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Prevalence, incidence, risk factors and treatment of Atrial Fibrillation in Australia: the Australian Diabetes, Obesity and Lifestyle (AusDiab) longitudinal, population cohort Study

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Keywords: atrial fibrillation, prevalence, incidence, risk factors

Abstract

Objective: We sought to describe the prevalence, incidence, risk factors and treatment (according to stroke risk) of atrial fibrillation (AF) in the national, population-based Australian Diabetes, Obesity and Lifestyle (AusDiab) Study cohort.

Methods: ECG data were available from 8273/11247 participants of AusDiab study in 1999/2000 and from 5422 participants in 2004/2005. Minnesota coding was used to identify prevalent and incident cases of AF.

Results: 90 prevalent cases of AF (14.1 per 1000) comprising 56 men (mean age 70.5±1.9 years) and 34 women (aged 78.3±1.2 years) were identified in 1999-2000. AF prevalence was associated with sedentary behavior versus physically active (PR 2.0, 95% CI 1.2–3.6). 53 incident cases of AF (2.0, 95%, CI 1.5–2.6 per 1000 person-year) were subsequently identified in 2004-2005. Increased risk of incident AF was associated with male sex, obesity, history of angina, myocardial infarction and stroke. Both increased weight gain and increased weight loss appeared to be associated with increased risks of developing AF in women, while no obvious association was observed in men. Despite their high risk for stroke, anti-thrombotic therapy was observed in only 39.3% of participants with CHA_2DS_2-VASC scores ≥2.

Conclusions: This study contributes to a better understanding of the AF burden. With the aging population, coordinated efforts will be needed to anticipate the future health care costs related to AF and its impacts on the health care system. This will include appropriate application of anti-thrombotic according to risk of thrombo-embolic events.

Keywords: atrial fibrillation, epidemiology risk factors, treatments

Introduction

Affecting more than 33 million individuals in the world [1], atrial fibrillation (AF) is the most common cardiac arrhythmia and one of the most common cardiac conditions overall [2]. As originally confirmed by the Renfrew-Paisley Study cohort in Scotland, independent of other factors, AF is not a benign condition in respect to conveying a markedly higher risk of long-term mortality [3]. In particular, AF is associated with increased risks of morbidity and mortality from complications including stroke, other embolic complications and heart failure [4-6]. The worldwide burden of AF is increasing, with more than 5 million new cases each year [1]. Ball et al. estimated that without any changes in incidence of AF or survival rates in patients with AF, the number of individuals affected by AF in Australia will double between 2014 and 2034 (300 000 to 600 000) [7]. The lack of Australian data on AF prevalence and incidence mainly explains why Ball and colleagues applied international AF prevalence statistics to the Australian adult population aged ≥55 years to estimate the current and potential future prevalence of AF in Australia [7]. Although hospital admissions data may provide useful information on the predictors and outcomes associated with AF [8], they may be limited in describing the broader epidemiology of AF.

With AF becoming a greater public health burden, AF prevalence and incidence figures as well as predictors of AF in the Australian population are urgently needed to facilitate future health care planning. Using data from the Australian Diabetes, Obesity and Life Style Study (AusDiab) [9], therefore, we sought to describe the epidemiology and risk factors of AF in this national, population-based cohort. Given the importance of prescribing anti-thrombotic therapy

to prevent stroke in high risk individuals with AF (those with CHA_2DS_2-VASC ≥2) [10], we also sought to characterise the application of such therapy in identified cases of AF. To our knowledge, this is the first report on the prevalence, incidence and risk factors of AF derived from a national population-based sample of the Australian adult population.

