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ORIGINAL ARTICLE

# Cardiovascular fitness in early adulthood and future suicidal behaviour in men followed for up to 42 years

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**Background.** Cardiovascular fitness influences many aspects of brain function. However, the relationship between cardiovascular fitness and suicidal behaviour is unknown. Therefore, we aimed to determine whether cardiovascular fitness at age 18 years is associated with future risk of suicide attempt/death.

**Method.** We performed a population-based Swedish longitudinal cohort study of male conscripts with no previous or ongoing mental illness ($n$=1 136 527). The conscription examination, which took place during 1968–2005, included the cycle ergonometric test and tests of cognitive performance. Future risk of suicide attempt/death over a 5- to 42-year follow-up period was calculated with Cox proportional hazards models controlling for several confounders including familial factors.

**Results.** At least one suicide attempt was recorded for 12 563 men. Death by suicide without a prior attempt was recorded in 4814 additional individuals. In fully adjusted models low cardiovascular fitness was associated with increased risk for future attempt/death by suicide [hazard ratio (HR) 1.79, 95% confidence interval (CI) 1.64–1.94]. The HR changed only marginally after exclusion of persons who received in-patient care for depression (HR 1.76, 95% CI 1.61–1.94). Poor performance on both the cardiovascular fitness and cognitive tests was associated with a fivefold increased risk of suicide attempt or suicide death (HR 5.46, 95% CI 4.78–6.24).

**Conclusions.** Lower cardiovascular fitness at age 18 years was, after adjustment for a number of potential confounders, associated with an increased risk of attempt/death by suicide in adulthood. It remains to be clarified whether interventions designed to improve fitness in teens can influence the risk of suicidal behaviour later in life.

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**Key words:** Adolescence, intelligence quotient, mental health, physical fitness, prevention, suicide, suicide attempt.

## Introduction

Suicide is a major public health concern worldwide and the second most common cause of death amongst young adults in the European Union (WHO, 2001). Suicide attempt is the strongest known risk factor for suicide (Leon *et al.* 1990; Yoshimasu *et al.* 2008).

For effective prevention, knowledge of key risk factors for suicide attempt and completed suicide is essential. The epidemiology is complex and a range of factors, including childhood risk factors (Sourander *et al.* 2009; Bruffaerts *et al.* 2010; Niederkrotenthaler *et al.* 2012), familial clustering (Tidemalm *et al.* 2011), low intelligence quotient (Batty *et al.* 2010*a*; Sörberg *et al.* 2013), low body mass index (BMI) (Batty *et al.* 2010*b*; Kinoshita *et al.* 2012), short stature (Jiang *et al.* 1999; Whitley *et al.* 2010), low socio-economic status (Andres *et al.* 2010), history of psychiatric disorders (Qin, 2011) and somatic illness (Gradus *et al.* 2010; Saitta *et al.* 2011; Kendal & Kendal, 2012), are associated with increased risk.

There are a few cross-sectional studies that indicate physical activity in adolescence as a protective factor against suicidal ideation (Brown & Blanton, 2002; Babiss & Gangwisch, 2009), but the relationship with more serious forms of suicidal behaviour (suicide attempt or suicide death) remains unclear. Previous studies have relied on questionnaires or self-rating scales for the measurement of physical activity. Prospective

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studies are lacking. Cognitive performance (Gunnell *et al.* 2005), BMI (Magnusson *et al.* 2006) and height (Whitley *et al.* 2010) at conscription have all been shown to be associated with future risk of suicide and both cognitive performance and BMI are also associated with cardiovascular fitness (Åberg *et al.* 2009; Pahkala *et al.* 2013). Further, we recently showed that lower cardiovascular fitness at conscription was associated with increased risk of serious depression in adulthood (Åberg *et al.* 2012).

We performed a prospective cohort study of all Swedish men born in 1950–1987 who at conscription at age 18 years had no history of mental illness. The first aim was to determine whether cardiovascular fitness at conscription was associated with future risk of suicide attempt or suicide death during a follow-up time of 5–42 years. The second aim was to examine how cognitive performance, BMI, height and depression would make an impact on the hypothesized relationship between fitness and suicide attempt or suicide death. A third aim was to study the relationship between cardiovascular fitness and cognitive performance and future risk of suicidal behaviour.

