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Maintaining or increasing cardiorespiratory fitness is associated with reduced hospital admission rate

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Aims The aim of this study was to investigate the association between change in cardiorespiratory fitness (CRF) and cardiovascular disease (CVD)-related and all-cause hospital admission and explore if the association varies dependently on prior admission, baseline CRF, sex, and age.

Methods and results A total of 91 140 adult participants (41.5% women) with two examinations from occupational health profile assessments between 1986 and 2019 were included (mean of 3.2 years between examinations). Cardiorespiratory fitness was assessed as maximal oxygen consumption and estimated through a submaximal cycle test. Cardiorespiratory fitness change was defined as annual percentage change in relative CRF (mL/min/kg) and further divided into 'decliners' (≤1%), 'maintainers' (−1% to 1%), and 'increasers' (>1%). Hospital admissions were followed over a mean of 7 years. Natural cubic splines and Cox proportional hazards model were applied. Additionally, prevented fraction for the population was calculated. Increase in CRF was associated with a lower risk of CVD [hazard ratio (HR) = 0.99] and all-cause hospital admission (HR = 0.99), after multilevel adjustment for confounders and change in smoking, diet, and stress. Compared with a decline, maintenance of CRF was associated with 9% and 7% lower risk of CVD and all-cause admission, respectively. Increase in CRF reduced the risk by 13% and 11% and, for individuals with prior admission, by 20% and 14%. The burden of CVD and all-cause admission was 6% and 5% lower than if the whole cohort had declined CRF, with large potential cost savings.

Conclusion Efforts to maintain or improve CRF should be included in disease-preventive strategies, regardless of change in other lifestyle-related risk factors. Preventing the age-associated decline in CRF can lessen healthcare utilization and costs.

Lay summary Moderate to high cardiorespiratory fitness has been associated with lower risk of cardiovascular disease and overall morbidity and mortality, but since it is not known whether a change in cardiorespiratory fitness influences the risk of future hospitalization, the present study investigated this, with the following key findings:

- Maintenance of cardiorespiratory fitness, compared with a decline, was associated with 9% lower risk of cardiovascular-related hospital admission and 7% lower risk of all-cause admission, while an increase in cardiorespiratory fitness was associated with 13% and 11% lower risk, respectively.
- Individuals who previously had been hospitalized and managed to increase their cardiorespiratory fitness had 20% and 14% lower risk of future cardiovascular and all-cause hospital admission, respectively.

Keywords Cardiorespiratory fitness • Cardiovascular diseases • Prevention • Hospitalization • Working population

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Introduction

It is well established that regular physical activity has wide-ranging health benefits, including a protective effect against premature death[1] and the development of lifestyle-related diseases, especially cardiovascular disease (CVD).[2] The World Health Organization has classified physical activity as one of the primary modifiable risk factors for CVD.[3] Over the last decades, however, physical inactivity has increased worldwide, also in the Swedish population,[4] with a simultaneous deterioration in cardiorespiratory fitness (CRF).[5]

Cardiorespiratory fitness is a measurement of maximal oxygen consumption (VO_2max) and represents the capacity of the cardiovascular and respiratory systems to transport oxygen to skeletal muscle and vital organs and is mainly improved through regular aerobic physical activity of sufficient intensity. Prior studies have identified an accelerating decline in CRF with age in both women and men,[6] although the level of physical activity can mitigate this decline somewhat.[7] Extensive data suggest that CRF is independently correlated to cardiovascular risks, such as the metabolic syndrome and coronary artery calcification,[8,9] to cardiovascular events,[10–13] and to CVD-related and all-cause mortality.[11,13–15] Cardiorespiratory fitness is also a potentially stronger indicator for all-cause mortality than traditional risk factors such as smoking, high blood pressure, and type 2 diabetes.[16] Even so, CRF is the only major clinical risk factor that is not routinely controlled for in clinical risk assessment, today.