Methods

Study population

The AusDiab study methods have been previously reported [9]. Briefly, AusDiab is a national, population-based survey of adults aged ≥25 years, with baseline examination in 1999-2000. Information was collected during a household interview and a subsequent biomedical examination. Of the 20 347 eligible people who completed a household interview, 11 247 (55.3%) attended for the biomedical examination including 55.1% of females [9]. Over 85% of the sample was born in Australia, New Zealand or UK, while 0.8% were of Aboriginal or Torres Strait Islander background. Over 94% of the participants spoke English as their first language. In 2004–2005, all living eligible participants were invited to attend follow-up. Among those eligible, 6537 (61%) returned in 2004-05 for follow-up, at which the baseline assessment was repeated [11]. Compared with those who did not attend follow-up, participants who attended follow-up were significantly less likely to have hypertension, to have a lower level of education, to be smokers and had lower levels of 2-hour plasma glucose and smaller waist circumferences at baseline [11]. The study was approved by the International Diabetes Institute Ethics Committee [9].

Data collection

Among 11 247 participants of AusDiab-baseline, 8273 individuals aged ≥35 years (84.0% of those aged ≥35years) had ECGs in 1999-2000 and 5422/6174 (87.8%) had ECGs at follow-up in 2004-2005. These ECGs were classified according to the Minnesota coding system [12], and AF status at baseline and at follow-up was defined as a Minnesota code 8.3 and included atrial flutter.

At baseline and follow-up, socio-demographics factors (age and education), behavioural factors (smoking and alcohol drinking habits), physical activity, previous cardiovascular events (such as angina, myocardial infarction and stroke) and medication use were recorded by self-report questionnaire. Education was classified according to the highest level attained ('secondary school qualification', 'trade, technician's certificate', 'Associate, undergraduate diploma or a higher degree'). Smoking status was classified as non-smoker, current-smoker, ex-smoker, and alcohol drinking was classified according to the usual intake when drinking (non-drinker, one to three drinks, five drinks or more). Anthropometric measures were taken at baseline and at follow-up. Body mass index (BMI) was calculated as weight (in kg) divided by the square of the height (in metres). Participants were classified as normal weight (BMI <25kg/m^2), overweight (BMI 25-29.9 kg/m^2) and obese (BMI ≥30 kg/m^2). The percentage of BMI change between baseline and follow-up was calculated as: (*follow-up BMI minus baseline BMI / baseline-BMI.)*100*.

The methods for ascertainment of physical activity [13], blood glucose and blood pressure [13] and diabetes [11] have been described elsewhere. Total physical activity time for the previous week was categorized according to Australian national health recommendations: no

physical activity ('sedentary'), 1-149 minutes ('insufficient physical activity'), and ≥ 150 minutes ('sufficient physical activity') [14].

Stroke risk measured by the CHA_2DS_2-VASC score [10] was estimated for patients with AF at follow-up. The CHA_2DS_2-VASC score was calculated by assigning 1 point each for the presence of congestive heart failure (not recorded in this study), hypertension, age 65–74 years, diabetes mellitus, vascular disease (e.g. myocardial infarction) and female gender and by assigning 2 points for history of stroke (or transient ischemic attack) and age ≥75 years [10]. Participants were thereafter classified in categories of CHA_2DS_2-VASC score ('CHA_2DS_2-VASC score ≤1' and 'CHA_2DS_2-VASC score ≥2'). Medications use over the last three months was recorded at follow-up only. Anti-platelet agents reported in this study included aspirin, dipyridamole and clopidogrel. Anti-coagulants included warfarin and enoxaparin. Anti-arrhythmic agents included amiodarone, digoxin, sotalol, flecainide, quinidine and disopyramide.

Statistical Analysis

To adjust for nonresponse, the AuDiab-baseline data have been weighted to match the age and gender distribution of the 1998 estimated residential population of Australia aged ≥25 years [15]. The weighting factor was based on the probability of selection in each sampling cluster [15]. Therefore, all prevalences provided relate to the total 1998 Australian population aged ≥25 years [15]. Prevalences of AF (per 1000) were computed in categories of age for men and women. Baseline characteristics of individuals included in this study were described and prevalences of AF in categories of baseline characteristics were examined on an age-adjusted basis. Categorical variables were standardized by the direct method using data from the Australian total population in 1998 [16]. Adjusted associations between prevalent AF and baseline characteristics of

participants were assessed with a multivariable log-binomial regression model for which the point estimates are interpretable as prevalence ratios or risk ratios.

