Title: Association between walking pace and stroke incidence: findings from the UK Biobank prospective cohort study

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Abstract

Background and Purpose

Stroke incidence in younger and middle-aged people is growing. Despite this, its associations in this subset of the stroke population are unknown and prevention strategies are not tailored to meet their needs. This study examined the association between self-reported walking pace and incident stroke.

Methods

Data from the UK Biobank was used in a prospective population-based study. 363,137 participants aged 37 to 73 years (52% women) were recruited. The associations of self-reported walking pace with stroke incidence over follow-up were investigated using Cox-proportional hazard models.

Results

Among 363,137 participants, 2,705 (0.7%) participants developed a fatal or non-fatal stroke event over the mean follow-up period of 6.1 years (interquartile range: 5.4 to 6.7). Slow walking pace was associated with a higher hazard for stroke incidence (HR 1.45, 95% CI: 1.26 to 1.66, $p<0.0001$). Stroke incidence was not associated with walking pace among people under 65 years. However, slow walking pace was associated with a higher risk of stroke among participants aged ≥65 years (HR 1.42, 95% CI: 1.17 to 1.72, $p<0.0001$). A higher risk for stroke was observed on those with middle (HR 1.28, 95% CI: 1.01 to 1.63, $p=0.039$) and higher (HR 1.29, 95% CI: 1.05 to 1.69, $p=0.012$) deprivation levels but not in

the least deprived individuals. Similarly, overweight (HR 1.30, 95% CI: 1.04 to 1.63, *p*=0.019) and obese (HR 1.33, 95% CI: 1.09 to 1.63, *p*=0.004) but not normal weight individuals had a higher risk of stroke incidence.

Conclusions

Slow walking pace was associated with a higher risk of stroke among participants over 64 years in this population-based cohort study. The addition of the measurement of self-reported walking pace to primary care or public health clinical consultations may be a useful screening tool for stroke risk

Introduction

Stroke is a preventable disease with 91% of the incidence attributable to modifiable risk factors such as smoking, poor diet, and low levels of physical activity (PA)[1]. A low level of PA makes the second highest contribution to stroke incidence[1]. Cohort studies consistently support the association between PA and primary stroke prevention[2-5] and the promotion of PA is therefore a critical component of any effective primary prevention strategy. In the context of primary stroke prevention, pragmatic methods of measuring PA are needed to inform accurate risk stratification and tailored intervention design. Given that self-reported walking pace is easy to examine, offering minimal burden to the patient and healthcare professional, it may prove to be a valuable routine test to help determine the associations of stroke incidence among people of younger and middle-age. Ganna and Ingelsson (2015)[6] investigated predictors of mortality among UK Biobank participants during a 5-year period. Results demonstrated that self-report measures, obtained by verbal interview without physical examination, are the strongest predictors of all-cause mortality in middle-aged and older people. Self-reported walking pace was a strong predictor of all-cause mortality in both men (C-index 0·72 [95% CI 0·71–0·73]) and women (0·69 [0·68–0·70); stronger than smoking habits and other lifestyle measurements.. Cohort studies demonstrate an association between objectively assessed walking pace and stroke risk in older adults[7] and post-menopausal women[8]. To date, self-reported walking pace has been demonstrated to be associated with cardiovascular health[9,10] and all-cause and cardiovascular mortality, using the UK Biobank data[11]. While there are some limitations in the use of a self-reported measure of walking pace, results of this study within a large national sample of UK adults demonstrate, that the strength of association persisted after adjustment for objectively measured handgrip strength[11]. Of note, stroke incidence or mortality was not included as an outcome in this study[11].

The incidence of stroke in people of working age is growing[12] with 20-25% of stroke survivors of working age in the United States, Australia and UK[13,14]. Despite this, the associations between many risk factors and stroke incidence in this population are unknown and prevention strategies are not tailored to meet the needs of this growing subset of the population. Younger and middle-aged people may have different patterns of risk whose impact is likely to be conditioned by lifestyle indicators.

Aim

To examine the associations of self-reported walking pace with incident stroke in participants from the UK Biobank dataset.

Methods

The UK Biobank data are available on application to the UK Biobank (http://www.ukbiobank.ac.uk/).

