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## **Age- and Gender-Specific Prevalence of Cardiovascular Risk Factors in 40 102 Patients With First-Ever Ischemic Stroke. A Nationwide Danish Study**

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*Stroke* published online Oct 21, 2010;

DOI: 10.1161/STROKEAHA.110.595785

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214

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ISSN: 1524-4628

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# Age- and Gender-Specific Prevalence of Cardiovascular Risk Factors in 40 102 Patients With First-Ever Ischemic Stroke

## A Nationwide Danish Study

Klaus Kaae Andersen, MS, PhD; Zorana Jovanovic Andersen, PhD; Tom Skyhøj Olsen, MD, PhD

**Background and Purpose**—We describe the prevalence of cardiovascular risk factors at stroke onset in men and women of all ages.

**Methods**—A registry started in 2001, designed to register all hospitalized stroke patients in Denmark, now holds 40 102 patients with first-ever ischemic stroke. Patients underwent evaluation including stroke severity (Scandinavian Stroke Scale), CT, and cardiovascular risk factors: hypertension, atrial fibrillation, diabetes mellitus, intermittent arterial claudication, previous myocardial infarction, body mass index, smoking, and alcohol consumption. We estimated the independent effect of gender and age on prevalence of cardiovascular risk factors and calculated age and gender-specific prevalence rates for each risk factor.

**Results**—The register contained 47.9% women and 52.1% men. Men had more often diabetes mellitus, previous myocardial infarction, intermittent arterial claudication, and over the limit alcohol consumption. Women had more often hypertension and obesity. Atrial fibrillation and smoking were equally frequent in both genders. Age stratification revealed that the lifestyle cardiovascular risk factors smoking, alcohol, and obesity were more common in the younger patients with stroke (<60 years), whereas prevalence of hypertension, diabetes mellitus, myocardial infarction, intermittent arterial claudication, and, in men, also atrial fibrillation decreases in the elderly (>70 to 80 years), the decrease being generally more pronounced in men than in women.

**Conclusion**—Cardiovascular risk factors were generally more prevalent in men. Lifestyle cardiovascular risk factors were more common in the young. Prevalence of hypertension, diabetes mellitus, coronary heart disease, and, in men, also atrial fibrillation go down after the age of 70 to 80 years. (*Stroke*. 2010;41:00-00.)

**Key Words:** gender ■ ischemic stroke ■ prevalence ■ risk factors

Women and men share the same traditional risk factors for stroke. However, at stroke onset, atrial fibrillation (AF) and hypertension are more prevalent in women in most reports, whereas in men, prevalence of heart disease, peripheral artery disease, diabetes mellitus (DM), smoking, and alcohol consumption is higher.<sup>1</sup>

Prevalence of stroke risk factors may vary with age and stroke due to individual risk factors may vary with age as well.<sup>2</sup> Life expectancy is longer for women<sup>3</sup> and women are older than men at stroke onset.<sup>4</sup> Risk factors that exert the highest effect in the elderly may, therefore, have higher overall impact in women compared with men. Traditional risk factors for stroke are all associated with excess mortality in men and women.<sup>3</sup> Therefore, so-called mortality displacement (ie, decrease in prevalence of the risk factor in the population due to excess mortality of individuals having the risk factor) may influence prevalence rates, especially in the elderly.<sup>5</sup> Neverthe-

less, the risk factor profile at stroke onset is usually presented as an average and not stratified according to age.<sup>6-11</sup>

An ongoing nationwide Danish stroke registry designed to include all patients hospitalized with acute stroke in Denmark now includes 40 102 patients with acute first-ever ischemic stroke, enabling a national study on cardiovascular risk factors at stroke onset separately in men and women at all ages.

### Methods

The study is based on data from the Danish National Indicator Project described in detail elsewhere.<sup>12,13</sup> Danish hospitals are committed to report a predefined set of data into the National Indicator Project database on all patients admitted to the hospital with acute stroke, including age, gender, admission stroke severity measured by the Scandinavian Stroke Scale (SSS),<sup>14</sup> stroke subtype, and a predefined cardiovascular profile.