## Method

### *Participants*

A cohort of 18-year-old Swedish males who enlisted for military service between 1968 and 2005 (i.e. born between 1950 and 1987; $n = 1\,353\,723$) was compiled from the Swedish Military Service Conscription Register. During that time Swedish law required all 18-year-old Swedish men to enlist. Exemptions were granted only for incarcerated males, severe chronic medical or mental conditions, or functional disabilities documented by a medical certificate (approximately 2–3% of the 18-year-old male population each year). When enlisting, males underwent extensive and highly standardized physical and psychological examinations prior to assignment in the Swedish Armed Forces. Conscripts with any history of mental illness or ongoing psychiatric disorders at the time of the examination ($n = 69\,609$) were excluded from the current study. All Swedes have a unique personal identification number making linkage to other registers possible. The Ethics Committee of the University of Gothenburg and Confidentiality Clearance at Statistics Sweden approved the study.

### *Swedish military service conscription register data*

#### *Cardiovascular fitness test*

Cardiovascular fitness was assessed using the cycle ergonometric test. The procedure, including elements of validity and reliability, has been described in detail previously (Nordesjö & Schéle, 1974). Briefly, after a normal resting electrocardiogram, 5 min of submaximal exercise was performed at work rates of 75–175 W, depending on body weight. The work rate was continuously increased by 25 W/min until volitional exhaustion. The subject was instructed to maintain pedal cadence between 60 and 70 revolutions per min. Heart rate was continuously measured. The final work rate ($W_{max}$) was recorded and divided by body weight. This measure was employed because it yielded a better correlation with maximum oxygen consumption ($V_{O_2max}$) (correlation coefficient about 0.9) than predicted $V_{O_2max}$ (correlation coefficient about 0.6–0.7). The resulting values ($W_{max}$/kg) were transformed into stanine (STAndard NINE) scores that served as a measure of cardiovascular fitness.

#### *Cognitive tests*

The cognitive performance tests are described in detail elsewhere (Carlstedt, 2000) and data have been employed in other studies (Gunnell *et al.* 2005; Åberg *et al.* 2009; Sörberg *et al.* 2013). Four cognitive tests were used during the period of assessment covered by the current study: logical performance test, verbal test of synonym and opposites, test of visuospatial/geometric perception, and technical/mechanical skills including mathematical/physics problems. Results from all four tests were combined yielding a combined intelligence score, which was regarded as a measure of general cognitive performance. Procedures for carrying out the cognitive tests changed in 1980 (Carlstedt, 2000) but others who have used these conscription data (Gunnell *et al.* 2005) as well as our own group (Åberg *et al.* 2009) have shown that the procedural alteration did not affect the associations examined. Test results were standardized against data from previous years to give scores from 1 (low) to 9 (high) with a Gaussian/normal distribution for each of the five scores: combined intelligence, logical, verbal, visuospatial, and technical/physics scores. The standardization to a nine-point 'stanine' scale provided long-term stability of the datasets. Before 1996 raw data were not electronically recorded and only stanine scores could be accessed for statistical analysis.

#### *Diagnoses recorded at conscription*

Conscripts were assessed by psychologists and physicians during the conscription examination. Those ($n = 69\,609$) who met criteria for previous or ongoing psychiatric disorders [International Classification of Diseases (ICD)-8 and -9 codes 290–319; ICD-10 codes F00–F99; all mental and behavioural disorders] were excluded from the current analyses.

**Table 1.** *Numbers of male conscripts with hospital record of suicide attempt or suicide death without previous attempt during up to 42 years of follow-up by method-specific ICD codes*[a]

| Method | ICD-8/9 codes | ICD-10 codes | Attempted suicides, *n* | Completed suicides, *n* |
|---|---|---|---|---|
| All | E950–E959 | X60–X84 | 12563 | 4814 |
| Poisoning by solid or liquid substances | E950 | X60–X65, X68–X69 | 10057 | 747 |
| Sharp object | E956 | X78 | 1088 | 110 |
| Other poisoning | E951–E952 | X66–X67 | 328 | 676 |
| Hanging, strangulation and suffocation | E953 | X70 | 420 | 1806 |
| Jumping from high place | E957 | X80 | 286 | 182 |
| Firearms and explosives | E955 | X72–X75 | 121 | 827 |
| Drowning and submersion | E954 | X71 | 63 | 139 |
| Other | E958–E959 | X76–X77, X79, X81–X84 | 373 | 638 |

ICD, International Classification of Diseases.

