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## RESEARCH PAPER

## Stress resilience in male adolescents and subsequent stroke risk: cohort study

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**ABSTRACT****Objective** Exposure to psychosocial stress has been identified as a possible stroke risk, but the role of stress resilience which may be relevant to chronic exposure is uncertain. We investigated the association of stress resilience in adolescence with subsequent stroke risk.**Methods** Register-based cohort study. Some 237 879 males born between 1952 and 1956 were followed from 1987 to 2010 using information from Swedish registers. Cox regression estimated the association of stress resilience with stroke, after adjustment for established stroke risk factors.**Results** Some 3411 diagnoses of first stroke were identified. Lowest stress resilience (21.8%) compared with the highest (23.7%) was associated with increased stroke risk, producing unadjusted HR (with 95% CIs) of 1.54 (1.40 to 1.70). The association attenuated slightly to 1.48 (1.34 to 1.63) after adjustment for markers of socioeconomic circumstances in childhood; and after further adjustment for markers of development and disease in adolescence (blood pressure, cognitive function and pre-existing cardiovascular disease) to 1.30 (1.18 to 1.45). The greatest reduction followed further adjustment for markers of physical fitness (BMI and physical working capacity) in adolescence to 1.16 (1.04 to 1.29). The results were consistent when stroke was subdivided into fatal, ischaemic and haemorrhagic, with higher magnitude associations for fatal rather than non-fatal, and for haemorrhagic rather than ischaemic stroke.**Conclusions** Stress susceptibility and, therefore, psychosocial stress may be implicated in the aetiology of stroke. This association may be explained, in part, by poorer physical fitness. Effective prevention might focus on behaviour/lifestyle and psychosocial stress.relevant to stroke risk, such as cigarette smoking, physical inactivity and alcohol intake.<sup>7</sup>To date, the association between psychosocial stress and stroke has been investigated incompletely.<sup>8</sup> Recent case-control studies investigating this may have been limited by potential reporting bias, and exclusion of subjects who experienced fatal stroke, as the measure of exposure to stress was collected after onset of stroke.<sup>4 9 10</sup> While some prospective studies have been performed,<sup>3 5</sup> limited duration of follow-up has not allowed examination of *chronic* exposure, which may be of particular relevance.Stress susceptibility—or stress resilience—is an important determinant of the consequences of exposure to stress.<sup>11 12</sup> A poorly controlled stress response (potentially signalled by low stress resilience) results in a prolonged physiological response to stressful exposures, thus increasing the possible longer-term adverse consequences of psychosocial stress. Stress resilience may be a useful and under-used measure for investigating the consequences of chronic stress in relation to stroke risk. Here, we examine the association of stress resilience in adolescence with subsequent stroke risk in middle age within a general population-based cohort of male Swedish residents. Stress resilience was measured during the assessment for military conscription over 10 years prior to stroke and, therefore, not subject to differential reporting bias. A secondary aim was to examine whether other risk factors might mediate associations of stress resilience with stroke risk. At the end of follow-up the subjects were still relatively young, under age 60 years, so the study is of stroke risk during working age rather than the later ages when stroke is more common.**INTRODUCTION**Stroke is the second leading cause of death worldwide, and the leading cause of neurological disability in adults in developed countries.<sup>1 2</sup> Recognised risk factors include high blood pressure, heart disease, diabetes, obesity, smoking, alcohol and physical inactivity, but further environmental factors are likely to be relevant to stroke risk. Exposure to psychosocial stress has been identified by several recently conducted studies as a possible stroke risk.<sup>3–5</sup> Psychosocial stress, particularly with chronic exposure, is a feasible risk for stroke through its influence on the hypothalamic pituitary adrenal (HPA) axis and sympathetic nervous system, which can result in inflammation and altered metabolic and cardiac autonomic control.<sup>6</sup> Moreover, stress may be related to lifestyle factors**METHODS****Study population**The study cohort consists of male Swedish residents born between 1952 and 1956, who were eligible for military conscription and included in the Swedish Military Conscription Register.<sup>13</sup> At this time, conscription and the associated examinations were mandatory for all male citizens of the appropriate age (18 and 19 years, with a small number at later ages). During the years covered by this study, only men with significant disability or a severe chronic disease were exempted from conscription (approximately 2–3% annually).<sup>14</sup> The assessments included extensive and highly standardised physical and psychological examinations by physicians and**To cite:** Bergh C, Udumyan R, Fall K, et al. *J Neurol Neurosurg Psychiatry* Published Online First: [please include Day Month Year] doi:10.1136/jnnp-2013-307485

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psychologists. Stroke risk was assessed from 1987 (when the Swedish National Inpatient Register<sup>15</sup> attained full coverage) to 2010.