The SSS is a validated neurological stroke scale that evaluates stroke severity on a total score from 0 to 58 with lower scores indicating more severe strokes.<sup>14</sup> Distinction between ischemic and

Received July 4, 2010; final revision received August 31, 2010; accepted September 7, 2010.

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Stroke is available at <http://stroke.ahajournals.org>

DOI: 10.1161/STROKEAHA.110.595785

hemorrhagic stroke was determined after CT/MR scan. The cardiovascular profile included information on: alcohol consumption (14 and/21 drinks per week for women and men, respectively; under/over the limit set by the by the Danish National Board of Health), current daily smoking, body mass index (BMI), DM, AF (chronic or parasytic), arterial hypertension, previous myocardial infarction, previous stroke, and intermittent arterial claudication. Diagnosis of DM, AF, arterial hypertension, previous myocardial infarction, previous stroke, and intermittent arterial claudication was made based on current Danish standards<sup>12</sup> and was either known before onset of stroke or diagnosed during hospitalization. Stroke was defined according to the World Health Organization criteria.<sup>15</sup>

This study included only patients with first-ever ischemic stroke admissions (not allowing for any previous stroke) between March 1, 2001, when the National Indicator Project register was established, and November 30, 2009. For patients with multiple records (events), only the first event was included in the analysis. Patients with hemorrhagic stroke, transient ischemic attacks, or patients <18 years were excluded from the study as well as patients in whom CT/MR scan was not performed (0.4%) or unavailable (0.7%). The National Indicator Project registry coverage was by professional consensus estimated to be approximately 80% of all stroke admissions in Denmark.<sup>16</sup> The very high proportion of patients with stroke is admitted to the hospital (90%) due to free hospital care in Denmark.<sup>17</sup>

The study was approved by the board of National Indicator Project and the Danish Data Protection Agency.

## Statistical Analyses

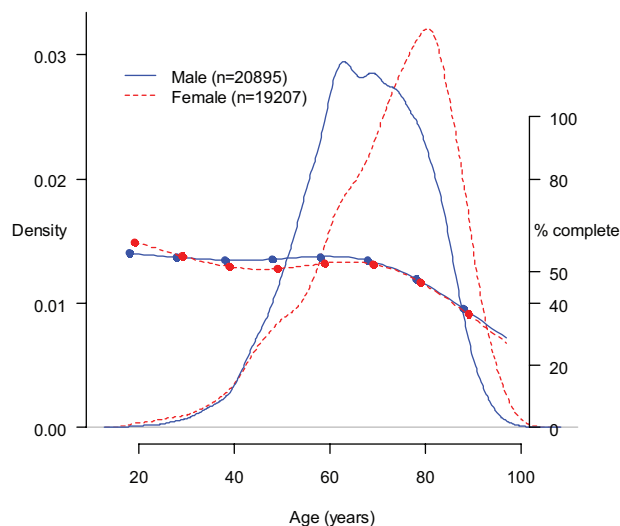
A generalized additive logistic regression model was used to estimate the effect of gender on prevalence of various cardiovascular risk factors. The model was fitted separately for each of the 9 cardiovascular risk factors defined as a binary outcome: DM (yes/no), previous myocardial infarction (yes/no), AF (yes/no), hypertension (yes/no), intermittent claudication (yes/no), smoking (current smoker/ex- or never smoker), alcohol ( $\leq 14/21$  drinks per week for women and men, respectively), and BMI (obese: BMI  $\geq 30$  kg/m<sup>2</sup>; not obese:  $< 30$  kg/m<sup>2</sup>) and adjusted for age, SSS score, and all other (than 1 used as an outcome) cardiovascular risk factors. Age and SSS score were modeled as continuous variables using smooth splines (penalized cubic regression spline with 4 degrees of freedom) to allow for the nonlinear effects of the 2. We performed analyses in R statistical software and estimated ORs and 95% CIs.