To analyse the incidence of AF, participants in sinus rhythm at baseline who had ECGs at follow-up were selected. Incidence rates of AF (per 1000 person-year) were computed in age categories for men and women and thereafter in categories of participants' baseline characteristics (combining men and women). Cox proportional hazard models with time to AF as the dependent variable were used to estimate the associations between incident AF and baseline characteristics. The models were first adjusted for age and thereafter were further adjusted for other socio-demographic and lifestyle factors. Data from the US reported non-linear associations between incident AF and weight changes in men and women [17]. Therefore, restricted cubic splines (choosing 5 knots corresponding to the quintiles of BMI change) were used to assess associations between the incidence of AF and percentage of BMI change in men and women [17].

Results

Among 8273 men and women aged ≥35 years who had ECGs at baseline, AF was found in 90 participants (a prevalence of 14.1 per 1000). Although the crude prevalence of AF was similar in men and women (14.6 per 1000 versus 13.6 per 1000 respectively), the pattern of age specific prevalence of AF was different in men compared to women. AF was more prevalent in men aged <75 years compared to women of the same age group: age <55 years (3.4 per 1000 versus 0.0 per 1000); 55-64 years (9.4 per 1000 versus 0.0 per 1000); and 65-74 years (31.3 per 1000 versus 12.8 per 1000). However, AF was more prevalent in women compared to men in those aged ≥75 years (103.8 per 1000 versus 66.1 per 1000).

Participants with AF were older than those in sinus rhythm (median age of 74.5 versus 54.0 years). On an adjusted basis, the prevalence of AF was higher among those classified as 'sedentary' compared to those classified as having 'sufficient physical activity' (prevalence ratio 2.1, 95% CI 1.2–3.6) (Table 1). Prevalent AF was not significantly more frequent among those who reported diabetes, angina, myocardial infarction and stroke compared to those who did not report these conditions (data no shown).

Among 5389 participants in sinus rhythm at baseline (1999-2000) who had ECGs at follow-up (2004-2005), 53 developed AF (incidence rate of 2.0 per 1000 person-year, 95% CI 1.5–2.6) (Table 2). Age specific incidence rates of AF were higher among men compared to women: age < 55 years (0.6 per 1000 versus 0.3 per 1000); 55-64 years (1.0 per 1000 versus 0.6 per 1000); 65-74 years (8.0 per 1000 versus 3.5 per 1000); and ≥75 years (21.2 per 1000 versus 10.7 per 1000). The follow-up time was 5.0 years on average and varied from 3.6 years to 6.0 years. The adjusted hazards of incident AF (Table 2) increased with age and were higher among men compared to women, among participants who were obese at baseline compared to those who had a normal weight and among those reporting angina, myocardial infarction and stroke (versus those who did report these conditions). No obvious association between incident AF and the percentage of BMI change was evident in men (Figure 1), while both BMI gain and BMI loss appeared to be associated with increased risks of developing AF in women.

Anti-platelet use was observed in 27.3% of participants with AF at follow-up with $CHADS_2DS_2$-VASC score ≤1 and in approximately a third of those with $CHADS_2DS_2$-VASC score ≥2 (Table 3). Despite their higher risk for stroke, only 39.3% of participants with $CHADS_2DS_2$-VASC score ≥2 reported anti-coagulant use, while they reported anti-arrhythmic use in 35.7% of cases.

Discussion

This study is the first report on the prevalence, incidence and risk factors of AF derived from a national population-based sample of the Australian adult population. AF prevalence was associated with sedentary behavior (sedentary versus physically active). Increased incidence of AF was associated with male sex, obesity and prior history of angina, myocardial infarction and stroke. Both increased weight gain and increased weight loss appeared to be associated with increased risks of developing AF in women, while no obvious association was found in men. Despite their high risk for stroke, antithrombotic therapy was observed in only 39.3% of participants with CHA_2DS_2-VASC scores ≥2.