From among a total of 284 198 men identified, we excluded 2564 subjects with unreliable data such as errors in the personal identification number or uncertain vital status. Those with implausible values for height (less than 144 cm), weight (above 178 kg), Body Mass Index, BMI, (below 15), systolic blood pressure (below 50 or above 230 mm Hg) and diastolic blood pressure (below 30 or above 135 mm Hg), were also excluded from the analysis; in total 225 men.<sup>16</sup> After excluding individuals who emigrated, died, or had a diagnosis of stroke before study entry in 1987, the sample comprised 271 767 men. Men with missing data for stress resilience, potential confounding factors (year of birth, geographic region, systolic and diastolic blood pressure, BMI, cognitive function, physical working capacity, parental socioeconomic index and household crowding) were also excluded (37 196 men; including 722 men with a stroke diagnosis at some time). The sample available for the main analysis comprised 237 879 men, 84% of the potential target population.

### Measures

#### Swedish military service conscription data

The men underwent a psychological examination to assess their potential ability to cope with war-time stress,<sup>17</sup> based on the ability to control and channel nervousness, tolerance of stress and disposition to anxiety.<sup>18</sup> During this assessment, the potential conscripts met a psychologist for a semistructured interview which covered areas relevant to general everyday life; including psychosocial dimensions, such as social maturity, leisure interests, psychological motivation, and emotional stability.<sup>18</sup> This interview was used to produce a stress resilience score from 1 to 9 which we grouped into low (1–3), medium (4–6) and high (7–9). Higher values indicate greater stress resilience. Details of the test are available in Swedish,<sup>19</sup> and it has been used in published research.<sup>16 17</sup> To ensure consistent evaluation, a central authority supervised the instruction and training of participating psychologists, supported by a written manual.

Height and weight were used to calculate BMI, which was categorised using the WHO criteria. Systolic and diastolic blood pressure was measured after rest in recumbent men using a sphygmomanometer. Physical working capacity was assessed using the cycle ergometric test. After a normal resting electrocardiogram, 5 min of submaximal exercise was performed at different work rates depending on body mass, directly followed by a maximal test with gradually increasing load until volitional exhaustion, or an estimate was derived from a nomogram for men who did not complete the full duration. The resulting value was transformed into scores with a range from 0 to 9. The cognitive test was a written assessment and comprised four domains: linguistic understanding, spatial recognition, general knowledge and ability to follow mechanical instructions: the results were transformed into a single score with a value ranging from 1 to 9. From the medical assessment at conscription, we identified diagnoses, and we used the International Classification of Diseases eighth revision, ICD-8, ICD-8 codes 393–458 to indicate diagnosis of any cardiovascular disease at the time of conscription.

### Stroke

Using the Swedish National Inpatient Register<sup>15</sup> and the Cause of Death Register,<sup>20</sup> we identified the dates of first fatal and non-fatal stroke diagnoses during the period 1969–2010.

The codes used for stroke were 430–434 and 436 in ICD-8, 430, 431, 433, 434 and 436 in ICD-9; and I60, I61, I63, I64 in ICD 10. For ischaemic stroke, they were 432–434 in ICD-8, 433, 434 in ICD-9, and I63 in ICD-10; for intracerebral haemorrhagic stroke 431 in ICD-8, 431 and 432 in ICD-9, and I61 in ICD-10.

### Socioeconomic and demographic characteristics

The government organisation, Statistics Sweden, provided socioeconomic and demographic data including information on vital status and emigration from the Total Population Register.<sup>21</sup> Childhood social and material circumstances were estimated using data from the 1960 census. The head of household's occupation was classified as manual, agricultural, farm owners/mangers, office workers, business owners/mangers, and others. Household crowding was divided into two categories to indicate a ratio of less than two persons per room, or more or equal to two persons per room.