Crude age- and gender-specific prevalence rates with 95% CIs were fitted for each of the 9 risk factors using generalized additive logistic regression model and presented graphically.

## Results

Of the 40 102 first-ever ischemic stroke hospital admissions, 19 207 (47.9%) were by women and 20 895 (52.1%) by men. Mean age in women was 73.2 years (SD 14.5) and in men 68.1 years (SD 12.8) years. Age distribution of male and female patients at hospital admission is shown in Figure 1. Mean SSS score was 42.1 (SD 16.1) in women and 45.7 (SD 14.1) in men. SSS score distributions for men and women are presented in Figure 2. SSS scores were missing for 5323 (13.2%) of the 40 102 patients with stroke, 2618 (12.9%) for men and 2705 (13.6%) for women. Percent of participants without missing observations for 8 risk factors (Table 1) appears in Figure 1 and 2.

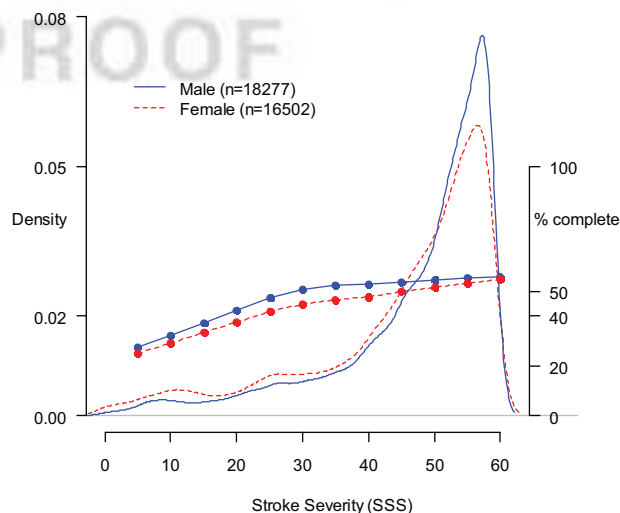
Descriptive statistics for cardiovascular risk factor profile variables can be seen in Table 1 and Table 2. Table 1 is based on data sets with maximum number of observations for each risk factor, whereas Table 2 is based on a data set in which all missing information for all covariates was excluded. Results were almost identical. Adjusting for age, gender, stroke severity, and cardiovascular risk profile variables (Table 2), it



**Figure 1.** Distribution of age and percent of participants without missing observations for 8 risk factors (dotted lines) for 40 102 patients admitted for first-ever ischemic stroke by gender.

appeared that men had more often DM, previous myocardial infarction, intermittent arterial claudication, and over the limit alcohol consumption than women. Women had more often hypertension and were more often obese (BMI  $\geq 30$  kg/m<sup>2</sup>). No significant difference in prevalence of AF and smoking were observed between men and women. Women had more missing data for each cardiovascular risk factor variable than men.

Prevalence of risk factors at stroke onset in patients with first-ever ischemic stroke stratified according to age and gender is shown in Figure 3 and 4. Figure 3 is based on data sets with maximum number of observations for each risk factor, whereas Figure 4 is based on a data set in which all missing information for all covariates was excluded. Results were almost identical.



**Figure 2.** Distribution of SSS score (lower score indicating more severe strokes) and percent of participants without missing observations for 8 risk factors (dotted lines) for 34 779 patients admitted for first-ever ischemic stroke by gender who had available SSS scores.

**Table 1. Cardiovascular Risk Profile (Overall and by Gender) for 40 102 Patients With Ischemic Stroke With First-Ever Stroke and Nonadjusted Associations Between Gender and Each Cardiovascular Risk Profile Variable**