[a] For persons with repeat behaviours, only first episodes are shown.

### *Outcomes*

#### *Suicide attempt*

Attempted suicide diagnoses were obtained from the Swedish National Hospital Discharge Register, which is maintained at the National Board of Health and Welfare. The Swedish National Hospital Discharge Register covers virtually all in-patient care for psychiatric disorders since 1964. Discharge diagnoses are coded by the physician in accordance with the ICD versions 8, 9 or 10 (ICD-8, ICD-9 and ICD-10). We identified diagnostic codes for first episode of hospitalization for attempted suicide from 1968 to 31 December 2010. The specific ICD-8, ICD-9 and ICD-10 codes that were used in the analyses are shown in Table 1.

#### *Suicide death*

Suicide deaths were identified by linkage with the Cause of Death Register, which is maintained at the National Board of Health and Welfare. The Swedish Cause of Death Register, which covers virtually all deaths since 1961, is annually updated based on death certificate diagnoses. See Table 1 for specific ICD-8, ICD-9 and ICD-10 codes.

### *Covariates from other data sources*

#### *LISA*

Education and occupation information was obtained from the longitudinal integration database for health insurance and labour market studies (Swedish acronym LISA). The LISA database (http://www.scb.se/Pages/List____257743.aspx) at Statistics Sweden was initiated in 1990 and includes all registered residents aged 16 years and older. The database, which is annually updated, integrates data from the labour market, as well as educational and social sectors. Information on parental education was obtained from LISA (80% coverage) and was rated in seven levels: pre-high school education less than 9 years, pre-high school education 9 years, high school education, college education (less than 2 years), college education (2 or more years), postgraduate education and postgraduate research training.

#### *Multi-Generation Register*

Links to the Multi-Generation Register (http://www.scb.se/Pages/List____257501.aspx; website in Swedish) at Statistics Sweden enabled the identification of full brothers.

### *Statistical analysis*

All statistical calculations were performed with SAS version 8.1 (SAS Institute Inc., USA). The follow-up period began at the date of conscription (baseline) and subjects were censored at the time of (1) first suicide attempt or (2) suicide (in cases without prior attempt) or (3) death from other causes or (4) at the end of follow-up, i.e. on 31 December 2010 (minimum 5 years and maximum 42 years of follow-up). We used Cox proportional hazards models to assess the influence of cardiovascular performance at age 18 years and potential confounders on the occurrence of first onset of suicide attempt or suicide death during the observation period. Cardiovascular fitness scores were transformed to stanines that were categorized as 'low' (stanine score 1–3), 'medium' (stanine score 4–6) and 'high' (stanine score 7–9); the 'high' group was the reference category. Since cardiovascular fitness was not normally distributed (see online Supplementary Table S1), separate analyses were also performed with 'low' cardiovascular fitness as stanine score 1–4, 'medium' as stanine score 5–7 and 'high' as stanine score 8–9.

Age was used as the time axis in the Cox model, thus controlling for age. To assess effects of secular variation in rates of suicide attempt or suicide death and differences in conscription procedures over time, we adjusted for calendar years by stratifying the Cox model by conscription decade (1960s, 1970s, etc.).

To reduce the risk for possible reverse causation, i.e. suicidal thoughts affecting performance on the physical tests, we restricted the analysis to men with no mental illness at the conscription examination and no previous episodes of in-patient psychiatric care in accordance with the National Hospital Register. To further reduce baseline misclassification, we performed separate analyses excluding incident cases of suicide attempt or suicide death during the year following the conscription examination.

Because differences among regions and test centres could introduce bias, geographical region and conscription test centres were considered as possible confounders and were adjusted for.

Adjustment for the continuous variables BMI and height were performed. Education levels for each parent were included as confounders (Nock *et al.* 2013). Also adjustment for cognitive performance at conscription was performed.