Few studies have investigated the effects of change in CRF, using multiple time points of CRF measurements, and on long-term outcomes. Among existing studies, change in CRF has been associated with major CVD-related risk factors, including hypertension, type 2 diabetes, and hypercholesterolaemia.[17–20] Some studies have additionally assessed the effects of change in CRF on mortality as the primary outcome.[12,21,22] For instance, in 1995, Blair et al.[21] found that in a cohort of men, participants who maintained or improved their CRF (mean of 4.9 years between examinations) had lower risk of CVD-related and all-cause mortality. Specifically, the reduction in mortality risk was 44% from improved CRF in comparison with remaining unfit, over a mean 5.1-year follow-up.

Improvement in physical activity levels and CRF should therefore be of clinical relevance for healthcare utilization and associated costs for society. One way to assess healthcare utilization and costs is to investigate hospital admission rates. However, little is known about the association between change in CRF and actual hospital admissions. Although one prospective study from 2015 found that higher mid-life CRF was associated with a lower risk of heart-failure hospitalization, CRF was measured at a single time point only.[23]

In the present study, we have access to repeated measurements of CRF in a large cohort of women and men and aim to investigate the association between intra-individual change in CRF in adulthood and CVD-related and all-cause hospital admission. We further aim to explore if the association varies dependently on prior hospital admission, baseline CRF level, sex, age, and whether change in smoking, diet, and stress affects the association.

Methods

Health profile assessment database

Data were obtained from the Health Profile Assessment (HPA) database, which is managed by the Health Profile Institute (HPI, Stockholm, Sweden). The HPAs have been conducted since the 1970s in Sweden and comprise anthropometric measurements (including data on body weight and height), a submaximal cycle test for estimating VO_2max, an extensive questionnaire with data on lifestyle habits, and an in-depth interview with a HPA coach. The HPA is free of charge for the participant, who is offered the HPA through their employer, connected to an occupational or other health service in Sweden. The HPI is responsible for education of data collection staff and standardization of methods and for administrating the database.

For the present study, individuals with at least two HPAs between 1986 and 2019, and with valid measurements of estimated VO_2max on both occasions, were included. For individuals with more than two HPAs, the first and most recent HPAs were used. To minimize the influence of measurement errors and uncertainties in data collection and recording processes, individuals younger than 18 or older than 79 years of age at baseline, or that had an annual decline or increase in relative or absolute CRF of more than 20%, were excluded (see flow chart in Supplementary material online, *Figure S1*). In total, the study cohort consists of 91 140 participants in analyses on relative CRF (mL/min/kg) and 91 641 in analyses on absolute CRF (L/min) (analyses on absolute CRF are available in the supplement material online). Informed consent was provided from all participants prior to data collection. The study was approved by the Stockholm Ethics Review Board (Dnr 2015/1864-31/2 and 2016/9-32).

Cardiorespiratory fitness assessment

Cardiorespiratory fitness was assessed as estimated VO_2max through the standardized Åstrand submaximal test on a cycle ergometer.[24] Participants were requested to refrain from vigorous physical activity the day before the HPA, from consuming a heavy meal 3 h before testing, to refrain from smoking or snuff use at least 1 h before the test, and were encouraged to avoid stress. Each participant cycled on a calibrated ergometer at a submaximal work rate for 6 min to attain a steady-state pulse. Cardiorespiratory fitness was estimated in both relative and absolute terms, using age-correction factors.

For this study, change in CRF was defined as the annual percentage change in VO_2max between HPA screenings and was expressed as the difference between the second and first divided by first screening ((VO_2max test2 – VO_2max test1)/VO_2max test1) and was additionally divided by the number of years between screenings. To minimize the risk to extrapolate values for participants with shorter interval than 1 year between screenings, participants with an interval between 10 months and 1 year were given a value of '1-year follow-up' when calculating annual percentage change, and participants with an interval shorter than 10 months were excluded.

