Lifestyle Factors and Early Clinical Outcome in Patients With Acute Stroke
A Population-Based Study

Annette Ingeman, PhD; Grethe Andersen, DMSci; Reimar W. Thomsen, PhD;
Heidi H. Hundborg, PhD; Henrik H. Rasmussen, PhD; Søren P. Johnsen, PhD

Background and Purpose—We examined the associations of individual and combined lifestyle factors with early adverse stroke outcomes.

Methods—A total of 82 597 patients were identified from nationwide registries. Lifestyle factors at the time of stroke admission included body mass index (kg/m^2), smoking habits, and alcohol intake, which were grouped (healthy, moderately healthy, moderately unhealthy, and unhealthy). The associations between lifestyle and outcomes were examined using multivariable regression.

Results—A total of 18.3% had a severe stroke, 7.8% pneumonia, 12.5% urinary tract infection, and 9.9% died within 30 days. The association between lifestyle, stroke severity, and mortality, respectively, differed according to sex. Unhealthy lifestyle was associated with lower risk of severe stroke (adjusted odds ratio [OR], 0.73; 95% confidence interval [CI], 0.63–0.84) and 30-day mortality among men (adjusted OR, 0.71; 95% CI, 0.58–0.87), but not among women (severe stroke: adjusted OR, 1.14; 95% CI, 0.85–1.55, and mortality: adjusted OR, 1.34; 95% CI, 0.90–1.99). No sex differences were found for pneumonia and urinary tract infection. Unhealthy lifestyle was not associated with a statistically significant increased risk of developing in-hospital pneumonia (adjusted OR, 1.30; 95% CI, 0.98–1.73) or urinary tract infection (adjusted OR, 0.98; 95% CI, 0.72–1.33). Underweight was associated with a higher 30-day mortality (men: adjusted OR, 1.71; 95% CI, 1.50–1.96, and women: adjusted OR, 1.46; 95% CI, 1.34–1.60).

Conclusions—Healthy lifestyle was not associated with a lower risk of adverse stroke outcomes, in particularly among men. However, underweight may be a particular concern being associated with an increased risk of adverse outcomes among both sexes. (***Stroke***. 2017;48:611-617. DOI: 10.1161/STROKEAHA.116.015784.)

Key Words: body mass index ■ healthy lifestyle ■ pneumonia ■ registries ■ stroke

Obesity, high alcohol intake, and smoking are all well-established modifiable risk factors for stroke, and they all play a central role for global stroke incidence and mortality.[1] In contrast, there are still significant gaps in the understanding of the prognostic role of lifestyle factors in patients with stroke, including how the potential prognostic effects are mediated and how they potentially interplay.[2] Such knowledge is important because it may help identifying subgroups of patients in need of additional specialized care/attention in the early poststroke phase.

Existing studies on lifestyle factors and stroke outcomes have yielded inconsistent results, and most of the studies are small and have focused on selected individual lifestyle factors and on mortality as the only outcome.[3–10] In addition, most of the existing studies have not been population based and have often been conducted in specialized units which raise concerns about the generalizability of the findings. There is consequently a need for large-scale studies on unselected patients in order better to comprehend the impact of lifestyle on stroke outcomes, including stroke severity, the risk of important medical complications, and mortality in acute stroke care settings. We therefore examined the individual and the combined associations of different lifestyle factors with clinical outcomes among patients admitted with acute stroke in a nationwide study.

Methods

This population-based follow-up study was based on national Danish registries covering the entire population (≈5.6 million). All citizens are assigned a unique 10-digit civil registration number enabling

unambiguous linkage between the registries.[11] The National Health Service provides tax-supported health care to all residents, including free access to hospital care and general practitioners.

The study was approved by The Danish Data Protection Agency (J.no.2007-58-0010).

Study Population

Patients were identified from the Danish Stroke Registry. Reporting is mandatory for all hospitals treating patients for acute stroke (stroke units n=45). The sensitivity and predictive value of the registration of patients in the Danish Stroke Registry have been estimated to be >90%.[12]

We identified all Danes (≥18 years) admitted with acute stroke at any hospital in Denmark from January 13, 2003 to December 31, 2011 (n=82 597; Figure I in the online-only Data Supplement). We only included the first event for patients with multiple recorded events during the study period.

Data on in-hospital pneumonia or urinary tract infection (UTI) were only available from a subset of the stroke units (n=11).

Lifestyle Factors

We assessed body mass index (BMI; kg/m^2), smoking habits (current, former (>1/2 year), or never) and alcohol intake (≤21 versus>21 drinks per week for men and ≤14 versus>14 drinks per week for women, respectively). The cutoff was defined according to the recommendations on maximum alcohol consumption from The Danish National Board of Health.

The selection of the lifestyle factors reflected a combination of biological rationale and data availability. The factors were originally included in the Danish Stroke Registry based on the assumption that the physiological effects of being obese, smoking tobacco, and having a high alcohol intake would have an adverse prognostic effect for stroke patients and that it could be potential confounding factors when monitoring and comparing stroke outcomes over time or between hospitals. Using a standardized registration form, with detailed written instructions, data on the lifestyle factors were prospectively collected at the time of admission as part of the daily clinical work of the health professionals taking care of the patient. The data reflect the BMI, and smoking and alcohol habits at the time of admission.

The following lifestyle combinations were assessed:

Healthy: Nonsmoker, alcohol intake ≤21/14 drinks per week, BMI >18.5 and <24.9 kg/m^2.

Moderately healthy: One adverse lifestyle factor, either current/former smoker or alcohol intake >21/14 drinks per week, or BMI <18.5 or >24.9 kg/m^2.

Moderately unhealthy: Two of the following 4 adverse lifestyle factors: current/former smoker, alcohol intake >21/14 drinks per week, and BMI <18.5 or >24.9 kg/m^2.

Unhealthy: Current/former smoker, alcohol intake >21/14 drinks per week, and BMI <18.5 or >24.9 kg/m^2.