In terms of international comparisons, results from this study are consistent with previous reports of AF prevalence ranging from around one per 1000 in those aged <55 years to more than 100 per 1000 in those aged ≥80 years [2]. The prevalence of AF among women aged ≥75 years was greater than among men of the same age; this pattern has been previously described among individuals aged >80 years [7]. The age-specific prevalence of AF among participants aged <70 years was, in general, lower in the AusDiab study compared to the Rotterdam study [4], the Framingham study [18] and the Renfrew/Paisley cohort [19] (for example 17 per 1000 in those aged 60-64 years in the Rotterdam study versus 8 per 1000 in AusDiab) [4]. While in participants aged ≥70 years, the prevalence tended to be equivalent or higher in the AusDiab study; for example 58 per 1000 in AusDiab versus 48 per 1000 in the Framingham study in those aged 70-79 years [18]. While it might be tempting to speculate that the burden of AF in those aged around 70 years and below may be lower in Australia compared to some high income

countries, different factors may explain these differences such as random variation, differences in the studied populations or differences in the methods used for AF detection [20].

When factors associated with prevalent AF were analysed, the adjusted prevalence ratio of AF was higher among those who reported sedentary behaviour compared to those who reported being sufficiently active. The association between prevalent AF and sedentary behaviour may reflect a causal mechanism, but may also be due to exercise intolerance induced by AF [2].

Over five years of follow-up, incidence rates of AF found for men and women aged 55-64 years and 65-74 years in the AusDiab study appeared lower than those observed in the Framingham study and Rotterdam study [4]. While incidence rates observed in men and women aged 55-64 years in this study (1.0 per 1000 person-year and 0.6 per 1000 person-year respectively) were closer to those observed in the Renfrew/Paisley study (1.3 per 1000 person-years and 0.4 per 1000 person-year) [19]. As mentioned previously for prevalent AF, different factors including differences in the methods of detection of AF may be related to these differences in AF incidence rates; the Framingham study for example used a combination of different methods for AF detection (ECGs, physical examination, medical records review of hospitalisation, outside physicians' visits) while single ECGs were used in the current study [18, 20].

This study confirmed results of previous studies reporting predictors of AF [2]. The incidence of AF increased with age [19]; from a reference age group aged <55 years, each additional decade of age increased the risk of AF by around three-fold. In accordance with other studies, men were around twice as likely as women to develop AF [2]. This study also confirmed

the associations between obesity, angina, myocardial infarction and stroke with new onset of AF [2, 21, 22]. Previous reports found higher risks of developing AF in individuals with hypertension or diabetes compared to those who did not have these conditions [2]. However, our study may have lacked power to detect these associations. Data from the Atherosclerosis Risk in Communities (ARIC) study reported marked increases of AF incidence in both men and women who lost >5% of their weight between baseline and follow-up and in men who gained >10% body weight compared to those who gained <5% [17]. In this study, the magnitude of BMI changes was larger in women compared to men and may partly explain why the associations between BMI changes and incident AF were found in women but not in men. The mechanisms linking weight loss and the incidence of AF are not clearly understood [17]. The reasons for weight loss have not been recorded in this study. It has been previously speculated that unintentional weight loss due to underlying medical conditions may explain the association between weight loss and increased incidence of AF [17].

Data from this study suggests that around 60% of Australians with AF who present a high risk of stroke may not be on optimal anti-coagulation therapy [10]. Despite the lack of evidence for their beneficial effects in high-risk individuals with AF (even when combined with anti-coagulants), anti-platelet therapies are frequently prescribed for individuals with AF (approximately a third of individuals with CHA_2DS_2-VASC ≥ 2 in AusDiab) [23].

This study has some limitations. Participants to the AusDiab follow-up study were less likely to be socio-economically disadvantaged and presented lower risks of chronic conditions compared to the Australian total population. Single ECGs taken during medical examinations at baseline and at follow-up were used for AF detection. This may have underestimated the burden of AF. In addition, it was not possible to distinguish paroxysmal to sustained AF cases. The

burden of AF may be higher among Aboriginal and Torres Strait Islander compared to other Australians [7]. However, this study is under-powered to report these comparisons.

