary healthcare data: experience from the Stockholm health care system. *Int J Cardiol*. 2013; 170:208–214. [PubMed: 24239153]
4. Bajpai A, Savelieva I, Camm AJ. Treatment of atrial fibrillation. *Br Med Bull*. 2008; 88:75–94. [PubMed: 19059992]
5. Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. *Am J Cardiol*. 1998; 82:2N–9N.
6. Humphries KH, Kerr CR, Connolly SJ, Klein G, Boone JA, Green M, et al. New-onset atrial fibrillation: sex differences in presentation, treatment, and outcome. *Circulation*. 2001; 103:2365–2370. [PubMed: 11352885]
7. Michelena HI, Powell BD, Brady PA, Friedman PA, Ezekowitz MD. Gender in atrial fibrillation: Ten years later. *Gend Med*. 2010; 7:206–217. [PubMed: 20638626]
8. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation*. 1998; 98:946–952. [PubMed: 9737513]
9. Wandell P, Carlsson AC, Sundquist K, Johansson SE, Sundquist J. Effect of cardiovascular drug classes on all-cause mortality among atrial fibrillation patients treated in primary care in Sweden: a cohort study. *Eur J Clin Pharmacol*. 2013; 69:279–287. [PubMed: 22990327]
10. Forslund T, Wettermark B, Wandell P, von Euler M, Hasselstrom J, Hjemdahl P. Risks for stroke and bleeding with warfarin or aspirin treatment in patients with atrial fibrillation at different CHA(2)DS(2)VASc scores: experience from the Stockholm region. *Eur J Clin Pharmacol*. 2014; 70:1477–1485. [PubMed: 25219360]
11. Lip GY, Lane DA. Does warfarin for stroke thromboprophylaxis protect against MI in atrial fibrillation patients? *Am J Med*. 2010; 123:785–789. [PubMed: 20655037]
12. Lane DA, Lip GY. Atrial fibrillation and mortality: the impact of antithrombotic therapy. *Eur Heart J*. 2010; 31:2075–2076. [PubMed: 20685675]
13. Diez Roux AV. Investigating neighborhood and area effects on health. *Am J Public Health*. 2001; 91:1783–1789. [PubMed: 11684601]
14. Diez Roux AV, Merkin SS, Arnett D, Chambless L, Massing M, Nieto FJ, et al. Neighborhood of residence and incidence of coronary heart disease. *The New England journal of medicine*. 2001; 345:99–106. [PubMed: 11450679]
15. Winkleby M, Sundquist K, Cubbin C. Inequities in CHD incidence and case fatality by neighborhood deprivation. *Am J Prev Med*. 2007; 32:97–106. [PubMed: 17234484]
16. Nakaya T, Honjo K, Hanibuchi T, Ikeda A, Iso H, Inoue M, et al. Associations of all-cause mortality with census-based neighbourhood deprivation and population density in Japan: a multilevel survival analysis. *PLoS One*. 2014; 9:e97802. [PubMed: 24905731]
17. Ross NA, Oliver LN, Villeneuve PJ. The contribution of neighbourhood material and social deprivation to survival: a 22-year follow-up of more than 500,000 Canadians. *Int J Environ Res Public Health*. 2013; 10:1378–1391. [PubMed: 23549228]
18. Zoller B, Li X, Sundquist J, Sundquist K. Neighbourhood deprivation and hospitalization for atrial fibrillation in Sweden. *Europace*. 2013; 15:1119–1127. [PubMed: 23447572]
19. Sundquist K, Li X. Coronary heart disease risks in first- and second-generation immigrants in Sweden: a follow-up study. *J Intern Med*. 2006; 259:418–427. [PubMed: 16594910]
20. Almgren T, Wilhelmsen L, Samuelsson O, Himmelmann A, Rosengren A, Andersson OK. Diabetes in treated hypertension is common and carries a high cardiovascular risk: results from a 28-year follow-up. *J Hypertens*. 2007; 25:1311–1317. [PubMed: 17563546]
21. Bottai M, Zhang J. Laplace regression with censored data. *Biom J*. 2010; 52:487–503. [PubMed: 20680972]
22. Orsini N, Wolk A, Bottai M. Evaluating percentiles of survival. *Epidemiology*. 2012; 23:770–771. [PubMed: 22872120]