Additionally, annual change in CRF was categorized into 'decliners' ($\leq$1%), 'maintainers' (−1% to 1%), and 'increasers' (>1%). In extended analyses on relative CRF, five categories were applied: 'large decliners' ($\leq$3%), 'small decliners' (−3% to $\leq$1%), 'maintainers' (−1% to 1%), 'small increasers' (>1% to 3%), and large increasers (>3%). Similar cut-offs for annual change in CRF have been applied in prior research. For instance, a decline of −1% to $\leq$3% in absolute CRF (L/min) has been associated with a 21% increased risk of hypertension.[20]

Hospital admission or death

All participants were followed from their last HPA to first hospital admission, death, or until 31 December 2019. Records of hospital admission were retrieved from the Swedish National Inpatient Registry and death of any cause from the Swedish Cause of Death Registry. Cardiovascular disease-related hospital admission was extracted based on international classification of disease (ICD) codes and includes main and secondary diagnoses of hypertension-related diseases (ICD8: 400-404; ICD9: 401-405; and ICD10: I10-I15), ischaemic heart diseases (ICD8: 410-414; ICD9: 410-414; and ICD10: I20-I25), other forms of heart diseases (ICD8: 420-429; ICD9: 420-429; and ICD10: I30-I52), and cerebrovascular diseases (ICD8: 430-438; ICD9: 430-438; and ICD10: I60-69).

Covariates

Prior hospital admission was defined as any admissions that occurred before the first HPA and was dichotomized (0/1). Baseline CRF level was divided into five categories: 'very low', 'low', 'average', 'high', and 'very high' based on the sex- and age-dependent cut-offs for relative VO_2max by Blair et al.[1] To ensure a large enough number of participants in each category, the five CRF categories were merged into three: 'low' ('very low' plus 'low'), 'average', and 'high' ('high' plus 'very high'). Sex and age were self-reported in the HPA questionnaire.

Smoking habits, diet, and perceived overall stress were self-reported. Smoking habits were assessed using the following statement: *I smoke*, with the alternatives: 'at least 20 cig/day', '11–19 cig/day', '1–10 cig/day', 'occasionally', or 'never'. Diet included the following components: *I consider my diet, regarding both meal frequency and nutrition content to be*, with the alternatives: 'very poor', 'poor', 'neither good nor bad', 'good', or 'very good'. Overall stress was measured by the following statement: *I perceive stress in life, both personally and at work*, with the alternatives: 'very often', 'often', 'sometimes', 'rarely', or 'never'.

For the present paper, covariates for risk level/behaviour were defined and dichotomized. For smoking, risk level/behaviour was defined as '>1 cigarette per day', for diet as 'poor'/'very poor', and for stress as 'often'/'very often'. Change in risk level/behaviour was subsequently categorized into four groups: *maintained risk* (risk at first and second screening), *deteriorated* (no risk at first but risk at second screening), *improved* (risk at first but not at second screening), and *maintained non-risk* (no risk at first and no risk at second screening). Spearman and Pearson correlation was used to investigate collinearity between predictor, outcome, and covariates.

Other variables

Body weight was measured using a calibrated scale wearing light-weight clothing and rounded to the nearest 0.5 kg. Height was assessed using a wall-mounted stadiometer and rounded to the nearest 0.5 cm. Subsequently, body mass index (BMI) (kg/m^2) was calculated. Systolic and diastolic blood pressure (mmHg) was measured manually in the right arm after 20 min of seated rest, using a standardized auscultatory method. Intake of CVD medication was self-reported with the alternatives 'yes' or 'no'.

Exercise habits were self-reported using the statement: *I exercise for the purpose of maintaining/improving my physical fitness, health and well-being*, with the alternatives: 'never', 'occasionally', '1–2 times/week', '3–5 times/week', or '>6 times/week'. Overall health was reported as follows: *I perceive my physical and mental health as*, with the alternatives: 'very poor', 'poor', 'neither good or bad', 'good', or 'very good'. The highest educational level at the time of the HPA was obtained from Statistics Sweden through linking of personal identity numbers. Educational level was expressed as 'low' = pre-secondary education ≤9 years, 'medium' = secondary education 2–3 years or post-secondary education <3 years, and 'high' = post-secondary education ≥3 years or postgraduate education.