To further assess potential effects of familial factors, subanalyses were performed within full brother pairs of conscripts. We used the Cox's proportional hazards model adjusting for the above-listed confounders including also suicide attempt or suicide death in one or more male siblings as an additional explanatory variable. This inclusion was independent of temporal relation to the brother's suicidal behaviour within the observation period.

The fact that the study spans a long time could have made an impact on our results due to latency of effect. To study how follow-up time affected the associations, separate analyses were performed with the follow-up times: 1–10, 11–20, 21–30 and 31–42 years.

Separate Cox models were performed to assess the influence of cardiovascular performance and potential confounders on the occurrence of suicide death during the observation period.

In a final set of analyses focusing on the suicidal behaviour outcome, we looked specifically at interactions involving both cardiovascular and cognitive performance data, first by stratifying by level of cognitive performance and second by combining low, medium and high performance in nine separate groups; the high cardiovascular/high cognitive performance group was the reference category.

Due to the large number of observations, the *p* values were very small [in all analyses when the 95% confidence interval (CI) was separated from 1 the *p* values were $<0.0001$]. Therefore *p* values are not reported and the risk for type I errors is considered very low.

## Results

Our analyses are based on the 1 136 527 mentally healthy conscripts with no prior history of attempted suicide and with complete information from military conscription. At least one suicide attempt was registered for 12 563 individuals during the observation period (Table 1). Suicide was the cause of death for a total of 5857 of the men in the cohort; 4814 of these had no previous registration of attempted suicide. In all, there were 17 377 cases with first onset of suicide attempt or suicide death during the observation period, corresponding to 1.53% of the total sample. The mean time from assessment of cardiovascular fitness at age 18 years to the first admission for attempted suicide was 14.1 years. For those with no previous attempt, the mean time from the evaluation and death by suicide was 15.5 years. Numbers with first onset of suicide attempt or suicide death are shown by level of follow-up time in online Supplementary Fig. S1.

### *Cardiovascular fitness at age 18 years and future suicide attempt or suicide*

Numbers and proportions with suicide attempt or suicide death during the observation period are shown by level of cardiovascular fitness at age 18 years in online Supplementary Table S1. Poor performance on the cardiovascular fitness test was associated with an increased risk for suicide attempt/death (Table 2). We found an inverse relationship with the highest hazard ratios (HRs) for suicidal behaviour in the low cardiovascular fitness group (stanine score 1–3). The strength of the associations changed little in models that controlled for calendar year, BMI, conscription test centre, parental education and height. However, the HR in the low cardiovascular fitness group was attenuated by 29% [the relative change between HRs 2.23 and 1.87 calculated as $(HR_{unadj} - HR_{adj})/(HR_{unadj} - 1.0)$] when controlling for cognitive performance at conscription. Data were reanalysed using a different categorization of cardiovascular fitness

**Table 2.** *Risk for suicide attempt/death in relation to cardiovascular fitness in a national cohort of 18-year-old male conscripts (n=1 136 527)*

| | Age-adjusted | Adjusted 1[c] | Adjusted 2 | Adjusted 3 | Adjusted 4 |
|---|---|---|---|---|---|
| Suicidal behaviour[a,b] (*n*=17 377) | | | | | |
| Cardiovascular fitness | | | | | |
| Low[d] | 2.16 (2.02–2.30) | 2.14 (2.00–2.28) | 2.23 (2.06–2.43)[e] | 1.87 (1.72–2.04)[f] | 1.79 (1.64–1.94)[g] |
| Medium[d] | 1.55 (1.50–1.60) | 1.55 (1.50–1.60) | 1.56 (1.50–1.63)[e] | 1.43 (1.37–1.49)[f] | 1.39 (1.33–1.45)[g] |
| Depression excluded and 1 year latency time[h] | | | | | |
| Suicidal behaviour[b] (*n*=14 029) | | | | | |
| Cardiovascular fitness | | | | | |
| Low[d] | 2.16 (2.02–2.32) | 2.15 (2.00–2.31) | 2.23 (2.03–2.45)[e] | 1.86 (1.70–2.05)[f] | 1.76 (1.61–1.94)[g] |
| Medium[d] | 1.54 (1.49–1.60) | 1.55 (1.50–1.61) | 1.56 (1.49–1.64)[e] | 1.43 (1.36–1.50)[f] | 1.38 (1.32–1.45)[g] |
| Conscripts with brothers only[i] | | | | | |
| Suicidal behaviour[b] (*n*=4607) | | | | | |
| Cardiovascular fitness | | | | | |
| Low[d] | 1.98 (1.74–2.26) | 1.96 (1.72–2.24) | 1.99 (1.74–2.27)[j] | 1.58 (1.38–1.80)[k] | 1.51 (1.32–1.73)[l] |
| Medium[d] | 1.53 (1.44–1.63) | 1.52 (1.43–1.62) | 1.52 (1.43–1.62)[j] | 1.35 (1.26–1.44)[k] | 1.31 (1.23–1.40)[l] |
| Brother[m] | 3.25 (2.85–3.71) | 3.26 (2.86–3.72) | 3.26 (2.85–3.72)[j] | 3.01 (2.63–3.43)[k] | 2.99 (2.62–3.42)[l] |