Cardiovascular Profile	Variable Definition	All (n=40 102) No. (%)	Men (n=20 895) No. (%)	Women (n=19 207) No. (%)	Men Versus Women Univariate OR (95% CI)
Hypertension	Yes	18 369 (45.8)	9183 (43.9)	9186 (47.8)	0.85 (0.82–0.88)
	No	20 612 (51.4)	11 141 (53.3)	9471 (49.3)	
	Missing	1121 (2.8)	571 (2.7)	550 (2.9)	
AF	Yes	6111 (15.2)	2742 (13.1)	3369 (17.5)	0.70 (0.67–0.74)
	No	33 250 (82.9)	17 781 (85.1)	15 469 (80.5)	
	Missing	741 (1.8)	372 (1.8)	369 (2.0)	
DM	Yes	5009 (12.5)	2836 (13.6)	2173 (11.3)	1.22 (1.15–1.30)
	No	34 590 (86.3)	17 830 (86.3)	16 760 (87.3)	
	Missing	503 (1.3)	229 (1.1)	274 (1.4)	
Previous myocardial infarction	Yes	3392 (8.5)	2196 (10.5)	1196 (6.2)	1.76 (1.63–1.89)
	No	35 880 (89.5)	18 330 (87.7)	17 550 (91.4)	
	Missing	830 (2.1)	369 (1.8)	461 (2.4)	
Intermittent arterial claudication	Yes	1260 (3.1)	757 (3.6)	503 (2.6)	1.37 (1.22–1.54)
	No	35 638 (88.9)	18 642 (89.2)	16 996 (88.5)	
	Missing	3204 (8.0)	1496 (7.2)	1708 (8.9)	
Alcohol consumption	Over limit*	2995 (7.5)	2387 (11.4)	608 (3.2)	3.77 (3.44–4.12)
	Under limit	31 901 (79.5)	16 276 (77.9)	15 625 (81.4)	
	Missing	5206 (13.0)	2232 (10.7)	2974 (15.5)	
Smoking	Current	13 718 (34.2)	8216 (39.3)	5502 (28.6)	1.15 (0.98–1.36)
	Previous/never	20 476 (51.1)	10 191 (48.8)	10 285 (53.5)	
	Missing	5908 (14.7)	2488 (11.9)	3420 (17.9)	
BMI	Obese†	4392 (11.0)	2395 (11.5)	1997 (10.4)	1.10 (1.04–1.18)
	Not obese	21 499 (53.6)	11 166 (53.4)	10 333 (53.8)	
	Missing	14 211 (35.4)	7334 (35.1)	6877 (35.7)	

\*Defined as &gt;14 and 21 drinks per week for women and men, respectively.

†Defined as BMI  $\geq 30$  kg/m<sup>2</sup>.

Hypertension was slightly more prevalent in men until the age of approximately 50 years, whereas in the age interval 50 to 70 years, prevalence of hypertension was the same in the 2 genders. However, after the age of 70 to 80 years, prevalence decreased in both genders; however, the decrease was slightly steeper in men. AF was equally prevalent in men and women until the age of 80, after which the prevalence increased slightly more in women as compared with men. After the age of approximately 85 years, the prevalence of AF decreased in men at the same time as showing a continued increase in women. DM was more prevalent in men up to the age of 80 years after which it became equally prevalent in men and women. A steep decrease in the DM prevalence among men was seen after the age of 70 years, whereas in women, a decrease of prevalence took place after the age of 80 years. Previous myocardial infarction was consistently more prevalent in men, reaching a maximum at the age of 75 and 85 years in men and women, respectively. Thereafter, prevalence decreased in both genders, however more steeply in men. Prevalence of intermittent arterial claudication showed almost identical age distribution in men and women with consistently higher prevalence in men and showing a decline in both genders after the age of 75 years and on. Over the limit

alcohol consumption was consistently higher in men. Notably, prevalence of over the limit alcohol consumption was as high as 20% in men aged 50 to 60 years of age compared with 7% in women of the same age. After the age of 50 to 60 years, the prevalence of over the limit alcohol consumption decreased in both genders, however more steeply in men. Smoking prevalence was slightly lower among women following a similar age distribution as in men. However, the gender difference in smoking prevalence was small, 7% at the highest at the age of 50 years, and gender was not a significant predictor of smoking in our multivariate analysis (Table 2). At a peak at the age of approximately 50 years, smoking prevalence was very high, approximately 60%, in both genders after which smoking prevalence continuously decreased in both genders. Prevalence of obesity was at the highest in the younger patients with stroke, decreasing with increasing age in both genders after the age of 50 to 60 years. Obesity was more prevalent among women until the age of 50 years, being equally prevalent afterward. After the age of 50 to 60 years, the prevalence of obesity gradually decreased in both genders.