23. Wandell P, Carlsson AC, Sundquist J, Johansson SE, Bottai M, Sundquist K. Effect of cardiovascular drugs on mortality in atrial fibrillation and chronic heart failure. *Scand Cardiovasc J.* 2014; 48:291–298. [PubMed: 25022789]
24. Major JM, Doubeni CA, Freedman ND, Park Y, Lian M, Hollenbeck AR, et al. Neighborhood socioeconomic deprivation and mortality: NIH-AARP diet and health study. *PLoS One.* 2010; 5:e15538. [PubMed: 21124858]
25. Blais C, Hamel D, Rinfret S. Impact of socioeconomic deprivation and area of residence on access to coronary revascularization and mortality after a first acute myocardial infarction in Quebec. *Can J Cardiol.* 2012; 28:169–177. [PubMed: 22200334]
26. Sundquist J, Li X, Sundquist K. Neighborhood deprivation and mortality in individuals with cancer: a multilevel analysis from Sweden. *Eur J Cancer Prev.* 2012; 21:387–394. [PubMed: 22495253]
27. Sridharan S, Koschinsky J, Walker JJ. Does context matter for the relationship between deprivation and all-cause mortality? The West vs. the rest of Scotland. *Int J Health Geogr.* 2011; 10:33. [PubMed: 21569408]
28. James WP, Nelson M, Ralph A, Leather S. Socioeconomic determinants of health. The contribution of nutrition to inequalities in health. *BMJ.* 1997; 314:1545–1549. [PubMed: 9183207]
29. Pickering T. Cardiovascular pathways: socioeconomic status and stress effects on hypertension and cardiovascular function. *Ann N Y Acad Sci.* 1999; 896:262–277. [PubMed: 10681903]
30. Bleich SN, Jarlenski MP, Bell CN, LaVeist TA. Health inequalities: trends, progress, and policy. *Annu Rev Public Health.* 2012; 33:7–40. [PubMed: 22224876]
31. Hawkins NM, Jhund PS, McMurray JJ, Capewell S. Heart failure and socioeconomic status: accumulating evidence of inequality. *Eur J Heart Fail.* 2012; 14:138–146. [PubMed: 22253454]
32. Agardh E, Allebeck P, Hallqvist J, Moradi T, Sidorchuk A. Type 2 diabetes incidence and socio-economic position: a systematic review and meta-analysis. *Int J Epidemiol.* 2011; 40:804–818. [PubMed: 21335614]
33. Wardle J, Steptoe A. Socioeconomic differences in attitudes and beliefs about healthy lifestyles. *J Epidemiol Community Health.* 2003; 57:440–443. [PubMed: 12775791]
34. Cubbin C, Winkleby MA. Protective and harmful effects of neighborhood-level deprivation on individual-level health knowledge, behavior changes, and risk of coronary heart disease. *Am J Epidemiol.* 2005; 162:559–568. [PubMed: 16093286]
35. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet.* 2012; 380:37–43. [PubMed: 22579043]
36. Marmot MG. Status syndrome: a challenge to medicine. *JAMA.* 2006; 295:1304–1307. [PubMed: 16537740]
37. Starrin B, Åslund C, Nilsson KW. Financial stress and shaming experiences and psychosocial ill-health – Studies into the finances-shame model. *Soc Indic Res.* 2009; 91:283–298.
38. Wilkinson, RG. *The Impact of Inequality – How to make Sick Societies Healthier.* New York Press; New York: 2005.
39. Carlsson AC, Starrin B, Gigante B, Leander K, Hellenius ML, de Faire U. Financial stress in late adulthood and diverse risks of incident cardiovascular disease and all-cause mortality in women and men. *BMC Public Health.* 2014; 14:17. [PubMed: 24406139]
40. Rosengren A, Hawken S, Ounpuu S, Sliwa K, Zubaid M, Almahmeed WA, et al. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study. *Lancet.* 2004; 364:953–962. [PubMed: 15364186]
41. McEwen BS. The neurobiology of stress: from serendipity to clinical relevance. *Brain Res.* 2000; 886:172–189. [PubMed: 11119695]
42. McEwen BS. Allostasis, allostatic load, and the aging nervous system: role of excitatory amino acids and excitotoxicity. *Neurochem Res.* 2000; 25:1219–1231. [PubMed: 11059796]
43. McEwen BS. Allostasis and allostatic load: implications for neuropsychopharmacology. *Neuropsychopharmacology.* 2000; 22:108–124. [PubMed: 10649824]