Conclusion

This study contributes to a better understanding of the AF burden. AF is a disease of the elderly and with the aging population, its impact will be largely amplified in the next decades. Co-ordinated efforts will be needed to anticipate its future health care costs and its impacts on the health care system. Future challenges will also include appropriate application of anti-thrombotic therapy according to risk of thrombo-embolic events.

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Figure legend

Figure 1: Association between atrial fibrillation and percentage of BMI change in women and men presented as hazard ratio (HR; solid line) and 95% confidence intervals (CIs; shaded area). Results from Cox proportional hazards model using restricted cubic splines, adjusted for age, gender, BMI, smoking status, usual number of alcoholic drinks, physical activity and level of education. Value zero (no weight change) was considered as a reference category. Q1 = first quartile; Me= median; Q3 = third quartile.

Table 1. Baseline characteristics of the study population and associations between prevalent atrial fibrillation and socio-demographic and life style factors: The Australian Diabetes, Obesity and Lifestyle (AusDiab) study.

	Baseline characteristics	Prevalence of AF	Adjusted PR of AF[†]
	% (n)	% (95% CI)	PR (95% CI)
N	8273	–	
Mean age (sd)	56.6 (11.7)	–	**4.1 (2.9 – 5.9)** [‡]
Women	51.6 (4494)	–	1.4 (0.8 – 2.4**)**
BMI Categories			
Normal	35.7 (2831)	1.2 (0.7 – 2.2)	reference
Overweight	41.5 (3459)	1.4 (0.8 – 2.4)	1.0 (0.7 – 1.5)
Obese	22.8% (1924)	2.0 (1.0 – 4.2)	1.4 (0.5 – 4.2)
Smoking status			
Non-smoker	56.8 (4476)	1.6 (1.0 – 2.5)	reference
Current-smoker	13.7 (1116)	0.5 (0.2 – 1.1)	0.5 (0.2 – 1.3)
Ex-smoker	29.5 (2553)	1.1 (0.7 – 1.7)	0.7 (0.4 – 1.4)
Usual number of alcoholic drinks			
Non-drinker	18.6 (1498)	1.8 (0.6 – 5.5)	reference
One to three drinks	69.3 (5681)	1.2 (0.8 – 1.8)	0.9 (0.3 – 2.5)
Five drinks or more	12.1 (1058)	1.4 (1.0 – 2.0)	1.5 (0.4 – 6.4)
Physical activity			

Sufficient	50.4 (4194)	1.1 (0.8 – 1.8)	reference
Insufficient	32.6 (2538)	1.1 (0.6 – 2.2)	0.9 (0.4 – 2.2)
Sedentary	17.0 (1504)	**2.4 (1.5 – 3.9)**	**2.1 (1.2 – 3.6)**
Education			
Secondary school qualification	40.3 (3546)	1.2 (0.8 – 2.1)	Reference
Trade, technician's certificate	30.0 (2386)	1.6 (1.0 – 2.4)	1.2 (0.7 – 2.0)
Associate, undergraduate diploma or a higher degree	29.7 (2284)	1.5 (0.9 – 2.5)	1.5 (0.7 – 2.9)

PR=prevalence ratio

‡ prevalence ratio for each additional decade of age

† The multivariable model included age, gender, BMI, smoking status, usual number of alcoholic drinks, physical activity and level of education

Table 2. Associations between baseline characteristics and 5-year incidence of atrial fibrillation. The Australian Diabetes, Obesity and Lifestyle (AusDiab) study.