## Discussion

Hypertension, DM, AF, and high cholesterol are the highest ranking controllable medical risk factors for stroke, whereas

**Table 2. Cardiovascular Risk Profile (Overall and by Gender) for 19 491 Patients With First-Ever Ischemic Stroke (Without Missing Observations for 8 Risk Factors) and Associations Between Gender and Each Cardiovascular Risk Profile Variable**

Cardiovascular Profile	Variable Definition	All (n=19 491) No. (%)	Men (n=10 584) No. (%)	Women (n=8907) No. (%)	Men Versus Women Univariate OR (95% CI)	Men Versus Women Multivariate* OR (95% CI)
Hypertension	Yes	9354 (48.0)	4869 (46.0)	4485 (50.4)		
	No	10 137 (52.0)	5715 (54.0)	4422 (49.6)	0.84 (0.80–0.89)	0.86 (0.82–0.90)
AF	Yes	2542 (13.0)	1207 (11.4)	1335 (15.0)		
	No	16 949 (87.0)	9377 (88.6)	7572 (85.0)	0.73 (0.67–0.79)	1.05 (0.99–1.12)
DM	Yes	2354 (12.1)	1398 (13.2)	956 (10.7)		
	No	17 137 (87.9)	9186 (86.8)	7951 (89.3)	1.26 (1.19–1.34)	1.22 (1.15–2.31)
Previous myocardial infarction	Yes	1525 (7.8)	1022 (9.7)	503 (5.6)		
	No	17 966 (92.2)	9562 (90.3)	8404 (94.4)	1.78 (1.60–1.78)	2.08 (1.92–2.22)
Intermittent claudication	Yes	685 (3.5)	403 (3.8)	282 (3.2)		
	No	18 806 (96.5)	10 181 (96.2)	8625 (96.8)	1.21 (1.03–1.41)	1.30 (1.18–1.44)
Alcohol consumption	Over limit†	1681 (8.6)	1352 (12.8)	329 (3.7)		
	Under limit	17 810 (91.4)	9232 (87.2)	8578 (96.3)	3.82 (3.37–4.32)	3.03 (2.78–3.32)
Smoking	Current	7782 (39.9)	4685 (44.3)	3097 (34.8)		
	Previous/never	11 709 (60.1)	5899 (55.7)	5810 (65.2)	1.05 (0.85–1.31)	1.07 (0.92–1.26)
BMI	Obese‡	3363 (17.3)	1885 (17.8)	1478 (16.6)		
	Not obese	16 128 (62.7)	8699 (82.2)	7429 (83.4)	1.08 (1.02–1.09)	0.89 (0.83–0.95)

\*Adjusted for age, SSS score and all other (than 1 used as an outcome) cardiovascular risk profile variables.

†Defined as >14 and 21 drinks per week for women and men, respectively.

‡Defined as BMI  $\geq$ 30 kg/m<sup>2</sup>.