44. Seeman TE, Singer BH, Rowe JW, Horwitz RI, McEwen BS. Price of adaptation--allostatic load and its health consequences. *MacArthur studies of successful aging. Arch Intern Med.* 1997; 157:2259–2268. [PubMed: 9343003]
45. Carlsson AC, Nixon Andreasson A, Wandell PE. Poor self-rated health is not associated with a high total allostatic load in type 2 diabetic patients - But high blood pressure is. *Diabetes Metab.* 2011
46. Hasson D, Von Thiele Schwarz U, Lindfors P. Self-rated health and allostatic load in women working in two occupational sectors. *J Health Psychol.* 2009; 14:568–577. [PubMed: 19383657]
47. Carlsson AC, Wandell P, Gasevic D, Sundquist J, Sundquist K. Neighborhood deprivation and warfarin, aspirin and statin prescription - A cohort study of men and women treated for atrial fibrillation in Swedish primary care. *Int J Cardiol.* 2015; 187:547–552. [PubMed: 25863300]
48. Raparelli V, Proietti M, Butta C, Di Giosia P, Sirico D, Gobbi P, et al. Medication prescription and adherence disparities in non valvular atrial fibrillation patients: an Italian portrait from the ARAPACIS study. *Intern Emerg Med.* 2014; 9:861–870. [PubMed: 24990547]
49. Carlsson AC, Wandell P, Sundquist K, Johansson SE, Sundquist J. Effects of prescribed antihypertensives and other cardiovascular drugs on mortality in patients with atrial fibrillation and hypertension: a cohort study from Sweden. *Hypertension research : official journal of the Japanese Society of Hypertension.* 2014; 37:553–559. [PubMed: 24599014]
50. Wandell P, Carlsson AC, Sundquist J, Johansson SE, Bottai M, Sundquist K. Effects of prescribed antithrombotics and other cardiovascular pharmacotherapies on all-cause mortality in patients with diabetes and atrial fibrillation - a cohort study from Sweden using propensity score analyses. *Diabetol Metab Syndr.* 2014; 6:2. [PubMed: 24397919]
51. Modesti PA, Agostoni P, Agyemang C, Basu S, Benetos A, Cappuccio FP, et al. Cardiovascular risk assessment in low-resource settings: a consensus document of the European Society of Hypertension Working Group on Hypertension and Cardiovascular Risk in Low Resource Settings. *J Hypertens.* 2014; 32:951–960. [PubMed: 24577410]
52. Sundquist K, Chaikiat A, Leon VR, Johansson SE, Sundquist J. Country of birth, socioeconomic factors, and risk factor control in patients with type 2 diabetes: a Swedish study from 25 primary health-care centres. *Diabetes Metab Res Rev.* 2011; 27:244–254. [PubMed: 21309045]
53. Winkleby MA, Jatulis DE, Frank E, Fortmann SP. Socioeconomic status and health: how education, income, and occupation contribute to risk factors for cardiovascular disease. *Am J Public Health.* 1992; 82:816–820. [PubMed: 1585961]