Between 2007 and 2010, UK Biobank recruited 502,628 participants, aged 37-73 years from the general population[15]. However, 363,137 with full data available were included in this study. Participants attended one of 22 assessment centres across England, Wales and Scotland [16]where they completed a touch-screen questionnaire, had physical measurements taken and provided biological samples[16,17]. Incident stroke (of any form) was the main outcome used in the current study; and self-reported walking pace (slow, average and brisk) was the exposure of interest. Sociodemographic factors (age, sex, ethnicity, employment status and area-based

deprivation), lifestyle factors (smoking status, self-reported discretionary screen time, total PA, grip strength and dietary intake), health related parameters (systolic blood pressure, diabetes, medication for cardiovascular disease, and self-reported health rating) and body mass index (BMI) were treated as potential confounders. All analyses were conducted using landmark analysis excluding events occurring in the first 2 years of follow-up, and participants with baseline medical diagnoses of depression, COPD, chronic asthma, chronic liver diseases, alcohol problems, substance abuse, eating disorders, schizophrenia, cognitive impartment, Parkinson's disease, dementia, chronic pain syndrome, heart diseases, diabetes and cancer were excluded (n=103,755). Those who reported to be unable to walk (n=1,929) or those who did not answer these questions were also excluded from the study (n=7,669). All participants provided written informed consent and the study was approved by the NHS National Research Ethics Service (Ref: 11/NW/0382).

Procedures

Date of death was obtained from death certificates held by the National Health Service (NHS) Information Centre (England and Wales) and the NHS Central Register Scotland (Scotland). Date and cause of hospital admissions were identified via record linkage to Health Episode Statistics and to the Scottish Morbidity Records (SMR01). Detailed information regarding the linkage procedure can be found at http://www.ic.nhs.uk/services/medical-research-information-service. For mortality endpoints, end of follow-up was recorded as the first of date of death or the end of data collection for the attended assessment centre (30 November 2016 for centres in Scotland; 31 January 2018 for centres in England/Wales). Hospital admission data were available until 31 March 2015, resulting in disease specific analyses being censored at this date, or the date of hospital admission or death if these occurred earlier. Incident stroke was defined as a hospital admission or death with ICD10 code I60, I61, I63, I64.

Walking pace was self-reported using a touch-screen questionnaire completed at the baseline visit. The participants who indicated they were able to walk were asked "How would you describe your usual walking pace?" and they could choose one of the following: slow pace defined as <3 miles per hour (mph); average pace defined as 3-4 mph; and brisk pace defined as >4 mph.

PA was measured using the IPAQ short form, and total PA was computed as the sum of walking, moderate and vigorous activity, measured as metabolic equivalents (MET-hours.week^{-1})[18]. Participants were asked "In a typical day, how many hours do you spend watching TV during your leisure time?", and this was expressed as hours per day. Grip strength was assessed using a Jamar J00105 hydraulic hand dynamometer and the mean of the three measurements for each hand were used, grip strength was expressed as kg[19]. Dietary information was collected via the Oxford WebQ; a web-based 24-hour recall questionnaire which was developed specifically for use in large population studies[20,21]. Area-based deprivation index was derived from postcode of residence, using the Townsend score[22]. Smoking status was self-reported as never, former or current smoking. Professional qualification, income, Employment status, ethnicity (White, Mixed, Asian, Black, Chinese, Other) and self-reported overall health rating (excellent, good, average and bad) were reported. Medical history (physician diagnosis of illness) was collected using the self-completed, baseline questionnaire. Height and body weight were measured by trained nurses during the initial assessment centre visit. BMI was calculated as (weight(kg)/height(m)^2) and the WHO criteria applied for classification into: underweight <18.5, normal weight 18.5-

24.9, overweight 25.0-29.9 and obese ≥30.0 kg.m^{-2}. Further details of these measurements can be found in the UK Biobank online protocol (http://www.ukbiobank.ac.uk)[23].

Statistical analyses

The associations of self-reported walking pace with stroke incidence over follow-up were investigated using Cox-proportional hazard models with age as the time variable. The results are reported as hazard ratios (HRs) and 95% confidence intervals (CI). The proportional hazards assumption was checked by tests based on Schöenfeld residuals. Walking pace was fitted into the model as an ordinal variable and average pace was used as reference group (0=slow pace, 1=average pace and 2=brisk pace). The models were conducted excluding participants with all relevant disease at baseline (n=103,755). We excluded from all analyses individuals who reported comorbidities which could affect walking pace or time spent walking, those with missing data or who were unable to walk.