Data are given as hazard ratio (95% confidence interval).
[a] With age-adjusted and fully adjusted models.
[b] Suicide attempt/death.
[c] Adjusted for calendar year, body mass index.
[d] Reference category: high.
[e] Adjusted for calendar year, body mass index, conscription test centre, parental education.
[f] Adjusted for calendar year, body mass index, conscription test centre, parental education, intelligence quotient.
[g] Adjusted for calendar year, body mass index, conscription test centre, parental education, intelligence quotient, height.
[h] Subanalyses after exclusion of conscripts (*n*=3348) with in-patient depression preceding or coinciding with the suicidal behaviour and with a latency time for suicide attempt/death within 1 year after conscription examination.
[i] Subanalyses for conscripts (*n*=336 055) with one or more full-brothers. Suicide attempt/death in one or more brother included in the model as an additional explanatory variable.
[j] Adjusted for calendar year, body mass index, conscription test centre.
[k] Adjusted for calendar year, body mass index, conscription test centre, intelligence quotient.
[l] Adjusted for calendar year, body mass index, conscription test centre, intelligence quotient, height.
[m] One or more brothers with suicidal behaviour.

(see Statistical analysis) and this procedure yielded similar HRs (results not shown). Therefore, stanine score 1–3 was used as 'low', stanine score 4–6 as 'medium' and stanine score 7–9 as 'high' cardiovascular fitness in all following analyses.

Separate analyses excluding individuals with in-patient treatment for depression preceding or coinciding with the first onset of suicide attempt or suicide death and excluding incident cases of suicide attempt or suicide death during the year following the conscription examination (i.e. a latency time of 1 year) yielded similar results.

In the total cohort there were 336 055 subjects with one or more full-brothers. While having one or more brothers with suicide attempt or suicide death was associated with a threefold increased risk of future suicidal behaviour, both low and medium cardiovascular fitness remained significant predictors in the model.

Three ICD versions were utilized during the long observation period. As this might affect results, we carried out separate analyses for each ICD system. These analyses showed similar associations between cardiovascular fitness and future suicidal behaviour but with twofold higher HRs within the ICD-10 compared with ICD-8/9. In order to see if there were changes in the effect size with greater follow-up time, subgroups were created for 10-year periods with respect to conscription year and length of follow-up. Higher HRs were observed closer to baseline within the same ICD version (Table 3).

There may be systematic differences between individuals who attempted suicide and those who committed suicide. Therefore, we performed separate analyses including only suicide death with or without previous suicide attempt as outcome (*n*=5857). In fully adjusted models poor performance on the cardiovascular fitness test was not associated with an

**Table 3.** *Risk for suicide attempt/death in relation to cardiovascular fitness at age 18 years by 10-year follow-up periods in male conscripts (n=1 136 527)*