Statistical analysis

The associations between annual percentage change in CRF and CVD-related and all-cause hospital admission were analysed using Cox regression models with natural cubic splines. The reference level was set to 0% and knots to −3% and 3%. The splines demonstrate covariates added in three adjustment models. Model 1 adjusted for prior hospital admission and baseline CRF, Model 2 additionally adjusted for sex and age at the second screening (and BMI at the second screening when analysing absolute CRF), and Model 3 additionally adjusted for change in smoking, diet, and stress level/behaviour between screenings. As blood pressure can have an effect on cardiac function and thereby the CRF, a supplemental sensitivity analysis was performed including mean arterial pressure in Model 4. Mean arterial pressure was calculated as follows: diastolic blood pressure + 1/3 (systolic blood pressure − diastolic blood pressure).

The adjusted Cox proportional hazards regression model was additionally used to study the association between change in CRF and hospital admission, with decliners set as reference. CVD-related and all-cause hospital admission were dichotomized (0/1). The hazard rate [hazard ratio (HR)] for hospital admission was assessed at 95% confidence interval (CI). Covariates were added in three adjustment models, as described above. Risk time from the last HPA screening until hospital admission, death, or end of study period was coded separately for CVD-related and all-cause hospital admission, respectively. To test for interaction between men and women, an interaction term (sex*annual percentage change in CRF) was introduced in the Cox model. The analyses were performed using IBM Statistical Package for Windows (IBM SPSS Statistics, version 28) and R with Tidyverse, Survival, Splines, and Patchwork package (R Core Team 2022, R Foundation for Statistical Computing, Vienna, Austria, version 4.2.1).

Prevented fraction for the population (PFP) was calculated using the following equation from Strain *et al.*[25] where P_d is the prevalence of exposure (maintenance of or increase in CRF) among cases: $PFP = P_d(1 - HR)/[1 - (1 - HR)(1 - P_d)]$. In turn, we estimated the hypothetical total number of hospital admissions that would have been observed if there had been a decline in CRF in the entire study population, by dividing the observed number of hospital admissions by 1 minus the prevented fraction.[25] Subsequently, we estimated the number of admissions averted from maintenance of or increase in CRF by taking the difference between the observed and hypothetical number of admissions. In addition, we calculated saved healthcare costs, alike the calculations in Strain *et al.*, by obtaining the total number of admissions, as well as the estimated cost per admission in Sweden, from the Swedish Association of Local Authorities and Regions data sets.[26] Number of admissions and cost per admission were based on inpatient treatment events in 2022. In 2022, there were approximately 170 000 CVD-related and 1 160 000 all-cause-related admissions in the Swedish population, and the average healthcare cost was approximately 95.000 Swedish crowns (SEK) [euros (EUR) ≍ 8.000] for a CVD admission and SEK ≍ 80.000 (EUR ≍ 6.700) for an all-cause admission.[26]

Results

A total of 91 140 participants (41.5% women) with a mean age of 41.8 [standard deviation (SD) 10.3] years at the first screening were included in the analyses. The mean interval between screenings was 3.2 (SD 2.3) years and ranged from 0.8 to 24.7 years. Mean follow-up time from the last screening until hospital admission, death, or end of study period was 7.8 (SD 5.0) years for CVD and 7.3 (SD 4.9) years for all-cause admission, ranging from 0 to 30 years. A total of 6709 participants had a CVD admission, 14 188 participants had an all-cause admission, and 1365 individuals died throughout the study period. At the first screening, 1832 participants had experienced a prior CVD admission and 13 971 a prior all-cause admission. The mean annual change in relative CRF was −0.3 (SD 2.6) mL/min/kg.