Three models including an increasing number of covariates were developed. All analyses where conducted using landmark analyses and excluding participants with previous stroke. Model 0 included socio-demographic variables (sex, age, area based deprivation status, professional qualification, income, current employment status, and ethnicity) and month of assessment. Model 1 included the same factors as model 1 and, in addition, health factors (mean arterial blood pressure, diabetes, systolic blood pressure, preventative CVD medication), self-reported health-rating and categories of BMI. Model 2 additionally adjusted for total PA, grip strength, smoking, TV-viewing and diet (processed meat, red meat, oily fish, alcohol intake, fruit and vegetables). All analyses were performed using STATA 14 statistical software (StataCorp LP).

Results

After conducting a 2-year landmark analysis and excluding individuals with major comorbidities at baseline (participants with previous stroke were also excluded), 363,137 participants were included in the analyses. The median follow-up period was 6.1 years [IQR: 5.4 to 6.7] for stroke incidence. Over the follow-up period, 2,705 (0.7%) participants developed a fatal or non-fatal stroke event.

The characteristics of the participants by walking pace category are presented in Table 1. The hazard ratios (HRs) for stroke incidence, both minimally and fully adjusted, are presented in Table 2. In summary, slow walking pace, compared to average walking pace was associated with a 45% higher hazard for stroke incidence (HR 1.45, 95% CI: 1.26 to 1.66, p<0.0001). Brisk walking pace, compared to average walking pace, was associated with reduced stroke incidence in minimally-adjusted models but not in the fully adjusted model (model 2).

To investigate whether the association between walking pace and stroke incidence differed by socio-demographic, clinical and lifestyle factors, multiplicative interactions terms were fitted in models. Significant interactions were noted between walking pace and age, deprivation and BMI, which justified stratifying the analysis accordingly. In the sub-group analysis by age, stroke incidence was not associated with walking pace among people under 55 years (448 events) and people aged 55 to 64 years (Table 3). In contrast, compared to average walking pace, slow walking pace was associated with a higher risk of stroke among participants aged over 65 years (HR 1.42, 95% CI 1.17 to 1.73, p<0.0001). Brisk walking pace was associated with a lower stroke risk among participants over 65 years in model 0, but not in models 1 and 2 2(Table 3). Sub-group analysis by sex (Table 4) demonstrated that slow walking pace was associated with increased risk of stroke in women (HR 1.50, 95% CI 1.23 to 1.84, p<0.0001)

but not men. Brisk walking pace was not associated with reduced risk of stroke in both men and women.

In the sub-group analyses by deprivation category, slow walking pace, compared to average walking pace, was associated with higher risk of stroke among participants within the second (average) and third (most deprived) tertiles of deprivation (HR 1.23, 95% CI 1.01 to 1.64, *p=0.04* and HR 1.29, 95% CI 1.06 to 1.59, *p*=0.01, respectively) (Table 3). Sub-group analysis by BMI categories demonstrated that slow walking pace was associated with a higher risk of stroke among participants in the overweight and obese categories, but not in participants in the normal weight category (743 events) (Table 3).

Discussion

This is the first study to demonstrate that within a large national sample of younger and middle-aged relatively healthy UK adults, self-reported slow walking pace was strongly positively associated with a higher risk of stroke, compared to average walking pace. The associations observed among women without previous stroke and remained robust after adjustment for many other variables. In relation to age, slow walking pace was significantly associated with stroke risk among people aged 65 years and over, but not among those aged 40 to 64years.

There is limited research with which to compare the current findings, as previous work has primarily focussed on associations of walking pace with total cardiovascular disease. An association between slow walking pace and stroke incidence is consistent with some previous work[7,8,24]. Prior studies however, have used less comprehensive, non-population-based data, in restricted samples, for example among older adults (mean age 73 years)[7], older men (mean