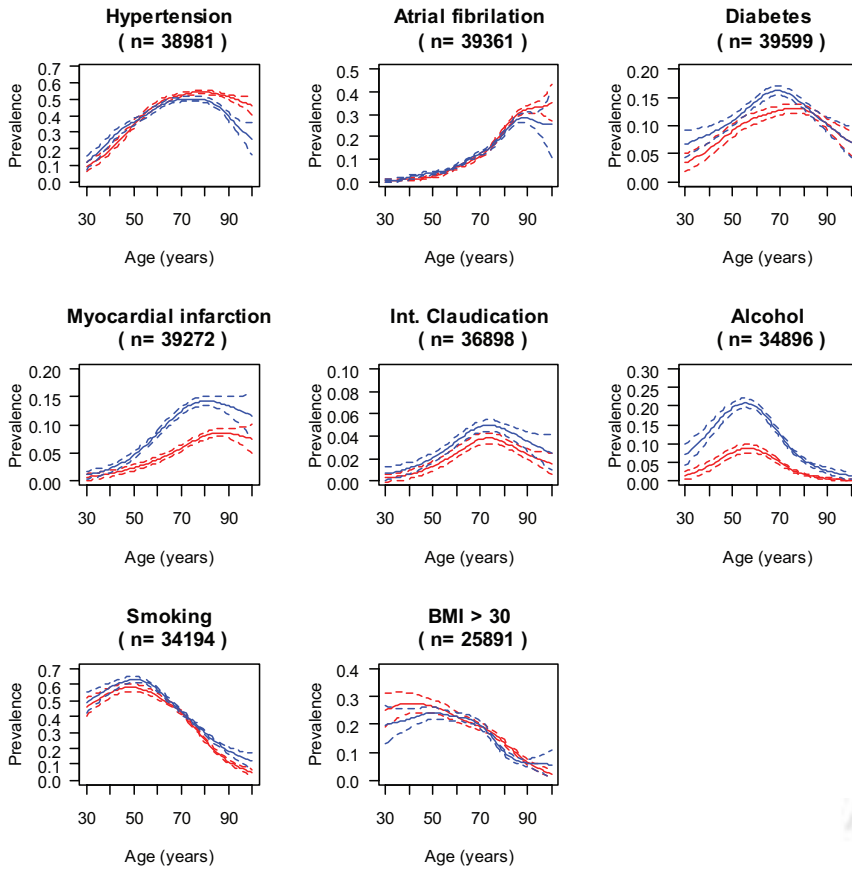
smoking, alcohol consumption, and obesity rank as the most important lifestyle stroke risk factors.<sup>2</sup> Among predisposing diseases, coronary artery diseases are particularly associated with a higher risk of stroke.<sup>2</sup> A recent review on gender differences in stroke concluded that women with stroke are more likely to have hypertension and AF, whereas in men with stroke, heart disease, myocardial infarction, peripheral arterial disease, DM, and alcohol and tobacco use were more likely.<sup>1</sup>

This study revealed complex interactions among age, gender, and prevalence of stroke risk factors in patients admitted with first-ever ischemic stroke. The prevalence of hypertension, DM, myocardial infarction, intermittent arterial claudication, and, in men, also AF decreases in the elderly (>70 to 80 years), the decrease being generally more pronounced in men than in women. Stroke risk factors were mostly more prevalent in men before the age of 70 to 80 years after which gender differences tended to equalize except for hypertension and AF, both being relatively more prevalent in women. The lifestyle cardiovascular risk factors, including smoking, alcohol, and obesity, were all more common in the younger patients with stroke (<60 years).

Our study's strength is first of all its large sample size. Second, our study is a nationwide study designed to include all hospitalized patients with stroke in Denmark without limitations on age, gender, or stroke severity. Third, our patients are well characterized on admission. Of the 40 102 patients, data completeness regarding DM, previous myocardial infarction, AF, and hypertension was very high (>97%). For alcohol consumption, smoking, and intermittent arterial claudication, data completeness was still quite high, >85%. Data completeness for BMI was only 64.6%; however,

approximately 26 000 patients with data on BMI is still to date the largest number published with respect to stroke. Generally, more data were missing for women for all risk factors, but women were also older and had more severe strokes at admission. As shown in Figures 1 and 2, the number of missing data was positively related to age and stroke severity, because it was more difficult to obtain data from older and sicker patients, and not to gender, and that our observations about gender differences are not result of selection bias. However, we cannot exclude the possibility of underestimation of the risk factors leading to severe strokes or strokes in very old patients, because there are more missing data in these groups. However, almost identical results observed with data with maximum number of observations for each risk factor and a reduced data set free of missing values for all covariates argue against selection bias.