Outcomes

Stroke Severity

Assessed using the Scandinavian Stroke Scale score and classified as severe (0–29 points) or nonsevere (≥30 points).[13–15]

Poststroke Pneumonia and UTI

Pneumonia was defined as clinical findings (fever, pleuritic chest pain, cough, purulent sputum, and either elevated infection parameters or microbiological results) in the medical records and a positive chest radiograph. UTI was defined as clinical symptoms of urinary infection combined with a positive culture (significant bacteriuria (>10⁵/mL). Pneumonia or UTI present already at the time of admission were not considered as poststroke complications. Pneumonia and UTI were included because they are among the most frequent poststroke complications. Furthermore, they are amenable for clinical intervention and prevention, and studies have identified pneumonia to be the most important complication in relation to early mortality.[16]

Thirty-Day Mortality

Assessed based on information from the Danish Civil Registration System, which holds daily updated electronic records on change of address, date of emigration, and changes in vital status.[11]

Covariates

Information on potential confounders was obtained from the Danish Stroke Registry, the National Registry of Patients,[17] the Danish Medicines Agency's Medical Register, and the Integrated Database for Labor Market Research. Data included sociodemographic and clinical factors, including age, sex, marital status, housing, previous stroke, type of stroke, comorbidity included in the Charlson Comorbidity Index, atrial fibrillation, hypertension, employment status, household income, educational level, medication use at the time of admission, quality of in-hospital care, and hospital characteristics (Table I in the online-only Data Supplement).

Statistical Analysis

Logistic (stroke severity, pneumonia, and UTI) and Cox regression (30-day mortality) was used to examined the association between lifestyle and the clinical outcomes. Follow-up started on the admission date and ended after 30 days, on the date of death or emigration, or at the end of the study period. We used a random effects model to correct for possible clustering by stroke unit in all analyses.

We used multiple imputation to impute any missing values among the covariates assuming that data were missing at random.[18] We created 5 data sets on the basis of aforementioned covariates. The outcome measures were averaged across the 5 imputations correction for between and within-imputations. Finally, we performed additional analyses to evaluate the robustness of our findings. First, we stratified all analyses according to age, sex, type of stroke, and Charlson Comorbidity index score to assess whether these acted as effect modifiers on the association between lifestyle factors (the individual or the joint effects) and the clinical outcomes. The prespecified interaction *P* value cutoff was 0.05. Indications of interaction by sex were found in the analyses on stroke severity and 30-day mortality but not for pneumonia and UTI.

Second, a complete case analysis, including only patients with available information on all covariates, was performed to evaluate the impact of missing data.

Results

Characteristics of the study population are presented in Table I in the online-only Data Supplement.

A total of 18.3% had a severe stroke. Table 1 presents the adjusted odds ratios (ORs) for the association between lifestyle factors and stroke severity, which seemed to differ according to sex. A healthy lifestyle was associated with a lower risk of severe stroke among men (adjusted OR, 0.73; 95% confidence interval [CI], 0.63–0.84) but not among women (adjusted OR, 1.14; 95% CI, 0.85–1.55; *P* for interaction: *P*=0.01). Among the individual adverse lifestyle factors, only underweight was associated with a significantly increased risk (men: adjusted OR, 1.51; 95% CI, 1.34–1.70, and women: adjusted OR, 1.34; 95% CI, 1.19–1.52).

During their hospitalization, 7.8% of the patients experienced pneumonia and 12.5% UTI. We found no interaction with sex and therefore present the results of the pooled analyses without stratifying for sex.

Table 1. SSS Outcome After Admission for Stroke According to Lifestyle Factors Present at Admission

Lifestyle Factors	All SSS Outcome Severe (0–29) n (%)	Men, Unadjusted OR (95% CI)	Men Adjusted OR* (95% CI)	Women Unadjusted MRR* (95% CI)	Women Adjusted MRR* (95% CI)
Healthy lifestyle					
Nonsmoker, alcohol intake ≤21/14, BMI >18.5 and <24.9 kg/m²	1048/5875 (17.8)	ref.	ref.	ref.	ref.
Moderate healthy					
1 lifestyle factor present	4260/25 442 (16.7)	0.68 (0.63–0.74)	0.78 (0.71–0.85)	0.77 (0.72–0.82)	0.95 (0.88–1.01)
Moderate unhealthy					
2 lifestyle factors present	4545/27 624 (16.5)	0.53 (0.48–0.58)	0.68 (0.61–0.75)	0.60 (0.56–0.64)	0.87 (0.79–0.95)
Unhealthy					
Smoker, alcohol intake >21/14, and BMI <18.5 and >24.9 kg/m²	579/3189 (18.2)	0.54 (0.49–0.60)	0.73 (0.63–0.84)	0.61 (0.48–0.78)	1.14 (0.85–1.55)
BMI†					
Normal weight, 18.5–24.9 kg/m²	4030/21 202 (19.1)	ref.	ref.		
Underweight, <18.5 kg/m²	873/2953 (29.6)	1.80 (1.62–1.99)	1.51 (1.34–1.70)	1.60 (1.42–1.79)	1.34 (1.19–1.52)
Overweight, 25–29.9 kg/m²	2570/17 327 (14.8)	0.73 (0.68–0.79)	0.85 (0.78–0.92)	0.77 (0.72–0.83)	0.88 (0.80–0.96)
Moderate obesity, 30.0–34.9 kg/m²	862/6205 (13.9)	0.63 (0.58–0.68)	0.76 (0.70–0.83)	0.66 (0.63–0.73)	0.86 (0.78–0.94)
Severe obesity, ≥35 kg/m²	305/2187 (14.0)	0.58 (0.48–0.70)	0.70 (0.60–0.82)	0.57 (0.49–0.67)	0.84 (0.72–0.97)
Alcohol intake§					
≤21/14 drinks per wk‡	9548/56 856 (16.8)	ref.	ref.		
>21/14 drinks per wk†	884/5272 (16.8)	0.90 (0.86–0.99)	1.03 (0.92–1.17)	0.79 (0.70–0.90)	1.06 (0.90–1.25)
Smoking habits‖					
Never smoker	3946/21 475 (18.4)	ref.	ref.		
Current smoker	3407/23 871 (14.3)	0.74 (0.70–0.79)	0.85 (0.79–0.92)	0.73 (0.68–0.78)	0.99 (0.92–1.08)
Former smoker	2365/15 107 (15.7)	0.70 (0.62–0.79)	0.70 (0.62–0.79)	0.62 (0.58–0.67)	0.72 (0.66–0.78)

BMI indicates body mass index; CI, confidence interval; MRR, mortality rate ratio; OR, odds ratio; and SSS, Scandinavian Stroke Scale.

*All analyses are corrected for clustering of patients by stroke unit, age, marital status, housing, profession, alcohol intake (except for lifestyle and alcohol intake), smoking habits (except for lifestyle and smoking), atrial fibrillation, previous stroke, hypertension, Charlson Comorbidity index, type of stroke, hospital setting (university/nonuniversity), stroke unit setting (neurological/non-neurological), patient volume, employment status, personal income, educational level (highest attained), medication use (platelet inhibitors, oral anticoagulants, ACE inhibitors/AT-II blockers, calcium antagonists, β-blockers, statins, thiazides, potassium-sparing and loop diuretics, oral glucose–lowering drugs and insulin), and proportion of relevant in-hospital processes of care received.