age 68 years)[24] and post-menopausal women (mean age 65 years)[8]. The current study is the first, therefore, to investigate associations in a relatively young population (40-69 years on entry to study). Soares-Miranda et al (2016)[7] reported that in a sample of 4207 US men and women of a mean age of 73 years, in comparison with slow walking pace (<2 mph), those that habitually walked at a pace >3 mph had a lower risk of stroke (HR 0.47; CI 0.33-0.66), demonstrating a 53% less risk of stroke among those of average walking pace. The current study differs in its inclusion of a larger, younger study sample. The magnitude and significance of the HR in the current study however, differs to that demonstrated by Soares-Miranda et al (2016)[7], wherein a HR of 0.93 (95% CI 0.85-1.03) was reported for brisk walkers compared to average-paced walkers, demonstrating a non-significant lower risk of stroke. This may be explained by the potential for underpowered analysis in the Soares-Miranda et al (2016)[7] study, however, due to the limited number of participants (n=4207) and events (n=563). Jeffris et al (2014)[24] examined the association between walking pace and stroke risk in a cohort study among 3435 men (195 incident strokes). The results demonstrated that the HR for stroke was significantly reduced in average or brisk pace compared with slow pace, HR 0.62 (95% CI 0.42–0.92) but was fully mediated on adjustment for walking distance. The current study however adds to this evidence base by presenting a much larger sample, with 2705 stroke events, across sex, age, deprivation and BMI categories. The current results align with those of Jeffris et al (2014)[24], demonstrating HRs of 1.50 (95% CI 1.23 to 1.84) among women for slow walkers compared to average-paced walkers, representing 50% higher risk of stroke in slow versus average-paced walkers in this population-based sample for women. However, the current findings show that this association did not remain significant in maximally-adjusted model (which included PA and muscle strength). One explanation could be that PA and strength may be more correlated with walking pace in men and not women. Men have higher PA and strength levels and therefore,

therefore adjusting for these variables in the final model could explain the lack of significance of the association between walking pace and stroke risk among men and not women. Whereas for women, PA and grip strength are low so these variables may not fully explain their walking pace levels.

Adding to this evidence base, we examined the associations between walking pace and stroke incidence across age categories. We did not find an association between walking pace and stroke incidence among participants younger than 64 years, perhaps reflecting the small number of events in this age group.

In the context of the increased incidence of stroke in younger and middle-aged people[12-14], the current findings have important implications for public health and general practice. Self-reported walking pace presents as a useful method of identifying people over 65 years with slow self-reported walking pace who are at high risk of stroke and who may benefit from further assessment of stroke risk factors and also from primary prevention strategies, including public health interventions to promote increased habitual walking pace. These findings have important implications for healthcare professionals and the general public, among which the diagnosis of stroke may be predominantly associated with older adults. Many clinical measures of ascertaining the PA habits of patients already include questioning around self-reported walking pace, for example the General Practice Physical Activity Questionnaire (GPPAQ). Therefore, the current findings, demonstrating the associations between slow walking pace and increased risk of stroke, do not suggest that substantial changes in clinical practice are needed but that more informed interpretation of information already being collected by many healthcare professionals is possible. These findings extend those of previous work by firstly confirming the substantial risk of stroke in a middle-aged

adult population, but also by identifying a relatively easily-applied association of stroke incidence to inform public health and primary care strategies.

Ten population attributable risk factors for first stroke have previously been identified using a multicentre case-control study design among over 26000 participants[1]. Results demonstrate that self-reported PA is the second-largest predictor of stroke[1]. However, the current study is the first to use a population-based cohort study design to examine the associations between an aspect of PA and stroke risk in a young to middle-aged sample. It must be noted that self-reported walking pace is not the same as PA. However, walking is frequently recommended as an intervention option to increase independence and PA levels post-stroke. Often, a primary recommendation has been to increase the time spent walking[25] with the pace of walking often receiving less focus. If future trials, examining the effectiveness of various dosages of PA post-stroke, confirm the findings of the current study, it may be prudent to also ensure promotion of a brisk walking pace, where the individual is capable, to further enhance the benefits of walking.

This study benefits from a large prospective population-based dataset with high follow-up rates and multiple physical function measures (walking pace, time spent in PA, handgrip strength). Inclusion of various measures of physical function allowed for more stringent adjustment of potential physical confounders of the association between walking pace and stroke incidence. Although we cannot exclude residual confounding as an explanation for our findings, we adjusted for a wide range of important potential confounders, mediators and effect modifiers. To reduce the risk of reverse causality, we excluded participants with pre-existing physician stroke diagnosis and any stroke diagnosis in the first 2 years of follow-up in sensitivity analyses.