	Incidence of AF		Hazard ratio (95% CI)	
	Cases/person-year	Rate per 1000 person-year (95% CI)	Age-adjusted	Multivariable model[†]
Overall incidence	**53/ 26890**	**2.0 (1.5 – 2.6)**		
Age		–	–	**3.6 (2.7 – 4.9)** [‡]
Gender				
Women	19/14716	**1.3 (0.8 – 2.0)**	**reference**	**Reference**
Men	34/12174	**2.8 (2.0 – 3.9)**	**2.1 (1.2 – 3.6)**	**2.3 (1.2 – 4.3)**
BMI Categories				
Normal	12/9741	1.2 (0.7 – 2.2)	**reference**	**Reference**
Overweight	26/11095	2.3 (1.6 – 3.4)	1.4 (0.7 – 2.8)	1.4 (0.7 – 2.9)
Obese	15/5823	2.6 (1.6 – 4.3)	**2.3 (1.1 – 4.8**)	**2.8 (1.3 – 6.2)**
Smoking status				
Non-smoker	28/15359	1.8 (1.3 – 2.6)	reference	Reference
Current-smoker	3/2988	1.0 (0.3 – 3.1)	0.9 (0.3 – 3.0)	0.8 (0.2 – 2.7)
Ex-smoker	22/8087	2.7 (1.8 – 4.1)	1.3 (0.7 – 2.2)	1.1 (0.6 – 1.9)
Usual number of alcoholic drinks				
Non-drinker	8/4078	2.0 (1.0 – 3.9)	reference	reference
One to three drinks	41/19161	2.1 (1.6 – 2.9)	1.6 (0.8 – 3.5)	1.6 (0.7 – 3.4)

Five drinks or more	3/ 3531	0.9 (0.3 – 2.6)	0.9 (0.2 – 3.5)	0.6 (0.1 – 2.2)
Physical activity (%)				
Sufficient	38/14422	2.6 (1.9 – 3.6)	reference	reference
Insufficient	9/8171	1.1 (0.6 – 2.1)	0.6 (0.2 – 1.0)	**0.4 (0.2 – 0.9)**
Sedentary	6/4167	1.4 (0.7 – 3.2)	0.7 (0.3 – 1.6)	0.7 (0.3 – 1.6)
Education				
Secondary school qualification	26/10146	2.6 (1.7 – 3.8)	reference	reference
Trade, technician's certificate	14/7865	1.8 (1.1 – 3.0)	0.9 (0.4 – 1.6)	0.6 (0.3 – 1.2)
Associate, undergraduate diploma or higher	13/8723	1.5 (0.9 – 2.6)	0.9 (0.5 – 1.8)	0.6 (0.3 – 1.3)
Pre-existing medical conditions at baseline*				
Diabetes				
No	28/19679	**1.4 (1.0 – 2.1)**	reference	reference
Yes	25/6987	**3.6 (2.4 – 5.3)**	1.5 (0.9 – 2.6)	1.2 (0.7 – 2.2)
Hypertension				
Normotensive	15/ 17719	**0.9 (0.5 - 1.4)**	reference	reference
Hypertensive	38/9081	**4.2 (3.0 – 5.8)**	1.6 (0.8 – 3.1)	1.2 (0.6 – 2.4)
Angina				
No	43/25461	**1.7 (1.3 – 2.3)**	reference	reference
Yes	10/1255	**8.0 (4.3 – 14.8)**	**2.0 (1.0 – 4.1)**	**2.3 (1.1 – 4.6)**
Myocardial infarction				

No	43/25745	**1.7 (1.2 – 2.3)**	reference	reference
Yes	10/966	**10.4 (5.6 – 19.2)**	**2.6 (1.3 – 5.3)**	**2.6 (1.2 – 5.4)**
Stroke				
No	48/26297	**1.8 (1.4 – 2.4)**	reference	reference
Yes	5/493	**10.1 (4.2 – 24.4)**	**2.6 (1.0 – 6.5)**	**2.9 (1.1 – 7.6)**

[†]The multivariable model included age, gender, BMI, smoking status, usual number of alcoholic drinks, physical activity and level of education

[‡] hazard ratio for each additional decade of age

[*] Adjustment for age, gender, BMI, smoking status, usual number of alcoholic drinks, physical activity and level of education

Table 3. Medication use among 68 individuals with atrial fibrillation at follow-up (2004-2005), according to CHA_2DS_2-VASC score categories: The Australian Diabetes, Obesity and Lifestyle (AusDiab) study.