| Conscription year | Cardiovascular fitness | Follow-up period 1969–1978 (ICD-8) | 1979–1988 (ICD-8/9) | 1989–1998 (ICD-9/10) | 1999–2010 (ICD-10) |
|---|---|---|---|---|---|
| 1968–1977 | | (*n*=770) | (*n*=2085) | (*n*=2064) | (*n*=2263) |
| | Low[a] | 2.32 (1.74–3.10) | 1.72 (1.42–2.09) | 2.03 (1.69–2.44) | 1.76 (1.46–2.10) |
| | Medium[a] | 1.69 (1.45–1.98) | 1.48 (1.35–1.62) | 1.40 (1.28–1.54) | 1.35 (1.23–1.47) |
| 1978–1987 | | | (*n*=1253) | (*n*=2371) | (*n*=2402) |
| | Low[a] | | 2.29 (1.84–2.86) | 2.48 (2.10–2.94) | 2.11 (1.78–2.50) |
| | Medium[a] | | 1.32 (1.16–1.49) | 1.67 (1.52–1.83) | 1.65 (1.50–1.80) |
| 1988–1997 | | | | (*n*=1319) | (*n*=2194) |
| | Low[a] | | | 3.29 (2.44–4.44) | 3.62 (2.90–4.52) |
| | Medium[a] | | | 1.93 (1.69–2.21) | 1.99 (1.79–2.21) |

Data are given as hazard ratio (95% confidence interval). Adjusted for calendar year, body mass index, conscription test centre.

ICD, International Classification of Diseases.

[a] Reference category: high.

increased risk for suicide death (HR 0.96, 95% CI 0.80–1.15). Separate analyses excluding individuals with in-patient treatment for depression preceding or coinciding with suicide death and excluding incident cases of suicide death during the year following the conscription examination (i.e. a latency time of 1 year) yielded similar results.

### *Relationships between physical and cognitive performance at age 18 years and future suicidal behaviour*

In the final set of analyses, we wanted to study interactions between cardiovascular fitness and cognitive performance and future risk of suicidal behaviour. Supplemental data regarding the relationship between cognitive performance and suicide attempt or suicide death are presented in online Supplementary Tables S1 and S2.

Table 4 shows that low and medium (compared with high) cardiovascular fitness was associated with an increased risk of future suicidal behaviour when stratified for 'low', 'medium' and 'high' cognitive performance. It demonstrates the lack of an interaction between cardiovascular fitness and cognitive performance. This indicates that cardiovascular fitness is an important predictor for later suicidal behaviour independent of cognitive performance.

Subsequently nine separate groups were created by combining 'low', 'medium' and 'high' performance; the 'high' cardiovascular/'high' cognitive performance group was the reference category (online Supplementary Table S3 and Fig. 1). Poor performance (category 'low') on both the cognitive and cardiovascular fitness tests was associated with a fivefold increased risk of attempted suicide/death by suicide. Having high cardiovascular fitness but low cognitive performance reduced the risk to threefold. Although cognitive performance seems to have a larger effect on later suicidal risk than cardiovascular fitness *per se*, a high cardiovascular fitness (compared with low) reduced future risk of suicidal behaviour in all cognitive performance levels.

## Discussion

In this national cohort study, we demonstrate that low cardiovascular fitness in early adulthood is associated with a twofold increased risk of suicidal behaviour during up to 42 years of follow-up. Relationships followed a dose–response pattern. Associations were only slightly attenuated after controlling for a number of possible covariates including serious depression. The associations between cardiovascular fitness and later suicidal risk were attenuated by 29% after controlling for cognitive performance. The combination of low cardiovascular fitness and low cognitive performance resulted in a fivefold increase in later risk of suicide attempt or suicide death.

The present study is a prospective study with a national population-based cohort of over a million individuals, objective measures of both cardiovascular

**Table 4.** *Risk for suicide attempt/death in relation to cardiovascular fitness by cognitive performance (intelligence quotient) at age 18 years in male conscripts (n=1 136 527)*

| Suicidal behaviour[a] (*n*=17 377) | Stratified for intelligence quotient | Age-adjusted | Adjusted 1[b] | Adjusted 2[c] | Adjusted 3[d] |
|---|---|---|---|---|---|
| Cardiovascular fitness | | | | | |
| Low[e] | Low | 1.74 (1.58–1.93) | 1.68 (1.51–1.86) | 1.92 (1.69–2.19) | 1.84 (1.62–2.10) |
| Medium[e] | | 1.41 (1.32–1.50) | 1.35 (1.26–1.44) | 1.40 (1.29–1.51) | 1.36 (1.25–1.47) |
| Low[e] | Medium | 1.84 (1.67–2.01) | 1.80 (1.64–1.97) | 1.85 (1.63–2.09) | 1.76 (1.55–2.00) |
| Medium[e] | | 1.42 (1.36–1.49) | 1.42 (1.36–1.48) | 1.47 (1.39–1.56) | 1.43 (1.35–1.52) |
| Low[e] | High | 1.70 (1.37–2.10) | 1.65 (1.33–2.04) | 1.74 (1.31–2.31) | 1.61 (1.21–2.14) |
| Medium[e] | | 1.32 (1.22–1.43) | 1.33 (1.22–1.44) | 1.34 (1.21–1.49) | 1.29 (1.16–1.43) |

Data are given as hazard ratio (95% confidence interval).