### Statistical analysis

Cox regression was used to examine the association of stress resilience in adolescence with subsequent stroke risk between ages 31 and 58 years. The follow-up period began on 1 January 1987 and ended at first stroke, death, emigration or 1 January 2010, whichever occurred first. Subjects with a diagnosis of stroke before 1987 were excluded (n=218). Non-fatal and fatal stroke were examined together and separately. In the analyses of aetiological subtypes (ischaemic and intracerebral haemorrhagic stroke), first event by each subtype was used.

Associations were examined using an unadjusted (model 1) and three further adjusted models. In Model 2, adjustment was for demographic and socioeconomic factors for the family of origin: birth year, geographical region, parents' socioeconomic index, and household crowding. Model 3 was additionally adjusted for characteristics in adolescence: cognitive function (continuous), systolic and diastolic blood pressure (continuous), and cardiovascular disease at conscription. In Model 4 lifestyle factors in adolescence (here represented by physical fitness and body mass) were also added to the model: BMI (in 4 categories) and physical working capacity score (continuous).

The proportional hazards assumption for stress resilience in relation to stroke was tested graphically, as well as using a test based on Schoenfeld residuals, and no evidence was found that it was violated. As this was assessed using age as the underlying time scale, it indicates that the association between stress resilience and stroke was constant and did not diminish with increasing age. Statistical significance was defined as 95% CIs that do not include 1.00. Analyses used SPSS statistical software V.21 and Stata V.12 SE.

## RESULTS

All analyses are based on the 237 879 conscripts with complete information for the required variables, after exclusion of individuals who emigrated, died, or had a diagnosis of stroke before the beginning of follow-up in 1987. During the follow-up period of 1987–2010, 3411 men (1.4%) received an inpatient diagnosis of stroke (or stroke was recorded as the underlying cause of death). The stroke incidence rate was 64 per 100 000 person-years in our study population, compared with 101 per 100 000 person-years in the excluded subset with missing data on covariates.

Table 1 presents characteristics by stress resilience. Men with low resilience tended to have lower physical capacity, lower cognitive function scores, higher blood pressure, were underweight,

**Table 1** Population (n=237 879) characteristics by stress resilience levels

	High (7–9) stress resilience n=56 293 (%)	Moderate (4–6) stress resilience n=129 746 (%)	Low (1–3) stress resilience n=51 840 (%)	p Values
Parental SEI 1960 n (%)				<0.001
Manual workers	19 107 (33.9)	55 116 (42.5)	24 622 (47.5)	
Agricultural workers	1450 (2.6)	5318 (4.1)	2459 (4.7)	
Farm owners/managers	5285 (9.4)	14 132 (10.9)	4324 (8.3)	
Office workers	20 424 (36.3)	34 134 (26.3)	11 428 (22.0)	
Business owners/managers	6954 (12.4)	13 817 (10.6)	4729 (9.1)	
Others/unknown	3073 (5.5)	7229 (5.6)	4278 (8.3)	
Household crowding, 1960 n (%)				<0.001
≤2 people/room	47 484 (84.4)	101 462 (78.2)	36 846 (71.2)	
>2 people/room	8809 (15.6)	28 284 (21.8)	14 994 (28.8)	
Cognitive function*	6.1 (1.7)	5.2 (1.9)	4.2 (2.0)	<0.001
Diastolic blood pressure* (mm Hg)	71.3 (8.5)	71.6 (8.6)	72.1 (8.8)	<0.001
Systolic blood pressure* (mm Hg)	127.6 (11.1)	127.7 (11.1)	127.6 (11.2)	0.028
CVD diagnosis				0.009
Yes	1479 (2.6)	3631 (2.8)	1521 (2.9)	
No	54 814 (97.4)	126 115 (97.2)	50 319 (97.1)	
Physical working capacity*	7.2 (1.7)	6.2 (1.7)	5.5 (1.7)	<0.001
Body Mass Index (kg/m <sup>2</sup> ) n (%)				<0.001
Underweight (<18.499)	3719 (6.6)	15 403 (11.9)	8535 (16.5)	
Normal weight (18.5–24.999)	48 623 (86.4)	104 698 (80.7)	38 892 (75.0)	
Overweight (25.0–29.999)	3624 (6.4)	8331 (6.4)	3660 (7.1)	
Obese (≥30.0)	327 (0.6)	1314 (1.0)	753 (1.5)	

\*Mean (SD).