As the UK Biobank sample is relatively representative of the general working-age UK population in terms of age, sex, ethnicity and socioeconomic status, this study had sufficient power to undertake analyses by sex and age which overcomes limitations from previous studies[8,24]. However, the potential for healthy volunteer bias must be considered as a potential limitation to the generalisation of the findings.

Conclusions

Slow walking pace was strongly associated with a high risk of stroke compared to those of average pace among participants of 64 years and older in this population-based cohort study. We found that this association persisted after multivariate adjustment for known stroke risk factors, variables associated with walking speed, other aspects of physical function, socioeconomic and behavioural variables. Future research, using a randomised controlled trial design, is needed to determine if the current observations reflect a causal association and, if so, these findings could have import implications for PA recommendations for older adults . The addition of the measurement of self-reported walking pace to primary care or public health clinical consultations may be a useful, screening for risk of stroke among people of younger and middle-age.

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Disclosures

None

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Table 1. Participant characteristics by self-reported walking pace. Continuous variables are presented as mean (SD); categorical variables are presented as n (%)

	Slow	**Average**	**Brisk**
N (%)	18,442 (5.1)	191,598 (52.7)	153,097 (42.2)
Fatal and non-fatal stroke events	285	1,525	895
Incident rate (fatal and non-fatal stroke events) (per 1,000 person year)	2.58	1.30	0.96
Socio-demographics			
Age	58.73 (7.54)	56.85 (8.04)	54.96 (8.08)
Ethnicity			
White	16,518 (89.57)	181,005 (94.47)	148,202 (96.80)
Mixed	471 (2.55)	2,798 (1.46)	1,653 (1.08)
Asian	861 (4.67)	4,019 (2.10)	1,447 (0.95)
Black	466 (2.53)	3,068 (1.60)	1,551 (1.01)
Chinese	126 (0.68)	708 (0.37)	244 (0.16)

Townsend Deprivation index (quartile)			
1 (Least deprived)	4,756 (25.79)	66,595 (34.76)	56,988 (37.22)
2	5,798 (31.44)	66,087 (34.49)	52,990 (34.61)
3 (Most deprived)	7,888 (42.77)	58,916 (30.75)	43,119 (28.16)
Income			
<18,000	6,342 (41.83)	36,480 (22.09)	19,491 (14.26)
18,000 to 30,999	3,961 (26.12)	44,497 (26.94)	30,684 (22.44)
31,000 to 51,999	2,969 (19.58)	44,305 (26.82)	38,959 (28.50)
52,000 to 100,000	1,564 (10.32)	32,316 (19.56)	36,440 (26.65)
Greater than 100,	326 (2.15)	7,578 (4.59)	11,142 (8.15)
Professional qualifications			
College or University degree	5,112 (39.83)	67,910 (43.18)	70,226 (51.01)
A levels*/AS levels† or equivalent	1,686 (13.14)	20,935 (13.31)	19,463 (14.14)
O levels‡/GCSEs§ or equivalent	3,763 (29.32)	43,438 (27.62)	31,751 (23.06)
CSEs or equivalent/ NVQ| | or	2,272 (17.70)	24,981 (15.88)	16,226 (11.79)

HND# or HNC* * or equivalent			
Employment status			
In paid employment/self-employed	6,730 (36.49)	111,488 (58.19)	103,671 (67.72)
Retired	8,097 (43.91)	67,248 (35.10)	40,967 (26.76)
Looking after home and or family	562 (3.05)	5,534 (2.89)	4,334 (2.83)
Unable to work due to sickness or disability	2,537 (13.76)	2,756 (1.44)	935 (0.61)
Unemployed	399 (2.16)	3,248 (1.70)	2,028 (1.32)
Doing unpaid / voluntary work	67 (0.36)	867 (0.45)	738 (0.48)
Full- or part-time student	50 (0.27)	457 (0.24)	424 (0.28)
Health			
Systolic BP†† (mmHg) ‡‡	138.79 (18.63)	138.79 (18.63)	135.85 (18.36)
Diastolic BP†† (mmHg) ‡‡	82.82 (11.08)	82.71 (10.68)	81.39 (10.58)
Handgrip strength (kg)	30.59 (10.87)	30.59 (10.87)	32.43 (10.84)