[a] Suicide attempt/death.

[b] Adjusted for calendar year, body mass index.

[c] Adjusted for calendar year, body mass index, conscription test centre, parental education.

[d] Adjusted for calendar year, body mass index, conscription test centre, parental education, height.

[e] Reference category: high.

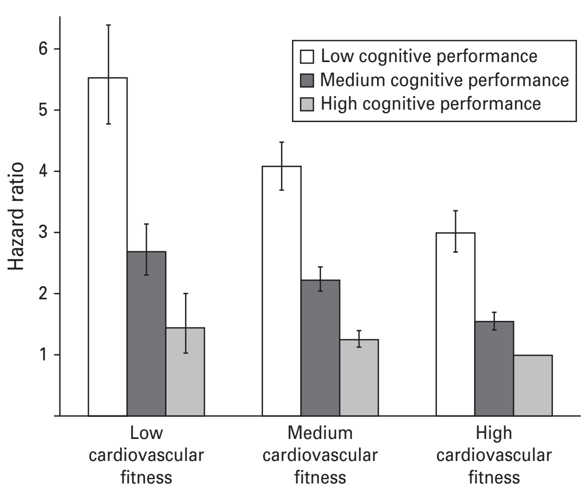


**Fig. 1.** Risk for suicidal behaviour for 18-year-old male conscripts (*n*=1 136 527) with different levels of cognitive performance, shown by level of cardiovascular fitness. All values are from fully adjusted models in online Supplementary Table S3 (Depression excluded and 1 year latency time section). Data are hazard ratios, with 95% confidence intervals represented by vertical bars.

fitness and cognitive performance, and a long follow-up time. The Swedish National Hospital Discharge Register enables us to cover virtually all in-patient care for suicide attempts during 42 years. Similarly, the Swedish Cause of Death Register covers all confirmed suicides during these years.

As the use of three separate ICD systems might affect results, we carried out separate analyses for each ICD version (8/9/10). Indeed, the associations between cardiovascular fitness and suicidal behaviour differed depending on which ICD version was used. Specifically, higher HRs were observed within the ICD-10. We have previously reported the same phenomenon for other associations (Åberg *et al.* 2012). While this may be an artifact it could also reflect a true secular variation that might be related to differences in diagnosis rate or treatment regimens over time. Also, while ICD-8 and ICD-9 are considered to be very similar, the ICD-10 is somewhat different. Clinical diagnoses are more clear and specific in this later version. More specific diagnoses would be expected to yield higher HRs.

An additional strength of this study is the reliance on psychologists and physicians for baseline assessment of mental health history, allowing us to exclude individuals with pre-existing psychiatric disorders, thereby reducing the risk of reverse causation. Also by including parental educational level as a confounder and by performing subanalyses within full-brother pairs, many early childhood risk factors could be accounted for, including genetics and parental treatment and upbringing.

However, there are also drawbacks of the current design. Data on cardiovascular fitness were available at baseline only. The incidence of attempted suicide is underestimated, as some do not seek hospital care in connection with a suicide attempt. Similarly, some actual suicides may have been categorized as deaths of uncertain cause.

Although we could adjust for parental education and suicidal behaviour in brothers we were not able to adjust for specific early developmental influences such as childhood psychiatric problems which did not require in-patient care or parental death that may have affected the associations (Sourander *et al.* 2009; Kuramoto *et al.* 2013). Further, although the conscripts underwent extensive examinations by psychologists, subsyndromal states that might have affected the future risk of suicidal behaviour may have been missed, and some may have opted not to tell about previous episodes of suicidal behaviour. Suicide attempts are common in youth, with accumulated prevalence figures as high as 1% in Swedish and 2% in American male teens up to the age of 18 years (Zetterqvist *et al.* 2012; Nock *et al.* 2013). Conscripts who neglected to report previous suicide attempts or episodes of mental ill-health would be inappropriately included in our study if they had no previous record of psychiatric hospitalization. Results from our study cannot be directly extrapolated to women or to other settings, as patterns of suicidal behaviour differ between men and women and among different cultures (Nock *et al.* 2008, 2013).