	Anti-platelet	Anti-coagulant	Anti-arrhythmic
	(n = 65)	(n = 68)	(n = 68)
	% (n)	% (n)	% (n)
CHA_2DS_2-VASC ≤1	27.3 (3)	16.7 (2)	25.0 (3)
CHA_2DS_2-VASC ≥2	37.0 (20)	39.3 (23)	35.7 (20)

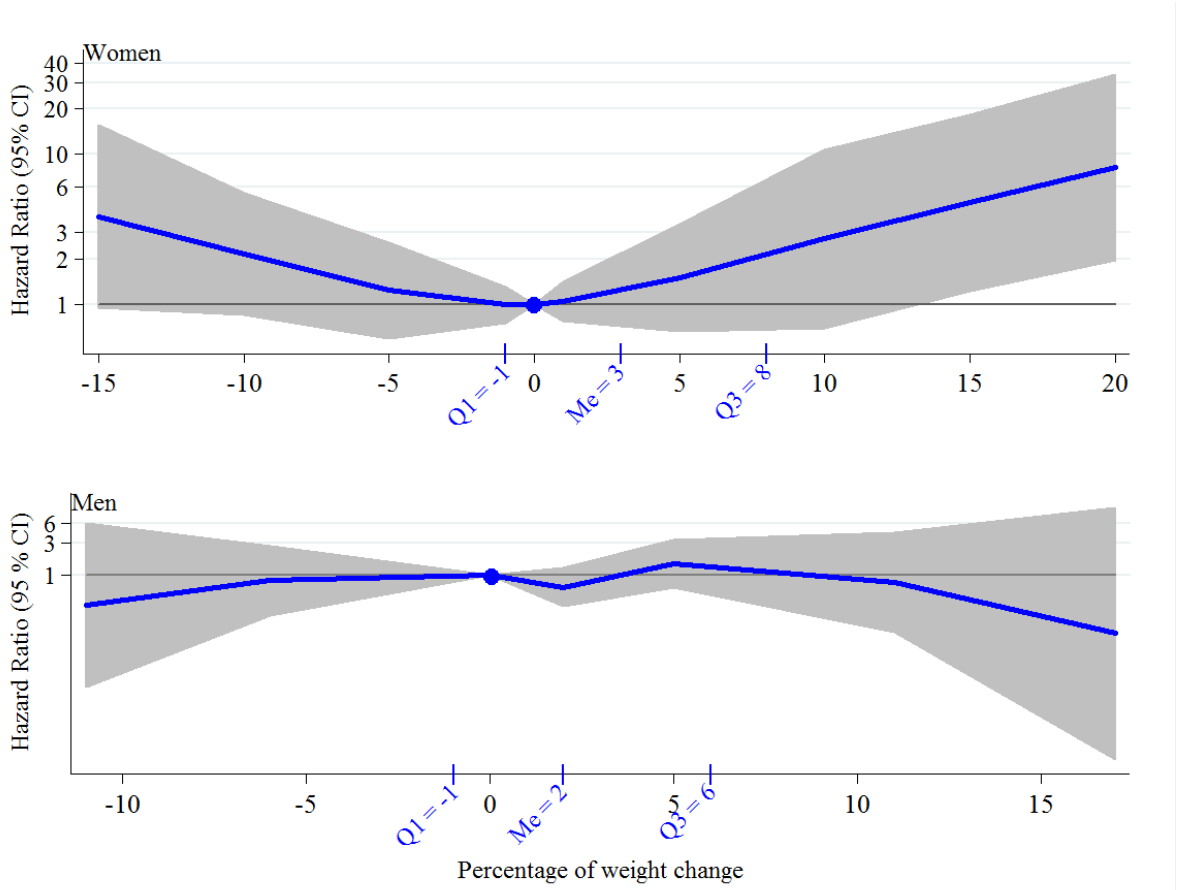

Figure 1