CVD, cardiovascular disease; SEI, socioeconomic index.

overweight or obese, more often had a diagnosis of cardiovascular disease at conscription, and had parents with a lower socioeconomic index and experienced greater household crowding in childhood.

The associations with stroke for stress resilience and the other measures are reported in [table 2](#). All characteristics investigated are statistically significantly associated with stroke. The lowest stress resilience group (21.8% with scores 1–3) compared with the highest (23.7% with score 7–9) was associated with increased risk of all stroke types. The intermediate category of stress resilience lay between the low and high groups, indicating a graded association. When adjusted for the demographic and socioeconomic factors in childhood, the association attenuated slightly but remained statistically significant. Additional adjustment for health and development characteristics in adolescence again attenuated the association somewhat. Further adjustment for physical fitness indicated by BMI and physical capacity had the most notable impact on the HRs, but despite the reduction in magnitude, statistical significance remained. Blood pressure was modelled as continuous variables to ensure the most effective adjustment: the magnitude of the associations appears small as the HRs are for each unit change per mm Hg, but statistical significance for associations with stroke remained after adjustment for all other measures.

[Table 3](#) presents the outcomes for the stroke subgroups, fatal (n=308), ischaemic (n=2060) and intracerebral haemorrhagic (n=676) stroke. All showed a significant association with stress resilience, with higher magnitude associations for fatal than non-fatal stroke; and for haemorrhagic than ischaemic stroke. In adjusted models, a similar pattern as for all stroke appeared, but the association of stress resilience and ischaemic stroke was more notably attenuated by adjustment for BMI and physical capacity.

## DISCUSSION

Low stress resilience in adolescence was associated with a higher risk of stroke in men of working age between 31 years and 58 years, a relatively young age group to experience stroke. This association was independent of childhood socioeconomic circumstances, as well as health and developmental characteristics in adolescence. The association was attenuated more notably (but not eliminated) by adjustment for BMI and physical working capacity as indicators of physical fitness in adolescence, likely to signal future lifestyle characteristics.

Our results from a general population-based cohort of men are consistent with recent studies suggesting a role for psychosocial stress in influencing stroke risk.<sup>3–5 9 10</sup> Similarly, poorer adaptation to social adversity—possibly signalling lower stress resilience—has also been linked with an increased risk of stroke.<sup>22</sup> Stress resilience in adolescence does not measure exposure to stress but does indicate susceptibility, such that the adversities of daily life may have a greater impact and conspire to produce a more chronic pattern stress arousal over adult life. Another study has found associations with stress independent of lifestyle factors.<sup>4</sup> This difference with our findings may be due to methodological variations, as we have a measure of resilience rather than stress exposure, it was collected prospectively, many years before stroke, and we adjusted for some characteristics in adolescence that may themselves be consequences of low stress resilience, as discussed below.

We hypothesise that low resilience to psychosocial stress could indicate exposure to psychosocial stress in earlier life, resulting in poorer control of the stress response that can continue across the life course. Animal studies have demonstrated that early life stress can alter HPA axis function in a way that can persist over the life course, producing persistent low resilience to stress.<sup>23 24</sup> Stress resilience may also be a characteristic of personality type, and

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**Table 2** Stroke risk associated with stress resilience and other characteristics