MABP‖ || | (mmHg) ‡‡	101.78 (12.27)	101.41 (12.19)	99.58 (12.58)
Smoking			
Never	8,946 (48.51)	106,011 (55.33)	90,139 (58.88)
Previous	6,934 (37.60)	66,891 (34.91)	50,507 (32.99)
Current	2,562 (13.89)	18,696 (9.76)	12,451 (8.13)
BMI§§			
Underweight	46 (0.25)	606 (0.32)	1,096 (0.72)
Normal	2,603 (14.11)	52,034 (27.16)	68,617 (44.82)
Overweight	6,133 (33.26)	86,266 (45.02)	64,429 (42.08)
Obese	9,660 (52.38)	52,692 (27.50)	18,955 (12.38)
Diabetes			
Yes	2,342 (12.70)	9,263 (4.83)	3,344 (2.18)
BP history			
Yes	9,106 (40.78)	51,612 (25.94)	27,594 (17.69)

Medication			
Cholesterol lowering medication	3,289 (17.83)	20,029 (10.45)	137,018 (89.50)
BP medication	1,129 (6.12)	9,076 (4.74)	10,678 (6.97)
Diabetes medication (insulin)	24 (0.13)	115 (0.06)	66 (0.04)
Self-reported overall health rating			
Excellent	655 (3.55)	25,660 (13.39)	40,897 (26.71)
Good	6,514 (35.32)	120,807 (63.05)	94,343 (61.62)
Fair	7,883 (42.74)	41,324 (21.57)	16,684 (10.90)
Poor	3,390 (18.38)	3,807 (1.99)	1,173 (0.77)
Lifestyle			
Total PA (MET/minute/week)	2804.92 (3016.41)	2804.92 (3016.41)	3064.30 (3130.28)
TV viewing	2.85 (1.49)	2.85 (1.49)	2.41 (1.37)
Fruit/Vegetables (g/day)	195.07 (144.32)	195.07 (144.32)	213.15 (146.12)
Red meat intake (portion/week)	2.13 (1.41)	2.13 (1.41)	2.00 (1.36)

Oily fish (portion/week)	1.62 (0.91)	1.62 (0.91)	1.71 (0.91)
Alcohol intake (frequency/week)	3.47 (1.66)	2.93 (1.49)	2.68 (1.41)

*: **Advanced Levels, †: Advanced subsidiary levels, ‡: Ordinary levels,** §: **General Certificate of Secondary Education; ǁ: National Vocational Qualification; #: Higher National Diploma; * *: Higher National Certificate;** ††: **Blood pressure;** ‡‡: **millimetres of mercury;** §§: **Body Mass Index; ǁ ǁ: Mean Arterial Blood Pressure**

Table 2 Cox proportional hazard models of the associations between self-reported walking pace and risk of incident stroke

	Total (n)*	**Events (n)**	**HR (95% CI†)**	**p-value**
Model 0	363,137	2705		
Slow pace			1.58 (1.39; 1.80)	<0.0001
Brisk pace			0.89 (0.82; 0.97)	0.007
Model 1	363,137	2705		
Slow pace			1.36 (1.19; 1.56)	<0.0001
Brisk pace			0.89 (0.81;0.98)	0.02
Model 2	363,137	2705		

Slow pace			1.45 (1.26; 1.66)	<0.0001
Brisk pace			0.96 (0.86; 1.05)	0.36

***: number of participants, †: Confidence interval. The reference category was "average walking pace", with HRs of 1.00**

Table 3- Association between walking pace and incident stroke, up to October 2016- by age group, deprivation, and BMI

Age	**<55 years**				**55-64years**				**65+years**			
	Total n	**Events**	**HR (95%CI)**	**p-value**	**Total n**	**Events**	**HR (95%CI)**	**p-value**	**Total n**	**Events**	**HR (95%CI)**	**p-value**
Model 0	146,942	448			152,188	1177			64,007	1080		
Slow pace			1.57 (1.06; 2.32)	0.02			1.50 (1.22; 1.84)	<0.001			1.70 (1.41; 2.03)	<0.0001
Brisk pace			0.89 (0.73; 1.08)	0.25			0.90 (0.80; 1.02)	0.10			0.85 (0.74; 0.97)	0.02