†Also corrected for smoking habits and alcohol intake.

‡Also corrected for smoking habits and BMI.

§Drinks per wk for men and women, respectively.

‖Also corrected for alcohol intake and BMI.

Unhealthy lifestyle was not associated with a statistically significantly higher risk of pneumonia (adjusted OR, 1.30; 95% CI, 0.98–1.73) or UTI (adjusted OR, 0.98; 95% CI, 0.72–1.33; Table 2; Table II in the online-only Data Supplement). Among the individual lifestyle factors, underweight was associated with a higher risk of pneumonia (adjusted OR, 1.36; 95% CI, 1.10–1.69) and high alcohol intake with an increased risk of both pneumonia and UTI (adjusted OR, 1.24; 95% CI, 1.14–1.36, and 1.12; 95% CI, 1.02–1.22, respectively). In contrast, overweight and obese patients had a lower risk of pneumonia (adjusted OR ranged from 0.72 to 0.79). No association with pneumonia and UTI was found for the remaining lifestyle factors.

The overall 30-day mortality rate was 9.9%. The association between lifestyle and mortality differed according to the sex (Table 3). Men with an unhealthy lifestyle at admission had a statistically significant lower risk of dying within 30 days from admission compared with men with a healthy lifestyle (adjusted OR, 0.71; 95% CI, 0.58–0.87), whereas statistically significant association was found for women (adjusted OR, 1.34; 95% CI, 0.90–1.99; P for interaction=0.01).

Overweight and obesity were associated with lower mortality rates (adjusted mortality rate ratios ranging from 0.64 to 0.74 for men and 0.64 to 0.85 for women). In contrast, underweight patients had a significantly higher mortality rate (adjusted mortality rate ratio for men, 1.71; 95% CI, 1.50–1.96, and for women, 1.46; 95% CI, 1.34–1.60) compared with patients with normal BMI.

Discussion

Previous studies have reported a healthy lifestyle to be associated with a lower long-term risk of adverse outcomes/

Table 2.   Pneumonia After Admission for Stroke According to Lifestyle Factors Present at Admission

Lifestyle Factors	Pneumonia, n (%)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Healthy lifestyle			
Nonsmoker, alcohol intake ≤21/14, BMI >18.5 and <24.9 kg/m²	132/1374 (9.6)	ref.	ref.
Moderate healthy			
1 lifestyle factor present	512/5590 (9.2)	0.88 (0.77–1.01)	1.02 (0.88–1.18)
Moderate unhealthy			
2 lifestyle factors present	513/5976 (8.6)	0.72 (0.61–0.87)	0.96 (0.79–1.17)
Unhealthy			
Smoker, alcohol intake >21/14, and BMI <18.5 and >24.9 kg/m²	90/863 (10.4)	0.84 (0.64–1.11)	1.30 (0.98–1.73)
BMI†			
Normal weight, 18.5–24.9 kg/m²	585/5171 (11.3)	ref.	ref.
Underweight, <18.5 kg/m²	140/831 (16.9)	1.53 (1.27–1.83)	1.36 (1.10–1.69)
Overweight, 25–29.9 kg/m²	307/3819 (8.0)	0.70 (0.62–0.79)	0.79 (0.70–0.89)
Moderate obesity, 30.0–34.9 kg/m²	84/1310 (6.4)	0.52 (0.40–0.67)	0.62 (0.49–0.79)
Severe obesity, ≥35 kg/m²	26/479 (5.4)	0.45 (0.30–0.68)	0.63 (0.41–0.96)
Alcohol intake‡			
≤21/14 drinks per wk§	1100/12 314 (8.9)	ref.	ref.
>21/14 drinks per wk	147/1489 (9.9)	1.00 (0.90–1.11)	1.24 (1.14–1.36)
Smoking habits‖			
Never smoker	401/4592 (8.7)	ref.	ref.
Current smoker	470/5623 (8.4)	0.92 (0.81–1.04)	1.12 (0.95–1.31)
Former smoker	353/3316 (10.7)	1.06 (0.85–1.32)	1.08 (0.84–1.39)

BMI indicates body mass index; CI, confidence interval; and OR, odds ratio.

*All analyses are corrected for clustering of patients by stroke unit, age, sex, marital status, housing, profession, alcohol intake (except for lifestyle and alcohol intake), smoking habits (except for lifestyle and smoking), atrial fibrillation, previous stroke, hypertension, Charlson Comorbidity index, type of stroke, hospital setting (university/nonuniversity), stroke unit setting (neurological/non-neurological), patient volume, employment status, personal income, educational level (highest attained), medication use (platelet inhibitors, oral anticoagulants, ACE inhibitors/AT-II blockers, calcium antagonists, β-blockers, statins, thiazides, potassium-sparing and loop diuretics, oral glucose–lowering drugs, and insulin), and proportion of relevant processes of care received.

†Also corrected for smoking habits and alcohol intake.

‡Also corrected for smoking habits and BMI.

§Drinks per wk for men and women, respectively.

‖Also corrected for alcohol intake and BMI.

mortality.[19–21] However, variations in the timing of the assessment of lifestyle, length of follow-up, and choice of outcome measure (all-cause or stroke-specific mortality) between the studies make direct comparisons difficult. To the best of our knowledge, our study is the first study to examine the association between lifestyle factors assessed at the time of admission (combined and individual factors) and a broader range of early outcomes.

Our findings that obese patients had a lower risk of adverse outcomes support results from previous studies that have reported a lower mortality in overweight/obese patients.[8,10,22–24] However, recently, the obesity paradox was challenged by a study focusing on cause-specific rather than all-cause mortality and reporting no indication of an obesity paradox among stroke patients, when focusing on stroke-specific deaths.[25] In our study, we found that overweight/

obese patients also had lower risk of a severe stroke and poststroke pneumonia. These findings add further support to the obesity paradox hypothesis and are in accordance with some[8,10,23] but not all previous studies.[24] A higher BMI has also been associated with a better outcome in several other chronic diseases, and the mechanisms underlying the phenomenon have been debated for years.[26] It may be of importance that BMI is a crude anthropometric measure that does not reflect the fat mass/fat-free mass ratio, nutritional status, cardiorespiratory fitness, body fat distribution, or other factors associated with obesity and affecting the clinical outcome.[27]

Our finding of a lower risk of severe strokes for current/former smokers is in accordance with the findings of Edjoc et al[28] who found former smoking to be associated with a lower risk of severe stroke and close to the findings of Ali et al[3] who

Table 3. Thirty-day All-Cause Mortality According to Lifestyle Factors Present at Admission