	Events/n	Unadjusted Model 1 HR (95% CI)	Adjusted		
			Model 2 HR (95% CI)	Model 3 HR (95% CI)	Model 4 HR (95% CI)
<b>Stress resilience</b>					
1. High (7–9)	690/56 293	Reference	Reference	Reference	Reference
2. Moderate (4–6)	1751/129 746	1.09 (1.00 to 1.19)	1.07 (0.98 to 1.16)	1.01 (0.92 to 1.10)	0.94 (0.86 to 1.03)
3. Low (1–3)	970/51 840	1.54 (1.40 to 1.70)	1.48 (1.34 to 1.63)	1.30 (1.18 to 1.45)	1.16 (1.04 to 1.29)
<b>Parental SEI 1960</b>					
Manual workers	1527/98 845	1.21 (1.11 to 1.31)	1.14 (1.04 to 1.24)	1.08 (0.98 to 1.18)	1.06 (0.97 to 1.16)
Agricultural workers	129/9227	1.08 (0.90 to 1.30)	1.00 (0.82 to 1.20)	0.92 (0.76 to 1.09)	0.90 (0.74 to 1.09)
Farm owners/managers	321/23 741	1.03 (0.91 to 1.17)	1.02 (0.89 to 1.16)	0.96 (0.84 to 1.10)	0.96 (0.84 to 1.10)
Office workers	836/65 896	Reference	Reference	Reference	Reference
Business/owners managers	349/25 500	1.08 (0.95 to 1.22)	1.06 (0.93 to 1.20)	1.03 (0.91 to 1.17)	1.02 (0.90 to 1.15)
Others/unknown	249/14 580	1.35 (1.17 to 1.56)	1.24 (1.08 to 1.44)	1.18 (1.02 to 1.36)	1.16 (1.01 to 1.34)
<b>Household crowding, 1960</b>					
≤2 people/room	2543/185 792	Reference	Reference	Reference	Reference
>2 people/room	868/52 087	1.22 (1.13 to 1.32)	1.15 (1.06 to 1.24)	1.12 (1.03 to 1.21)	1.11 (1.03 to 1.20)
<b>Cognitive function (per unit change, 1–9)</b>					
Diastolic blood pressure (per 1 mm Hg change)		0.92 (0.90 to 0.93)		0.94 (0.92 to 0.95)	0.94 (0.93 to 0.97)
Systolic blood pressure (per 1 mm Hg change)		1.01 (1.01 to 1.01)		1.01 (1.00 to 1.01)	1.00 (1.00 to 1.01)
<b>CVD diagnosis</b>					
Yes	107/6631	1.13 (0.94 to 1.38)		1.10 (0.90 to 1.33)	1.09 (0.90 to 1.32)
No	3304/231 248	Reference		Reference	Reference
<b>Physical working capacity (per unit change, 0–9)</b>					
		0.91 (0.90 to 0.93)			0.92 (0.90 to 0.94)
<b>Body Mass Index (kg/m<sup>2</sup>)</b>					
Underweight (<18.49)	374/27 657	0.99 (0.89 to 1.01)			0.85 (0.76 to 0.95)
Normal weight (18.5–24.99)	2636/192 213	Reference			Reference
Overweight (25.0–29.99)	321/15 615	1.51 (1.34 to 1.69)			1.45 (1.29 to 1.63)
Obese (≥30.0)	80/2394	2.52 (2.02 to 3.15)			2.14 (1.71 to 2.68)

Model 1. Unadjusted.

Model 2. Adjusted for socio/material background factors (birth year, region, parental SEI and household crowding).

Model 3. Adjusted for 2+ characteristics in adolescence (cognitive function, diastolic and systolic blood pressure and CVD diagnosis at conscription).

Model 4. Adjusted for 2+3+ physical fitness in adolescence (physical working capacity and BMI).

CVD, cardiovascular disease; SEI, socioeconomic index.