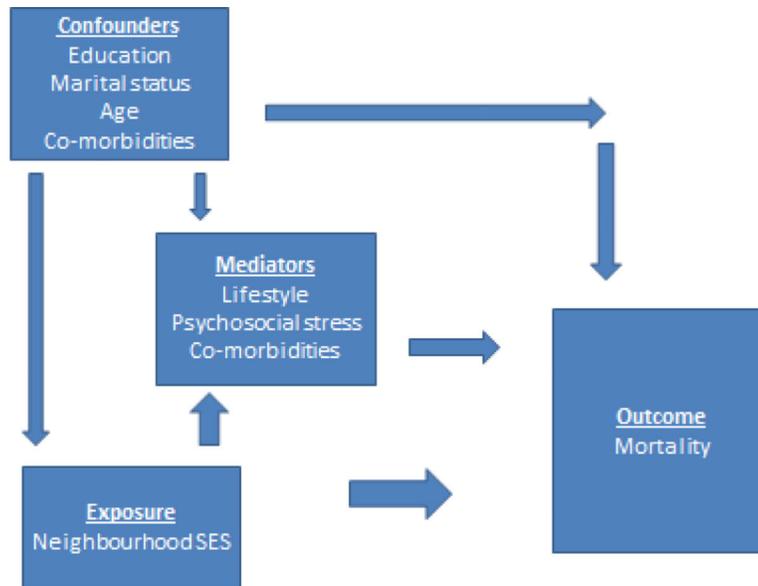


Figure 1. Diagram of the causal pathway to all-cause mortality

Neighbourhood SES categories are likely to affect mortality either by a direct route or by mediators within the causal pathway (in this case lifestyle factors, psychosocial stress or com-morbidities). Educational level, marital status, age and co-morbidities were regarded as confounders. N.b. co-morbidities could be regarded as both confounders and mediators.

Table 1
 Characteristics of patients with atrial fibrillation (AF) by neighborhood socio-economic status

	Men				Women			
	High n=2,656	Middle n=3,030	Low n=960	Difference p-value trend	High n=1,948	Middle n=2,777	Low n=912	Difference p-value trend
Age (years), mean (SD)	72.1 (10.1)	72.5 (10.1)	71.2 (10.1)	0.005 <0.001	77.1 (9.2)	77.5 (9.1)	75.9 (9.9)	<0.001 <0.001
Age group (years)								
45-54	131 (4.9)	172 (5.7)	67 (7.0)		25 (1.3)	49 (1.8)	31 (3.4)	
55-64	518 (19.5)	508 (16.8)	196 (20.4)		193 (9.9)	225 (8.1)	103 (11.3)	
65-74	836 (31.5)	914 (30.2)	292 (30.4)		461 (23.7)	593 (21.4)	212 (23.3)	
75-84	878 (33.1)	1,136 (37.5)	326 (34.0)		847 (43.5)	1,299 (46.8)	388 (42.5)	
85+	293 (11.0)	300 (9.9)	79 (8.2)		422 (21.7)	611 (22.0)	178 (19.5)	
Marital status				<0.001				<0.001
Married	1,896 (72.0)	1,852 (61.5)	545 (57.7)		900 (46.6)	1,000 (36.3)	315 (35.1)	
Unmarried	168 (6.4)	330 (11.0)	148 (15.7)		103 (5.3)	225 (8.2)	72 (8.0)	
Divorced	326 (12.4)	492 (16.4)	173 (18.3)		241 (12.5)	430 (15.6)	115 (12.8)	
Widowed	243 (9.2)	336 (11.2)	79 (8.4)		689 (35.6)	1,004 (40.0)	396 (44.1)	
Educational level				<0.001				<0.001
Compulsory school	379 (21.9)	857 (45.5)	329 (52.8)		254 (29.0)	541 (47.9)	249 (61.2)	
Secondary school	717 (41.5)	695 (36.9)	227 (36.4)		352 (40.2)	430 (38.1)	113 (27.8)	
College/university	634 (37.7)	330 (17.5)	67 (10.8)		269 (30.7)	159 (14.1)	45 (11.1)	
AF-related disease								
Hypertension	1,077 (40.6)	1,297 (42.8)	425 (44.3)	0.078	920 (47.2)	1,393 (50.1)	474 (52.0)	0.034
Coronary heart disease	450 (16.9)	659 (21.8)	229 (23.9)	<0.001	353 (18.1)	595 (21.4)	228 (25.0)	<0.001
Heart failure	415 (15.6)	561 (18.5)	179 (18.7)	0.009	361 (18.5)	586 (21.1)	206 (22.6)	0.021
Valvular disease	126 (4.7)	130 (4.3)	38 (4.0)	0.53	89 (4.6)	148 (5.3)	40 (4.4)	0.36
Cardiomyopathy	26 (1.0)	23 (0.8)	11 (1.2)	0.47	11 (0.6)	14 (0.5)	5 (0.6)	0.96
Cerebrovascular disease	287 (10.8)	350 (11.6)	105 (10.9)	0.65	231 (11.9)	345 (12.4)	93 (10.2)	0.20
Intracranial bleeding	16 (0.6)	19 (0.6)	4 (0.4)	0.75	9 (0.5)	4 (0.1)	3 (0.3)	0.12
Peripheral embolism	10 (0.4)	9 (0.3)	2 (0.2)	0.71	11 (0.6)	12 (0.4)	7 (0.8)	0.47
Diabetes mellitus	476 (17.9)	611 (20.2)	225 (23.4)	0.001	302 (15.5)	561 (20.2)	230 (25.2)	<0.001