Lifestyle factors	All, n (%)	All 30-Day Mortality, n (%)	Men Unadjusted MRR (95% CI)	Men Adjusted MRR* (95% CI)	Women Unadjusted MRR* (95% CI)	Women Adjusted MRR* (95% CI)
Healthy lifestyle						
Nonsmoker, alcohol intake ≤21/14, BMI >18.5 and <24.9 kg/m²	6516 (9.3)	393/5084 (7.7)	ref.	ref.		
Moderate healthy						
1 lifestyle factor present	28 421 (40.6)	1924/5084 (37.8)	0.64 (0.58–0.70)	0.80 (0.73–0.88)	0.77 (0.71–0.84)	1.00 (0.92–1.09)
Moderate unhealthy						
2 lifestyle factors present	31 350 (44.8)	2468/5084 (48.5)	0.45 (0.40–0.52)	0.68 (0.60–0.78)	0.57 (0.51–0.64)	0.94 (0.84–1.06)
Unhealthy						
Smoker, alcohol intake >21/14, and BMI <18.5 and >24.9 kg/m²	3680 (5.3)	299/5084 (5.9)	0.37 (0.30–0.46)	0.71 (0.58–0.87)	0.49 (0.35–070)	1.34 (0.90–1.99)
BMI†						
Normal weight, 18.5–24.9 kg/m²	24 489 (29.6)	1491/3007 (49.6)	ref.	ref.		
Underweight: <18.5 kg/m²	2638 (3.2)	429/3007 (14.3)	2.07 (1.84–2.34)	1.71 (1.50–1.96)	1.70 (1.53–1.89)	1.46 (1.34–1.60)
Overweight: 25–29.9 kg/m²	19 226 (23.2)	760/3007 (25.3)	0.62 (0.56–0.69)	0.74 (0.67–0.82)	0.72 (0.64–0.80)	0.85 (0.75–0.96)
Moderate obesity: 30.0–34.9 kg/m²	6881 (8.3)	235/3007 (7.8)	0.53 (0.47–0.61)	0.68 (0.58–0.79)	0.50 (0.42–0.60)	0.64 (0.52–0.78)
Severe obesity: ≥35 kg/m²	2426 (2.9)	92/3007 (3.1)	0.47 (0.37–0.61)	0.64 (0.51–0.81)	0.42 (0.33–0.52)	0.66 (0.53–0.82)
Alcohol intake‡						
≤21/14 drinks per wk§	64 023 (77.4)	4695/5084 (92.4)	ref.	ref.		
>21/14 drinks per wk	6088 (7.4)	389/5084 (7.7)	0.68 (0.59–0.75)	0.95 (0.83–1.09)	0.66 (0.56–0.79)	1.12 (0.91–1.38)
Smoking habits‖						
Never smoker	24 083 (29.1)	1878/4589 (40.9)	ref.	ref.		
Current smoker	27 057 (32.7)	1456/4589 (31.7)	0.69 (0.63–0.75)	0.95 (0.86–1.05)	0.70 (0.64–0.76)	1.06 (0.95–1.18)
Former smoker	16 863 (20.4)	1255/4589 (27.4)	0.73 (0.64–0.82)	0.72 (0.65–0.80)	0.68 (0.63–0.74)	0.84 (0.77–0.91)

BMI indicates body mass index; CI, confidence interval; MRR, mortality rate ratio; and OR, odds ratio.

*All analyses are corrected for clustering of patients by stroke unit, age, marital status, housing, profession, alcohol intake (except for lifestyle and alcohol intake), smoking habits (except for lifestyle and smoking), atrial fibrillation, previous stroke, hypertension, Charlson Comorbidity index, type of stroke, hospital setting (university/nonuniversity), stroke unit setting (neurological/non-neurological), patient volume, employment status, personal income, educational level (highest attained), medication use (platelet inhibitors, oral anticoagulants, ACE inhibitors/AT-II blockers, calcium antagonists, β-blockers, statins, thiazides, potassium-sparing and loop diuretics, oral glucose–lowering drugs, and insulin), and proportion of relevant processes of care received.

†Also corrected for smoking habits and alcohol intake.

‡Also corrected for smoking habits and BMI.

§Drinks per wk for men and women, respectively.

‖Also corrected for alcohol intake and BMI.

found that current smoking was associated with lower mortality. The likelihood of a lower risk of severe strokes among current/former smokers might reflect ischemic preconditioning leading to increased collateral blood circulation, which may be induced by smoking. Another potential mechanism might be selection, that is, people who are able to tolerate a lifestyle with smoking into high age, where the stroke incidence increases substantially, may have a particular strong health constitution because they have survived this long with a high-risk lifestyle, including other smoking-related health risks, such as the risk of cancer, myocardial infarction, etc.

In contrast, Lee et al[29] found that current smoking was not associated with a good functional outcome after ischemic stroke.

Studies on the prognostic impact of alcohol intake are sparse. Some studies found, in accordance with our results, a higher risk of in-hospital pneumonia for patients with high alcohol intake and no clear association with stroke severity and short-term mortality.[6,30]

It could by hypothesized that the negative physiological effects of an unhealthy lifestyle would have an adverse effect on the patient's ability to overcome a stroke; however, the lack of an association between an unhealthy lifestyle and an increased risk of early phase adverse clinical outcome found in our study do not support this hypothesis. This may reflect that the physiological consequences of an unhealthy lifestyle on stroke outcomes are truly negligible; however, it may also reflect a possible survival bias, where patients with an unhealthy lifestyle surviving long enough to experience a stroke may be less susceptible to the potential adverse effects that the lifestyle may have in the early phase after the stroke. The interaction between sex and the composite lifestyle score used in our study is puzzling in this context. It may partly

reflect sex-related differences in the distribution of lifestyle factors, for example, a higher proportion of underweight women versus men, but it is worth noting that the risk estimates in general were more extreme among men compared with women also in the analyses on the individual lifestyle factors. This may indicate that men are more susceptible for the effects of lifestyle on stroke outcome and of the selection mechanisms mentioned above. Although the findings in our and other studies do not indicate that a need of specific awareness on the patient's lifestyle is required during the early phase of stroke, it is essential to keep in mind that unhealthy lifestyle factors, such as obesity, smoking, and a high alcohol intake, play a major role for the global patterns of stroke incidence and mortality and are also likely to play a role for the long-term outcome of stroke patients, including the risk of recurrent stroke and death.[1]

The main limitations of this study include the lack of more detailed information on lifestyle and stroke subtypes. Several other factors, in particular physical activity level and diet, may play an important role in outcome after stroke. Several measures were taken to minimize the impact of possible confounding, including control for a wide range of well-established prognostic factors. However, uncertainty may exist on the exact role of some of the covariates included in the multivariable analyses because some (eg, several comorbid conditions) may both be potential confounders and intermediate steps in the association between lifestyle and stroke outcomes. However, our overall results were not affected by the inclusion or exclusion of individual covariates.