**Table 3** Stress resilience and stroke subdivided by stroke characteristics

	Unadjusted Model 1 HR (95% CI)	Adjusted		
		Model 2 HR (95% CI)	Model 3 HR (95% CI)	Model 4 HR (95% CI)
<b>Fatal stroke (n=308)</b>				
<b>Stress resilience</b>				
1. High 7–9	Reference	Reference	Reference	Reference
2. Moderate 4–6	1.15 (0.84 to 1.58)	1.13 (0.83 to 1.55)	1.05 (0.77 to 1.44)	0.94 (0.68 to 1.30)
3. Low 1–3	2.21 (1.60 to 3.06)	2.17 (1.56 to 3.01)	1.82 (1.29 to 2.58)	1.50 (1.04 to 2.16)
<b>Haemorrhagic stroke (n=676)</b>				
<b>Stress resilience</b>				
High 7–9	Reference	Reference	Reference	Reference
Moderate 4–6	1.17 (0.95 to 1.43)	1.16 (0.94 to 1.42)	1.06 (0.86 to 1.30)	1.00 (0.81 to 1.24)
Low 1–3	1.76 (1.41 to 2.20)	1.72 (1.38 to 2.16)	1.40 (1.11 to 1.78)	1.28 (1.00 to 1.63)
<b>Ischaemic stroke (n=2060)</b>				
<b>Stress resilience</b>				
High 7–9	Reference	Reference	Reference	Reference
Moderate 4–6	1.06 (0.95 to 1.19)	1.04 (0.93 to 1.16)	0.99 (0.88 to 1.11)	0.92 (0.82 to 1.04)
Low 1–3	1.41 (1.24 to 1.60)	1.34 (1.18 to 1.53)	1.20 (1.05 to 1.38)	1.08 (0.94 to 1.24)

Model 1. Unadjusted.

Model 2. Adjusted for socio/material background factors (birth year, region, parents SEI, household crowding).

Model 3. Adjusted for 2+ characteristics in adolescence (cognition, systolic and diastolic blood pressure, CVD diagnosis at conscription).

Model 4. Adjusted for 2+3+ physical fitness in adolescence (physical working capacity and BMI).

CVD, cardiovascular disease; SEI, socioeconomic index.



thus, a persistent trait. For example, low resilience may reflect something like type A behaviour which, although controversial, has previously been related to increased cardiovascular risk.<sup>25</sup> It has been demonstrated that adverse socioeconomic conditions in childhood increase stroke risk<sup>26</sup>; so we adjusted for such factors, with little impact on the association of stress resilience with stroke. Markers of early life exposure to stress have been linked with poorer cognitive development<sup>27</sup> and higher blood pressure.<sup>28</sup> Thus, cognitive function and blood pressure may represent consequences of earlier stressful exposures and poorer stress resilience, and adjusting for these factors may have produced conservative estimates of association; arguably an over-adjustment. Markers of stressful exposures in early life are also linked with unhealthy weight gain,<sup>29</sup> which may influence physical exercise or be a consequence of low exercise levels.<sup>30</sup> Thus, even in adolescence, BMI and fitness could, in part, be a consequence of lower stress resilience and earlier stressful exposures. We believe the results suggest that a significant proportion of the association of stress and stress resilience with stroke risk is due to lifestyle risk factors. This is consistent with recent findings from a British cohort study with older participants, where the association of psychological distress with CVD risk was largely explained by behavioural/lifestyle processes.<sup>31</sup> Our findings suggest such processes have a long natural history, beginning in childhood or adolescence.

Our results were consistent among the different stroke subtypes (fatal, non-fatal, ischaemic and intracerebral haemorrhagic stroke) although there may be pathological heterogeneity. Previous studies investigating the association between psychosocial stress and stroke subtypes are few, but the results are mostly consistent with our findings suggesting a more notable association for fatal than for non-fatal stroke, and for haemorrhagic than ischaemic stroke. The stronger association with haemorrhagic than ischaemic stroke could also be a consequence of a greater aetiological heterogeneity in ischaemic stroke. Physical working capacity and BMI in adolescence most notably attenuated that association of stress resilience with ischaemic stroke, suggesting more significant mediation through lifestyle factors.

As this is a study of stress resilience measured in adolescence, it is possible that stressful *exposures* in adult life might represent a higher risk of stroke, particularly chronic exposures among the less stress resilient. Overweight, obesity and poorer physical capacity in adolescence are likely to signal an accumulation of behavioural/lifestyle health risks that continue through adulthood.<sup>32–33</sup> Other lifestyle risks in the years between conscription and stroke, such as smoking, alcohol and diet, are also likely to be relevant mediating factors. Further mediating factors might include type 2 diabetes, a stroke risk which tends to have its onset in adulthood some years after the time of conscription, which has also been linked with psychosocial stress.<sup>34–35</sup> As behaviours and diagnoses occurring between conscription and stroke are intermediate in the causal pathway, we have not included them in the model. Unfortunately, we have no data on smoking, diet or alcohol consumption, which could have added further to our understanding of lifestyle risks. Thus, major mediation between poor stress resilience and stroke risk may be through lifestyle factors and fitness, suggesting interventions for psychosocial stress and behaviour might be most effective in lowering stroke risk among younger men.