There are possible confounders that may increase risk for both poor fitness and suicide attempt or suicide death. A couple of cross-sectional epidemiological studies have documented an association between self-reported sedentary life-style in adolescence and suicidal behaviour (Brown & Blanton, 2002; Babiss & Gangwisch, 2009). They conclude that self-esteem and social support are important mediators of the relationships between sports participation and suicidal ideation. We were not able to control for self-esteem, personality and socio-environmental circumstances at the time of conscription/later in the life course that may have affected the associations.

Biological risk factors associated with major depression contribute to the aetiology of suicidal behaviour (Coryell, 2006). Several cross-sectional and a few prospective epidemiological studies have documented an association between self-reported sedentary life-style and depression (Farmer *et al.* 1988; Buckworth & Dishman, 2002; Strawbridge *et al.* 2002; Harvey *et al.* 2010). Therefore, a possible explanation for the association between cardiovascular fitness in young adulthood and suicidal behaviour later in life could be mediated via a protective effect of physical fitness on depression. Depression is indeed an important risk factor for suicidal behaviour; however, it is somewhat less salient at younger ages (Hunt *et al.* 2006). This paper focuses on first episode of suicidal behaviour, which in many cases occurred at a relatively young age, a time of life when depression might play a less prominent role in suicide-related outcomes. The association with cardiovascular fitness remained after exclusion of individuals with in-patient depression preceding or coinciding with the first episode of suicidal behaviour. Further, the association between cardiovascular fitness and suicidal behaviour appeared to be connected to suicide attempt in our study; associations with suicide death were not significant. If depression had been the main mediator of the association we would have expected to find larger HRs for death by suicide than for the combined suicide attempt/suicide death outcome as those who die by suicide would be more likely to be depressed than those with non-fatal attempts. Taken together, our findings suggest that the reduced risk for future suicidal behaviour observed in those with better cardiovascular performance at the age of 18 years might in part be attributed to a mechanism other than a protective effect of physical fitness on depression. There are data at the molecular biological level indicating that the increased susceptibility of certain individuals towards suicidal behaviour stems from disruptions in the hypothalamic–pituitary–adrenal axis (Wasserman *et al.* 2010) and expression of brain-derived neurotrophic factor (BDNF) (Dwivedi, 2009), which may be independent of depression. Interestingly, these disruptions are positively affected by physical exercise (Zheng *et al.* 2006; Griffin *et al.* 2011) and one may speculate that physical exercise in young adulthood could contribute to an increased brain reserve capacity (Nithianantharajah & Hannan, 2009) which might reduce the risk of suicidal behaviour in times of distress. One mechanism underlying these effects of exercise on brain function could be the robust increase in the generation of new neurons in the adult hippocampus (van Praag *et al.* 1999; Brown *et al.* 2003). There is emerging evidence of the possible involvement of hippocampal neurogenesis in mediating the beneficial effects of physical exercise on counteracting stress (Yau *et al.* 2011).

Both physical fitness and cognitive performance in late adolescence seem to be important predictors for later suicidal behaviour. We found that cardiovascular fitness was associated with future suicidal risk independently of cognitive performance. At the individual level it may be difficult to change cognitive performance; however, cardiovascular performance is possible to improve. A greater understanding of the mechanisms underlying these associations including complex bidirectional models may provide opportunities and strategies for prevention (de Jonge & Roest, 2012). While our results cannot be extrapolated to adolescents with previous episodes of mental illness and suicide attempts, future studies could test the usefulness of exercise programmes for these individuals. Evaluating new strategies could prove to be clinically important, considering the difficulty of reducing suicidal behaviours among young people (Gibbons *et al.* 2012).

## Supplementary material

For supplementary material accompanying this paper, please visit http://dx.doi.org/10.1017/S0033291713001207.

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## Declaration of Interest

None.

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