In conclusion, this study found that unhealthy lifestyle factors, including obesity, smoking, and high alcohol intake either individually or in combination, were in general not associated with increased risk of adverse early clinical outcomes, in particularly among men with stroke. However, underweight may be a particular concern because it was associated with an increased risk of adverse outcomes after stroke among both men and women, and further efforts to ameliorate this association seem warranted.

Disclosures

None.

References

1. O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, et al; INTERSTROKE Investigators. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. *Lancet*. 2010;376:112–123. doi: 10.1016/S0140-6736(10)60834-3.
2. Elkind MS. Epidemiology and risk factors. *Continuum*. 2011;17(6 2ndary Stroke Prevention):1213–1232. doi: 10.1212/01.CON.0000410031.34477.8d.
3. Ali SF, Smith EE, Bhatt DL, Fonarow GC, Schwamm LH. Paradoxical association of smoking with in-hospital mortality among patients admitted with acute ischemic stroke. *J Am Heart Assoc*. 2013;2:e000171. doi: 10.1161/JAHA.113.000171.
4. Andersen KK, Olsen TS. The obesity paradox in stroke: lower mortality and lower risk of readmission for recurrent stroke in obese stroke patients. *Int J Stroke*. 2015;10:99–104.
5. Dhamoon MS, Tai W, Boden-Albala B, Rundek T, Paik MC, Sacco RL, et al. Risk of myocardial infarction or vascular death after first ischemic stroke: the Northern Manhattan Study. *Stroke*. 2007;38:1752–1758. doi: 10.1161/STROKEAHA.106.480988.
6. Fekete K, Szatmári S, Szőcs I, Szekeres C, Szász J, Mihálka L, et al. Prestroke alcohol consumption and smoking are not associated with stroke severity, disability at discharge, and case fatality. *J Stroke Cerebrovasc Dis*. 2014;23:e31–e37. doi: 10.1016/j.jstrokecerebrovasdis.2013.08.006.
7. Movva R, Figueredo VM. Alcohol and the heart: to abstain or not to abstain? *Int J Cardiol*. 2013;164:267–276. doi: 10.1016/j.ijcard.2012.01.030.
8. Olsen TS, Dehlendorff C, Petersen HG, Andersen KK. Body mass index and poststroke mortality. *Neuroepidemiology*. 2008;30:93–100. doi: 10.1159/000118945.
9. Towfighi A, Ovbiagele B. The impact of body mass index on mortality after stroke. *Stroke*. 2009;40:2704–2708. doi: 10.1161/STROKEAHA.109.550228.
10. Vemmos K, Ntaios G, Spengos K, Savvari P, Vemmou A, Pappa T, et al. Association between obesity and mortality after acute first-ever stroke: the obesity-stroke paradox. *Stroke*. 2011;42:30–36. doi: 10.1161/STROKEAHA.110.593434.
11. Schmidt M, Pedersen L, Sørensen HT. The Danish Civil Registration System as a tool in epidemiology. *Eur J Epidemiol*. 2014;29:541–549. doi: 10.1007/s10654-014-9930-3.
12. Wildenschild C, Mehnert F, Thomsen RW, Iversen HK, Vestergaard K, Ingeman A, et al. Registration of acute stroke: validity in the Danish Stroke Registry and the Danish National Registry of Patients. *Clin Epidemiol*. 2014;6:27–36. doi: 10.2147/CLEP.S50449.
13. Andersen ZJ, Olsen TS, Andersen KK, Loft S, Ketzel M, Raaschou-Nielsen O. Association between short-term exposure to ultrafine particles and hospital admissions for stroke in Copenhagen, Denmark. *Eur Heart J*. 2010;31:2034–2040. doi: 10.1093/eurheartj/ehq188.
14. Jørgensen HS, Nakayama H, Reith J, Raaschou HO, Olsen TS. Stroke recurrence: predictors, severity, and prognosis. The Copenhagen Stroke Study. *Neurology*. 1997;48:891–895.
15. Lindenstrøm E, Boysen G, Christiansen LW, Nielsen PW. Reliability of Scandinavian neurological stroke scale. *Cerebrovasc Dis*. 1991;1:103–107.
16. Ingeman A, Andersen G, Hundborg HH, Svendsen ML, Johnsen SP. In-hospital medical complications, length of stay, and mortality among stroke unit patients. *Stroke*. 2011;42:3214–3218. doi: 10.1161/STROKEAHA.110.610881.
17. Lynge E, Sandegaard JL, Rebolj M. The Danish National Patient Register. *Scand J Public Health*. 2011;39(suppl 7):30–33. doi: 10.1177/1403494811401482.
18. Sterne JA, White IR, Carlin JB, Spratt M, Royston P, Kenward MG, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ*. 2009;338:b2393.
19. Eguchi E, Iso H, Tanabe N, Wada Y, Yatsuya H, Kikuchi S, et al; Japan Collaborative Cohort Study Group. Healthy lifestyle behaviours and cardiovascular mortality among Japanese men and women: the Japan collaborative cohort study. *Eur Heart J*. 2012;33:467–477. doi: 10.1093/eurheartj/ehr429.
20. Lin MP, Ovbiagele B, Markovic D, Towfighi A. "Life's simple 7" and long-term mortality after stroke. *J Am Heart Assoc*. 2015;4:e001470.
21. Towfighi A, Markovic D, Ovbiagele B. Impact of a healthy lifestyle on all-cause and cardiovascular mortality after stroke in the USA. *J Neurol Neurosurg Psychiatry*. 2012;83:146–151. doi: 10.1136/jnnp-2011-300743.
22. Andersen KK, Olsen TS. The obesity paradox in stroke: lower mortality and lower risk of readmission for recurrent stroke in obese stroke patients. *Int J Stroke*. 2015;10:99–104.
23. Doehner W, Schenkel J, Anker SD, Springer J, Audebert HJ. Overweight and obesity are associated with improved survival, functional outcome, and stroke recurrence after acute stroke or transient ischaemic attack: observations from the TEMPiS trial. *Eur Heart J*. 2013;34:268–277. doi: 10.1093/eurheartj/ehs340.
24. Semins MJ, Shore AD, Makary MA, Weiner J, Matlaga BR. The impact of obesity on urinary tract infection risk. *Urology*. 2012;79:266–269. doi: 10.1016/j.urology.2011.09.040.