### Strengths

The use of prospectively recorded data from several linked registers, and the long-term follow-up subsequent to the measure of susceptibility, increases the validity and reliability of the study, as

well as avoiding bias due to reverse causation or poor recall. The study population is largely representative of the male general population as only a small proportion of Swedish men were exempted from enlistment examinations. Extensive physical and psychological examinations were conducted in adolescence, so the information was objectively measured and were able to adjust for a variety of powerful stroke risk factors including, BMI and physical capacity which are objective physiological measures. The duration between conscription examination and start of follow-up means it is unlikely that prodromal characteristics of an impending stroke were driving the stress resilience measure, and it was possible to identify pre-existing cardiovascular diagnoses and adjust for blood pressure.

### Limitations

The potential limitations of the study include the inclusion of only men, as women also suffer from stroke. This was necessary as the measure of stress susceptibility was collected during military conscription, which at the time was almost exclusively available to men. As stress resilience was only measured once, we cannot be definitive about stability of this characteristic over time and how this may interact with stressful exposures. In these data, the association of stress resilience with stroke risk did not vary by age, indicating that this measure of stress resilience is a relatively stable characteristic over time, at least in terms of stroke risk. There is a possibility of misclassification of the stress resilience measure if potential conscripts attempted to obtain exemption from military service through 'false' responses. However such 'false' answers, if they exist, would most likely dilute the resilience measure and result in less precise estimates. The temporal relationship of stress resilience and physical fitness in adolescence cannot be established, but we hypothesise that poor stress resilience has an adverse influence on physical fitness. As stressful exposures were not examined, it is possible that the magnitude of associations with stress resilience is conservative.

A proportion of the cardiovascular diagnoses at conscription when the men in our cohort were 18–19 years old may not be directly relevant to stroke risk. We included this information in the models to ensure that poorer stress resilience was not a function of pre-existing cardiovascular disease, where a proportion of these diseases may increase subsequent stroke risk. Most stroke onset occurs at a higher age than in our study, so early stroke may be somewhat atypical and the aetiology may differ from stroke at older ages.<sup>36</sup> However, stroke incidence in younger adults (younger than 55 years of age) is increasing.<sup>37</sup> Stroke at young (working) age is a particular concern, as a reduction of working capacity increases the personal, social as well as economic burden of the disease. This is of public health significance, as stroke at early ages has the potential for greater lifetime burden of disability, and because some risks may be modifiable. The proportion of stroke diagnoses in the analytic sample is lower than among those who were not included. This is for two reasons, and the first is that men who had a stroke at an early age, close in time to the conscription examination, were excluded deliberately to avoid associations due to reverse causation. Some men in poor health, with very low levels of physical fitness, or low cognitive function at the time of the conscription examination, were identified as unsuitable for military service by the assessors and may not have completed all the examinations (including for stress resilience). As these men—excluded due to missing values on the assessments—may have the greatest risk of stroke, we may have underestimated the proportion at risk and conceivably produced a conservative estimate of stroke risk. The validity of some

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diagnoses recorded in the Swedish National Inpatient Register can be questionable, but the reliability of stroke diagnoses is satisfactory.<sup>38 39</sup>

### CONCLUSIONS

The association with stress resilience suggests that stress may be implicated in the aetiology of stroke, which is, in part, explained by poorer physical fitness among the less stress resilient. We hypothesise that the most effective interventions to prevent stroke would focus on behaviour and lifestyle factors, as well as psychosocial stress.

**Contributors** All authors fulfil the authorship requirements and have approved the final version of the manuscript. SM, KF and CB developed the research question and the study design. CB and RU conducted the data preparation and data analyses. CB and SM wrote the first draft of the manuscript to which all authors made significant subsequent contributions.

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**Competing interests** None.

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## Stress resilience in male adolescents and subsequent stroke risk: cohort study

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