Model 1	146,942	448			152,188	1177			64,007	1080		
Slow pace			1.35 (0.90; 2.01)	0.14			1.25 (1.01; 1.55)	0.04			1.51 (1.25; 1.83)	<0.0001
Brisk pace			0.96 (0.78; 1.16)	0.66			0.99 (0.87; 1.13)	0.93			0.89 (0.77; 1.03)	0.12
Model 2	146,942	448			152,188	1177			64,007	1080		
Slow pace			1.25 (0.84; 1.88)	0.27			1.16 (0.93; 1.45)	0.17			1.42 (1.17; 1.73)	<0.0001
Brisk pace			0.98 (0.80; 1.20)	0.87			1.04 (0.91; 1.18)	0.55			0.94 (0.81; 0.08)	0.34
Deprivation	**Tertile 1**				**Tertile 2**				**Tertile 3**			
Model 0	121,054	840			121,046	919			121,037	946		

Slow pace			1.48 (1.13; 1.95)	0.005			1.67 (1.33; 2.09)	<0.0001			1.65 (1.36 1.99)	<0.0001
Brisk pace			0.89 (0.11; 0.77)	0.11			0.88 (0.77; 1.02)	0.08			0.84 (0.72; 0.97)	0.02
Model 1	121,054	840			121, 046	919			121,037	946		
Slow pace			1.34 (0.01; 1.78)	0.04			1.33 (1.05; 1.69)	0.02			1.40 (1.15; 1.72)	0.001
Brisk pace			0.94 (0.81; 1.09)	0.45			0.99 (0.85; 1.14)	0.84			0.92 (0.79; 1.07)	0.25
Model 2	121,054	840			121, 046	919			121,037	946		
Slow pace			1.23 (0.92; 1.63)	0.16			1.23 (1.01; 1.64)	0.04			1.29 (1.06; 1.59)	0.01
Brisk pace			0.99 (0.85; 1.15)	0.91			1.03 (0.89;1.19)	0.73			0.97 (0.84;1.14)	0.75

BMI	Normal				Overweight				Obese			
	Total n	**Events**	**HR (95%CI)**	**p-value**	**Total n**	**Events**	**HR (95%CI)**	**p-value**	**Total n**	**Events**	**HR (95%CI)**	**p-value**
Model 0	125,002	743			156,828	1212			81,307	750		
Slow pace			1.36 (0.94; 1.96)	0.09			1.65 (1.33; 2.04)	<0.0001			1.50 (1.24; 1.80)	<0.0001
Brisk pace			0.89 (0.77; 1.03)	0.13			0.90 (0.79; 1.02)	0.11			0.97 (0.80; 1.18)	0.75
Model 1	125,002	743			156,828	1212			81,307	750		
Slow pace			1.15 (0.79; 1.67)	0.46			1.44 (1.15; 1.79)	0.001			1.38 (1.13; 1.68)	0.001
Brisk pace			0.95 (0.81; 1.67)	0.46			0.95 (0.84; 1.08)	0.44			1.01 (0.83; 1.22)	0.93

Model 2	125,002	743			156, 828	1212			81,307	750		
Slow pace			1.06 (0.73; 1.55)	0.75			1.31 (1.05; 1.63)	0.02			1.34 (1.09; 1.63)	0.004
Brisk pace			0.98 (0.84; 1.15)	0.84			1.01 (0.87; 1.14)	0.93			1.03 (0.85; 1.25)	0.79

***: number of participants, †: Confidence interval. The reference category was "average walking pace", with HRs of 1.00**

Table 4- Association between walking pace and incident stroke, up to October 2016- by sex

	Female				**Male**			
	Total n	**Events**	**HR (95%CI)**	**p-value**	**Total n**	**Events**	**HR (95%CI)**	**p-value**
Model 0	195,843	1093			167,294	1612		

Slow pace			1.87 (1.55; 2.27)	<0.0001			1.39 (1.17;1.66)	<0.0001
Brisk pace			0.94 (0.82; 1.07)	0.35			0.86 (0.77;0.96)	0.006
Model 1	195,843	1093			167,294	1612		
Slow pace			1.58 (1.29; 1.94)	<0.0001			1.22 (1.02;1.46)	0.03
Brisk pace			1.02 (0.89;1.17)	0.81			0.92 (0.82; 1.03)	0.13
Model 2	195,843	1093			167,294	1612		
Slow pace			1.50 (1.23; 1.84)	<0.0001			1.14 (0.95;1.36)	0.17
Brisk pace			1.06 (0.93; 1.02)	0.39			0.96 (0.86; 1.07)	0.45

***: number of participants, †: Confidence interval. The reference category was "average walking pace", with HRs of 1.00**