25. Dehlendorff C, Andersen KK, Olsen TS. Body mass index and death by stroke: no obesity paradox. *JAMA Neurol*. 2014;71:978–984. doi: 10.1001/jamaneurol.2014.1017.

26. Hainer V, Aldhoon-Hainerová I. Obesity paradox does exist. *Diabetes Care*. 2013;36(suppl 2):S276–S281. doi: 10.2337/dcS13-2023.

27. Heymsfield SB, Cefalu WT. Does body mass index adequately convey a patient's mortality risk? *JAMA*. 2013;309:87–88. doi: 10.1001/jama.2012.185445.

28. Edjoc RK, Reid RD, Sharma M, Fang J; Registry of the Canadian Stroke Network. The prognostic effect of cigarette smoking on stroke severity, disability, length of stay in hospital, and mortality in a cohort with cerebrovascular disease. *J Stroke Cerebrovasc Dis*. 2013;22:e446–e454. doi: 10.1016/j.jstrokecerebrovasdis.2013.05.001.

29. Lee JH, Lee JY, Ahn SH, Jang MU, Oh MS, Kim CH, et al. Smoking is not a good prognostic factor following first-ever acute ischemic stroke. *J Stroke*. 2015;17:177–191. doi: 10.5853/jos.2015.17.2.177.

30. Mogensen UB, Olsen TS, Andersen KK, Gerds TA. Cause-specific mortality after stroke: relation to age, sex, stroke severity, and risk factors in a 10-year follow-up study. *J Stroke Cerebrovasc Dis*. 2013;22:e59–e65. doi: 10.1016/j.jstrokecerebrovasdis.2012.04.006.

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Lifestyle Factors and Early Clinical Outcome in Patients With Acute Stroke: A Population-Based Study

Annette Ingeman, Grethe Andersen, Reimar W. Thomsen, Heidi H. Hundborg, Henrik H. Rasmussen and Søren P. Johnsen

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Correction to: Lifestyle Factors and Early Clinical Outcome in Patients With Acute Stroke: A Population-Based Study

In the article by Ingeman et al, "Lifestyle Factors and Early Clinical Outcome in Patients With Acute Stroke: A Population-Based Study," which published online ahead of print on January 16, 2017, and appeared in the March 2017 issue of the journal (*Stroke*. 2017;48:611–617. DOI: 10.1161/STROKEAHA.116.015784), a correction is needed.

On page 611, the corresponding author's e-mail address is incorrect. It should be: ai@dce.au.dk.

This correction has been made to the current online version of the article, which is available at http://stroke.ahajournals.org/content/48/3/611.

SUPPLEMENTAL MATRERIAL

SUPPLEMENTAL TABLE I. Descriptive characteristics of 82,597 patients with acute stroke admitted to stroke units in Denmark between 2003-2011.

Characteristics	N (%)	Men	Women
Whole population	82,597 (100)	43,220 (52.3)	39,377 (47.7)
Patients in Copenhagen and Aarhus areas	20,657 (25.0)	-	-
Age (y)			
18–64	23,679 (28.7)	14,988 (34.7)	8,691 (22.1)
>65–80	35,135 (42.5)	19,482 (45.1)	15,653 (39.8)
>80	23,783 (28.7)	7,750 (20.3)	15,033 (38.2)
Mean age(years)	71.5	69.2	74.1
Median (range)	73 (18, 107)	70 (18, 107)	77 (18, 106)
Marital status			
-Living with partner, family, or friend	43,03 (52.1)	27,895 (64.5)	15,137(38.4)
-Living alone	34,314 (41.5)	13,032 (30.2)	21,282 (54.1)
-Other	2,268 (2.8)	838 (1.9)	1,430 (3.6)
-Unknown	2,983 (3.6)	1,455 (3.4)	1,528 (3.9.)
Housing			
-Ownhome	70,965 (85.9)	38,276 (88.6)	32,689 (83.0)
-Nursing home or other institution	5,548 (6.7)	1,828 (4.2)	3,720(9.5)
-Other	1,798(2.2)	869(2.0)	929 (2.4)
-Unknown	4,286 (5.2)	2,247 (5.2)	2,039 (5.2)
Education			
- Short	35,142(42.6)	16,246 (37.6)	18,896 (47.8)

- Medium	25,187 (30.5)	16,410 (38.0)	8,777(22.3)
- Long term higher education	9,885 (12.0)	6,114 (14.2)	3,771 (9.6)
-Unknown	12,383 (15.0)	4,450 (10.3)	7,933(20.2)
Profession			
-Employed	16,674 (20.2)	11.662(27.0)	5,012(12.7)
-Unemployed or early retirement benefits	1,649 (2.0)	1,038(2.4)	611(1.6)
-Unemployed, public benifits / education	10,673 (12.9)	6,171(14.3)	4,502(11.4)
- Pensioner	51,131 (64.3)	24,024(55.6)	29,107(73.9)
-Unknown	470 (0.6)	325(0.8)	145 (0.4)
Type of stroke			
-Intracerebral hemorrhage	8,588 (10.4)	4,400 (10.2)	4,188 (10.6)
-Ischemic	61,032 (73.9)	32,165 (74.4)	28,857 (73.3)
-Unspecified	12,977 (15.7)	6,655 (15.4)	6,322 (16.1)
Scandinavian Stroke Scale on admission			
-Very severe, 0–14 points	7,594 (9.2)	3,127 (7.2)	4,467 (11.3)
-Severe, 15–29 points	7,506 (9.1)	3,529 (8.2)	3,977 (10.1)
-Moderate, 30–44 points	13,837 (16.8)	6,934 (16.0)	6,903 (17.5)
-Mild, 45–58 points	43,345 (52.5)	24,505 (56.7)	18,840 (47.9)
-Unknown	10,315 (12.5)	5,125 (11.7)	5,190 (13.2)
Previous stroke			
-Yes	15,845(19.2)	8,635 (20.0)	7,210 (18.3)
-No	62,556(75.7)	32,652 (75.6)	29,904 (75.9)
-Unknown	4,196(5.1)	1,933 (4.5)	2,263 (5.8)
Atrial fibrillation*			
-Yes	13,665(16.5)	6,190(14.3)	7,475(19.0)