Hypertension is slightly more prevalent in men until the age of 45 years.<sup>18</sup> Thereafter, prevalence becomes increasingly (although slightly) higher in women until the age of 65 after which the difference between men and women accelerates because prevalence in women continues to increase, whereas it levels off in men after that age.<sup>18</sup> We observed the same pattern in our stroke cohort. It cannot be excluded that our observation is due to decreasing risk of stroke due to hypertension after the age of approximately 70 years and that this is particularly the case for men. However, our observation might as well reflect mortality displacement,<sup>5</sup> that is, a decrease in the prevalence of hypertension in the population due to excess mortality of men with hypertension. In the latter case, a higher prevalence of hypertension among women than men with stroke might be considered an artifact due to



**Figure 3.** Age- and gender-specific prevalence rates with 95% CIs for the 8 risk factors for 40 102 patients admitted for first-ever ischemic stroke. Men, blue; women, red.

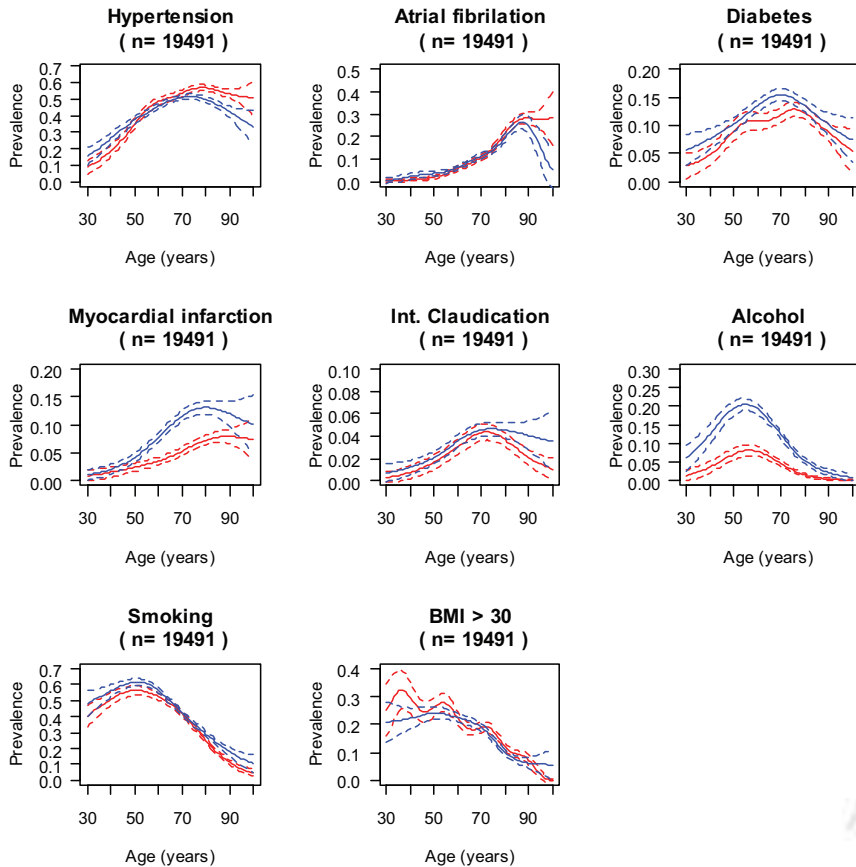
mortality displacement rather than a true gender difference in occurrence of hypertension.

AF is consistently more prevalent in men than in women.<sup>19</sup> Most studies report, however, higher prevalence of AF among women with stroke.<sup>6–11</sup> This contradictory finding could be explained by a higher risk of stroke in females with AF as reported from the Copenhagen City Heart Study and in the Stroke Prevention in Atrial Fibrillation (SPAF) studies.<sup>20,21</sup> In the latter studies, however, stroke risk was only higher in women with AF >75 years of age, and it cannot be excluded that higher risk of stroke in these women relative to men only reflects that excess mortality in men with AF reduces their chance to survive to that age, that is, mortality displacement. In our study, prevalence of AF did not differ much in men and women at any age except for the oldest patients, in which prevalence of AF in men declines. To determine whether excess mortality among men with AF or higher risk of stroke in women with AF is the cause of our observation, population-based studies of mortality in patients with AF are needed. Prevalence of DM is higher in men in all ages except for the oldest patients, in whom prevalence rates are similar for men and women.<sup>22</sup> We observed a similar pattern in our stroke cohort. Prevalence rates decreased after the age of 70 and 80 years in men and women, respectively, either as the result of mortality displacement or lower risk of stroke in the elderly with DM. Prevalence of previous myocardial infarction is higher in men until the 7th decade when prevalence rates become higher in women.<sup>23</sup> In our stroke cohort, prevalence rates of previous myocardial infar-