	Men				Women			
	High n=2,656	Middle n=3,030	Low n=960	Difference p-value trend	High n=1,948	Middle n=2,777	Low n=912	Difference p-value trend
Drugs								
Warfarin	1,629 (61.3)	1,612 (53.2)	475 (49.5)	<0.001	997 (51.2)	1,303 (46.9)	391 (42.9)	<0.001
ASA	675 (25.4)	974 (32.2)	313 (32.6)	<0.001	697 (35.8)	1,054 (38.0)	465 (40.0)	0.075
Statins	832 (31.3)	880 (29.0)	252 (26.3)	0.009	528 (27.1)	682 (24.6)	220 (24.1)	0.090
								0.044

Table 2

All-cause mortality of patients with atrial fibrillation by neighbourhood socio-economic status: the results of Cox regression

Group	Events/At Risk (n)	Incidence Rate per 100 Person-Years at Risk (95% CI)	Model A HR (95% CI)	Model B HR (95% CI)	Model C HR (95% CI)	Model D HR (95% CI)
Men n=6,646	701/6,646	3.02 (2.80-3.25)				
High	266/2,656	2.91 (2.58-3.29)	0.96 (0.82-1.13)	1.04 (0.87-1.26)	0.97 (0.79-1.18)	1.02 (0.83-1.24)
Middle	331/3,030	3.05 (2.73-3.40)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Low	104/960	3.20 (2.64-3.88)	1.06 (0.85-1.32)	1.10 (0.86-1.41)	1.49 (1.13-1.96)	1.39 (1.05-1.83)
Women n=5,637	744/5,637	3.78 (3.52-4.06)				
High	247/1,948	3.69 (3.26-4.18)	1.01 (0.86-1.18)	1.16 (0.95-1.43)	1.19 (0.96-1.48)	1.25 (1.01-1.56)
Middle	363/2,777	3.69 (3.33-4.09)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Low	134/912	4.25 (3.58-5.03)	1.16 (0.95-1.41)	1.02 (0.79-1.32)	1.17 (0.87-1.56)	1.14 (0.86-1.53)

Model A includes neighbourhood socio-economic score by three groups (high, medium and low) and age group, Model B as Model A but also includes educational level and marital status; Model C as Model B but also includes change of neighborhood level, and diagnoses (hypertension, coronary heart disease, congestive heart failure, cerebrovascular disease and diabetes, also including interaction term between age group and diabetes for men); Model D also includes prescribed anticoagulant treatment and statins

Years until death for 10% of the patients with atrial fibrillation by neighborhood socio-economic status: the results of Laplace regression

Table 3

Group	Model A years (95%CI)	Model B years (95%CI)	Model C years (95%CI)	Model D years (95%CI)
Men n=6,646				
High	0.18 (-0.23; 0.49)	-0.07 (-0.67; 0.52)	-0.07 (-0.62; 0.47)	-0.20 (-0.71; 0.31)
Middle	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Low	-0.70 (-1.19; -0.20)	-0.54 (-1.51; 0.43)	-1.45 (-2.42; -0.48)	-1.24 (-1.83; -0.66)
Women n=5,637				
High	0.10 (-0.20; 0.41)	-0.02 (-0.66; 0.61)	-0.15 (-0.72; 0.42)	-0.22 (-0.70; 0.27)
Middle	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Low	-0.07 (-0.43; 0.29)	0.24 (-0.85; 1.34)	-0.66 (-1.50; 0.19)	-0.46 (-1.19; 0.27)

Model A includes neighborhood socio-economic score by three groups (high, middle and low) and age group. Model B as Model A but also included educational level and marital status; Model C as Model B but also includes change of neighborhood level, and diagnoses (hypertension, coronary heart disease, congestive heart failure, cerebrovascular disease and diabetes, also including interaction terms between age group and diagnoses); Model D also included prescribed antithrombotic treatment and statins