-No	64,885 (78.6)	35,027(81.0)	29,858(75.8)
-Unknown	4,047(4.9)	2.003 (4.6)	2,044(5.2)
Hypertension*			
-Yes	40,513 (49.1)	20,646 (47.8)	19,867 (50.5)
-No	41,837 (50.7)	22,433 (51.9)	19,404 (49.3)
-Unknown	237 (0.3)	141 (0.3)	106 (0.3)
Smoking habits			
-Current	26,968 (32.7)	16,229 (37.6)	10,739 (27.3)
-Former	16,839 (20.4)	10,770 (24.9)	6,069 (15.4)
-Never	24,046 (29.1)	9,892 (22.9)	14,154 (35.9)
-Unknown	14,744 (17.9)	6,329 (14.6)	8.415 (21.4)
Alcoholintake[†]			
-≤21/14 drinks/week	63,908 (77.4)	32,787 (75.9)	31,121 (79.0)
->21/14 drinks/week	6,059 (7.4)	4,828 (11.2)	1,231 (3.1)
-Unknown	12,630 (15.3)	5,605 (13.0)	7,025 (17.8)
Medication use at admission			
Platelet inhibitors			
-Current user[‡]	27,255(33.0)	14,076 (32.3)	13,179 (33.5)
-Former[§]	9,246(11.2)	4,858 (11.2)	4,388 (11.1)
-Never	46,096 (55.8)	24,286 (56.2)	21,810 (55.4)
Oralanticoagulants			
-Current user	4,796 (5.8)	2,689 (6.2)	2,107 (5.4)
-Former	3,459 (4.2)	1,765 (4.1)	1,694 (4.3)
-Never	74,342 (90.0)	38,766 (89.7)	35,576 (90.4)
ACE inhibitors/AT-II blockers			

-Current user	23,564 (28.5)	12,461 (28.8)	11,103 (28.2)
-Former	7,846 (9.5)	3,938 (9.1)	3,908 (9.9)
-Never	51,187 (62.0)	26,821 (62.1)	24,366 (61.9)
Calcium antagonists			
-Current user	14,360 (17.4)	7,174 (16.6)	7,186 (18.3)
-Former	8,928 (10.8)	4,242 (9.8)	4,686 (11.9)
-Never	59,309 (71.8)	31,804 (73.6)	27,505 (69.9)
Beta blockers			
-Current user	18,532 (22.4)	8,938 (20.7)	9,594 (24.4)
-Former	7,771 (9.4)	3,835 (8.9)	3,936 (10.0)
-Never	56,294 (68.2)	30,447 (70.5)	25,847 (65.6)
Statins			
-Current user	15,398 (18.6)	8,814 (20.4)	6,584 (16.7)
-Former	5,455 (6.6)	3,014 (7.0)	2,441 (6.2)
-Never	61,877 (74.8)	31,392 (72.6)	30,352 (77.1)
Thiazides			
-Current user	14,155 (17.1)	5,736 (13.3)	8,419 (21.4)
-Former	15,347 (18.6)	6,575 (15.29)	8,772 (22.3)
-Never	53,095 (64.3)	30,909 (71.5)	22,186 (56.3)
Loop diuretics			
-Current user	11,842 (14.3)	5,118 (11.8)	6,724 (17.1)
-Former	6,860 (8.3)	3,006 (7.0)	3,854 (9.8)
-Never	63,895 (77.4)	35,096 (81.2)	28,799 (73.1)
Potassium sparing diuretics			
-Current user	2,587 (3.1)	1,237 (2.9)	1,350 (3.4)

-Former	2,157 (2.6)	1,023 (2.4)	1,334 (2.9)
-Never	77,853 (94.3)	40,960 (94.8)	36,893 (93.7)
Oral glucose-lowering drugs			
-Current user	6,384 (7.7)	3,775 (8,7)	2,609 (6.6)
-Former	1,668 (2.0)	925 (2.1)	733 (1.9)
-Never	74,555 (90.3)	38,520 (89.1)	36,035 (91.5)
Insulin			
-Current user	3,023 (3.7)	1,747 (4.0)	1,276 (3.2)
-Former	408 (0.5)	227 (0.5)	181 (0.5)
-Never	79,166 (95.9)	41,246 (95.4)	37,920 (96.3)
Body Mass Index (BMI) (kg/m^2)			
Mean	25.2	25.8	24.5
-Normal weight:18.5 -24.9 kg/m2	23,777 (28.8)	11,440 (26.5)	12,337 (31.3)
- Underweight: <18.5 kg/m2	3,397 (4.1)	919 (2.1)	2,478 (6.3)
-Overweight: 25 - 29.9 kg/m2	19,101 (23.1)	11,962 (27.7)	7,139 (18.3)
-Moderate obesity: 30.0 - 34.9 kg/m2	6,858 (8.3)	3,952 (9.1)	2,906 (7.4)
-Severe obesity: >= 35 kg/m2	2,416 (2.9)	1,155 (2.7)	1,261 (3.2)
-Unknown	27,048 (32,8)	13,792 (31.9)	13,256 (33.7)
Lifestyle factors at admission			
-Healthy: non smoker, alcohol intake <= 21/14, BMI >18.5 and < 24.9 kg/m2	6,516 (7.9)	2,198 (5.1)	4,318 (11.0)
-Moderate healthy: 1 lifestyle factor present	28,421(34.4)	13,440 (31.1)	14,981 (38.1)
-Moderate unhealthy: 2 lifestyle factors present	31,350 (38.0)	18,993 (43.9)	12,357 (31.4)
-Unhealthy : smoker, alcohol intake > 21/14,	3,680(4.5)	2,984 (6.9)	696 (1.8)

and BMI <18.5 or > 24.9 kg/m2

-Unknown	12,630 (15.3)	5,605 (13.0)	7,025 (17.8)
Charlson Comorbidity Index			
-No (0)	24,979 (30.2)	13,186 (30.5)	11,793 (30.0)
-Moderate (1–2)	37,848 (45.8)	19,618 (45.4)	18,230 (46.3)
-Severe (≥3)	19,770 (23.9)	10,416 (24.1)	9,354 (23.8)
Hospital setting			
-UniversityHospital	30,091 (36.4)	15,313 (35.4)	14,778 (37.5)
-Non-universityHospital	52,506 (63.6)	27,907 (64.6)	24,599 (62.5)
Stroke unit setting			
-Neurologic department	26,845(32.5)	13,667 (31.6)	13,178 (33.5)
-Non-neurologic department	55,772 (67.5)	29,553 (68.4)	26,199 (66.5)
Patient volume (departmental average number of stroke patients per year)			
-Median (range)	448 (18 - 859)	-	-
Complications after admission only for patients in Copenhagen and Aarhus areas (n=20,657)			
Pneumonia			
-Yes	1,605 (7.8)	855 (8.2)	750 (7.4)
-No	14,338 (69.4)	7,244 (69.1)	7,094 (69.8)
-Unknown	4,714 (22.8)	2,387 (22.8)	2,327 (22.9)
Urinarytractinfection			
-Yes	2,591 (12.5)	868 (8.3)	1,723 (16.9)
-No	13,295 (64.4)	7,198 (68.6)	6,097 (59.9)