tion in men was twice as high as in women and prevalence remained higher in men in all ages. Prevalence of previous myocardial infarction declined from the age of 75 and 85 years in men and women, respectively. Again, mortality displacement or lower risk of stroke in the elderly with previous myocardial infarction is the most likely explanation of our observation. Intermittent arterial claudication was more prevalent in men; however, prevalence rates paralleled in men and women, indicating that intermittent arterial claudication associates with stroke in the same way in men and women.

In Denmark, obesity is slightly more prevalent in men than in women, but the difference is small (14% in men versus 12% in women aged 45 to 79 years).<sup>24</sup> In the United States, prevalence of obesity is much higher than in Denmark and slightly higher in women (33% in men versus 37% in women aged 65 to 74 years).<sup>18</sup> In our stroke cohort, obesity was slightly more prevalent among women. Prevalence of obesity among patients with stroke in our cohort was at the highest in the young (40 to 50 years), whereas in the Danish background population, obesity is most prevalent in the age group 65 to 79 years. This is in line with findings of an association between obesity and risk of cardiovascular disease in middle-aged individuals and not in the elderly.<sup>25,26</sup>

Prevalence of alcohol consumption over the limit in the Danish background population (men >21 drinks, women >14 drinks per week) is on average 1.6 higher in men,<sup>24</sup> whereas in our stroke cohort, it was on average 3 times higher in men. Prevalence peaked at the age of 55 years. Excessive



**Figure 4.** Age- and gender-specific prevalence rates with 95% CIs for the 8 risk factors for 19 491 patients (without missing observations for 8 risk factors) admitted for first-ever ischemic stroke. Men, blue; women, red.

alcohol consumption is known to increase risk of stroke,<sup>2</sup> and this may explain the much higher prevalence of drinking over the limit among young and middle-aged men in our stroke cohort.

Smoking in the Danish background population is on the whole only 3% less prevalent in women compared with men (27.8% versus 31.6%).<sup>24</sup> Likewise, in our stroke cohort, prevalence was only slightly lower among women, and in our multivariate analysis, gender was not significantly associated with smoking. Prevalence paralleled in men and women and peaked, like in the background population, at the age of approximately 50 years in both genders,<sup>24</sup> indicating that smoking influences the risk of stroke in the same way and magnitude in men and women. Although the overall prevalence of smoking in our stroke cohort is 33% higher than in the Danish background population (40% versus 30%),<sup>24</sup> it is impressive to realize that at the age of 50 years, when prevalence of smoking is peaking, prevalence in the stroke cohort is twice the prevalence in the background population at the same age (approximately 60% versus 30%). We find this observation to indicate that smoking introduces a very high risk of stroke in young and middle-aged individuals.

### Conclusion

Age stratification in the evaluation of risk factor prevalence in patients with first-ever ischemic stroke revealed that prevalence of hypertension, DM, myocardial infarction, intermittent arterial claudication, and, in men, also AF declined after the age of 70 to 80 years. This might either be due to

lower risk of stroke associated with these risk factors in the elderly or mortality displacement reflecting continuous natural selection of individuals with the fewest cardiovascular risk factors. The lifestyle cardiovascular risk factors were most prevalent in the younger end of the age spectrum suggesting a high impact of lifestyle on risk of stroke in the young. Our study indicates that focus on lifestyle modification for primary as well as secondary prevention of stroke is of particular importance in the young.

### Disclosures

None.

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