-Unknown	4,771 (23.1)	2,420(23.12)	2,351 (23.1)
Proportion of relevant processes of care received within time frame			
0–24	5,034 (6.1)	2,348 (5.4)	2,686 (6.8)
25–49	8,465 (10.3)	4,152 (9.6)	4,313 (11.0)
50–74	21,466 (26.0)	10,884 (25.2)	10,582 (26.9)
75–100	47,632(57.7)	25,836 (59.8)	21,796 (55.4)
30-day mortality			
-Yes	8,195 (9.9)	3,667 (8.5)	4,528 (11.5)
-No	74,402 (90.1)	39,553 (91.5)	34,849 (88.5)
Number of patients by year of hospitalization			
– 2003	7,141 (8.7)	3,750 (8.7)	3,391(8.6)
– 2004	9,315 (11.3)	4,820 (11.2)	4,495 (11.4)
– 2005	9,373 (11.4)	4,792 (11.1	4,581 (11,6)
– 2006	9,963 (12.1)	5,219 (12.1)	4,744 (12.1)
– 2007	9,447 (11.4)	5,022 (11.6)	4,425 (11.2)
– 2008	9,084 (11.0)	4,739 (11.0)	4,345 (11.0)
– 2009	9,594 (11.6)	5,066 (11.7)	4,528 (11.5)
– 2010	9,455(11.5)	4,940 (11.4)	4,515 (11.5)
– 2011	9,225 (11.2)	4,872 (11.3)	4,353 (11.1)

*Known history or diagnosed during current admission.

†Drinks per week for men and women, respectively

‡ Current user: at least one filled prescription within 90 days beforehand of the stroke hospitalization index date. Persons who filled a prescription. The 90-day period was chosen to capture most current users.

§ Former user: more than 90 days beforehand of the stroke hospitalization index date.

SUPPLEMENTAL TABLE II. Urinary tract infection after admission for stroke according to lifestyle factors present at admission

Lifestyle factors	Urinary tract infection N (%)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Healthy lifestyle: - Non smoker, alcohol intake <= 21/14, bmi >18.5 and < 24.9 kg/m^2	270/1,372(19.7)	ref.	ref.
Moderate healthy: - 1 lifestyle factor present	966/5,569 (17.4)	0.76 (0.65–0.88)	0.97 (0.83–1.14)
Moderate unhealthy: - 2 lifestyle factors present	805/5,957 (13.5)	0.60 (0.51–0.70)	0.98 (0.82–1.18)
Unhealthy: - Smoker, alcohol intake > 21/14, and bmi <18.5 and > 24.9 kg/m^2	90/860 (10.5)	0.42 (0.32–0.56)	0.98 (0.72–1.33)
Body Mass Index[†]: - Normal weight:18.5 -24.9 kg/m^2	956/5,157 (18.5)	ref.	ref.
Body Mass Index: - Underweight: <18.5 kg/m^2	204/832 (24.5)	1.33 (1.07–1.65)	1.01 (0.82–1.26)
Body Mass Index: - Overweight: 25 - 29.9 kg/m^2	553/3,812 (14.5)	0.75 (0.68–0.84)	0.95 (0.84–1.06)
Body Mass Index: - Moderate obesity: 30.0 - 34.9 kg/m^2	199/1,310 (15.6)	0.76 (0.67–0.86)	1.03 (0.91–1.17)
Body Mass Index: - Severe obesity: >= 35 kg/m^2	75/481 (15.6)	0.76 (0.63–0.92)	1.13 (0.91–1.40)
Alcohol intake[‡]: - ≤21/14 drinks per week[§]	1,964/12,269 (16.0)	ref.	ref.
Alcohol intake: - >21/14 drinks per week	167/1,489 (11.2)	0.65 (0.60–0.71)	1.12 (1.02–1.22)
Smoking habits[‖]: Never smoker	828/4,579 (18.1)	ref.	ref.
Smoking habits: Current smoker	725/5,609 (12.9)	0.70 (0.62–0.79)	1.00 (0.88–1.14)
Smoking habits: Former smoker	487/3,299 (14.8)	0.73 (0.63–0.85)	0.93 (0.78–1.14)

*All analyses are corrected for clustering of patients by stroke unit, and age, sex, marital status, housing, profession, alcohol intake(except for lifestyle and alcohol intake), smoking habits (except for lifestyle and smoking), atrial fibrillation, previous stroke, hypertension, Charlson Comorbidity index, type of stroke, hospital setting (university/non-university),

stroke unit setting (neurologic/non-neurologic), patient volume, employment status, personal income, educational level (highest attained), medication use (platelet inhibitors, oral anticoagulants, ACE inhibitors/AT-II blockers, calcium antagonists, beta blockers, statins, thiazides, potassium sparing and loop diuretics, oral glucose-lowering drugs and insulin) and proportion of relevant processes of care received.

[†] Also corrected for smoking habits and alcohol intake

[‡] Also corrected for smoking habits and Body Mass Index

[§] Drinks per week for men and women, respectively.

[∥] Also corrected for alcohol intake and Body Mass Index

SUPPLEMENTAL FIGURE I. Flow chart of the study population

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┌─────────────────────────────────────────────────────────────────┐
│ All patients  with acute stroke in Denmark and registered in The  │
│ Danish Stroke Registry  (DSR) between January 13, 2003 and        │
│ December 31, 2011,  N = 101.515.                                  │
└─────────────────────────────────────────────────────────────────┘
                              │
                              ▼
┌─────────────────────────────────────────────────────────────────┐
│ All patients with first acute stroke registered in The Danish     │
│ Stroke Registry (DSR) in study period,  N = 91.345                │
└─────────────────────────────────────────────────────────────────┘
                              │
                              ▼
┌─────────────────────────────────────────────────────────────────┐
│ Only patients  >= 18 years, N = 91.345                            │
└─────────────────────────────────────────────────────────────────┘
                              │
                              ▼
┌─────────────────────────────────────────────────────────────────┐
│ Only patients  admitted to a stroke unit or transferred to a      │
│ stroke unit during hospitalization , N = Only patients  admitted  │
│ to a stroke unit or transferred to a stroke unit during           │
│ hospitalization , N = 83,479                                      │
└─────────────────────────────────────────────────────────────────┘
                              │
                              ▼
┌─────────────────────────────────────────────────────────────────┐
│ Only patients with a valid civil registration number to allow     │
│ follow up, N = 82,597                                             │
└─────────────────────────────────────────────────────────────────┘
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