At the first screening, the participants' baseline characteristics, including age, BMI, lifestyle habits, educational level, blood pressure, intake of medication, and disease history, were similar among decliners, maintainers, and increasers (*Table 1*). Estimated relative VO_2max at the first screening differed between the groups, with the highest mean VO_2max among decliners [39.6 (SD 9.9)] and the lowest mean among increasers [34.5 (SD 8.7)]. Similarly, 42.1% of decliners had a 'high' baseline CRF level in comparison with 21.0% among increasers. The corresponding table for absolute CRF values is presented in Supplementary material online, *Table S1*.

An increase (per annual percentage change) in relative CRF was associated with a lower risk of CVD admission [HR = 0.97, 95% CI (0.97–0.98)] and all-cause admission [HR = 0.98 (0.98–0.98)] in Model 1 (*Figure 1*). The associations remained in the fully adjusted model (Model 3) for both CVD [HR = 0.99 (0.98–0.99)] and all-cause admissions [HR = 0.99 (0.99–0.99)]. In comparison with a decline in CRF (set as reference), maintenance of CRF was associated with a risk reduction of CVD [HR = 0.91 (0.85–0.98)] and all-cause admission [HR = 0.93 (0.89–0.98)] after full adjustment (*Table 2*). An increase in CRF was associated with greater risk reduction of both CVD [HR = 0.87 (0.82–0.92)] and all-cause admissions [HR = 0.89 (0.86–0.93)]. No interactions for sex were observed, neither for the association with CVD hospital admission nor with all-cause hospital admission (see Supplementary material online, *Table S2*). Further, in the sensitivity analysis, including mean arterial pressure (Model 04) had a small attenuating effect on the association (see Supplementary material online, *Table S3*). Hazard curves and extended analyses are presented in Supplementary material online, *Figure S2* and *Table S4*. Corresponding natural cubic spline regression, Cox regression, and hazard curves for absolute values are also available in Supplementary material online, *Table S5* and *Figures S3* and *S4*.

Baseline cardiorespiratory fitness level

For participants with low baseline CRF, maintenance of CRF was not associated with any significant risk reduction of neither CVD nor

Table 1 **Baseline characteristics of the study cohort stratified for annual percentage change in mL/min/kg**

		Decliners (≤1%)	Maintainers (−1% to 1%)	Increasers (>1%)
n (% women)		43 348 (41.6%)	14 346 (39.5%)	33 446 (42.2%)
Age (years)		41.9 (10.2)	41.6 (10.0)	41.8 (10.4)
BMI		25.2 (3.7)	25.3 (3.7)	25.6 (3.9)
Estimated VO_2max (mL/min/kg)		39.6 (9.9)	37.0 (9.2)	34.5 (8.7)
CRF category at baseline (mL/min/kg)	Low	25.0%	35.5%	46.3%
	Average	32.9%	34.9%	32.7%
	High	42.1%	29.6%	21.0%
Exercise habits (never/occasionally)		32.1%	35.7%	36.3%
Smoking habits (>1 cig/day)		9.7%	8.7%	8.6%
Diet habits (very poor/poor)		7.0%	8.2%	6.8%
Overall stress (very often/often)		13.4%	12.9%	13.1%
Overall health (very bad/bad)		4.1%	4.4%	4.6%
Educational level	Low	9.6%	9.9%	8.7%
	Medium	66.9%	66.3%	66.1%
	High	23.4%	23.8%	25.2%
Systolic blood pressure		123.9 (14.1)	124.5 (14.0)	125.1 (14.6)
Diastolic blood pressure		76.6 (9.8)	76.8 (9.8)	77.1 (10.1)
Intake CVD medication		2.7%	2.3%	2.7%
Prior CVD hospital admission		2.1%	1.8%	2.0%
Prior all-cause hospital admission		15.8%	14.3%	15.1%

Baseline characteristics are demonstrated as mean [standard deviation (SD)] or percentage.

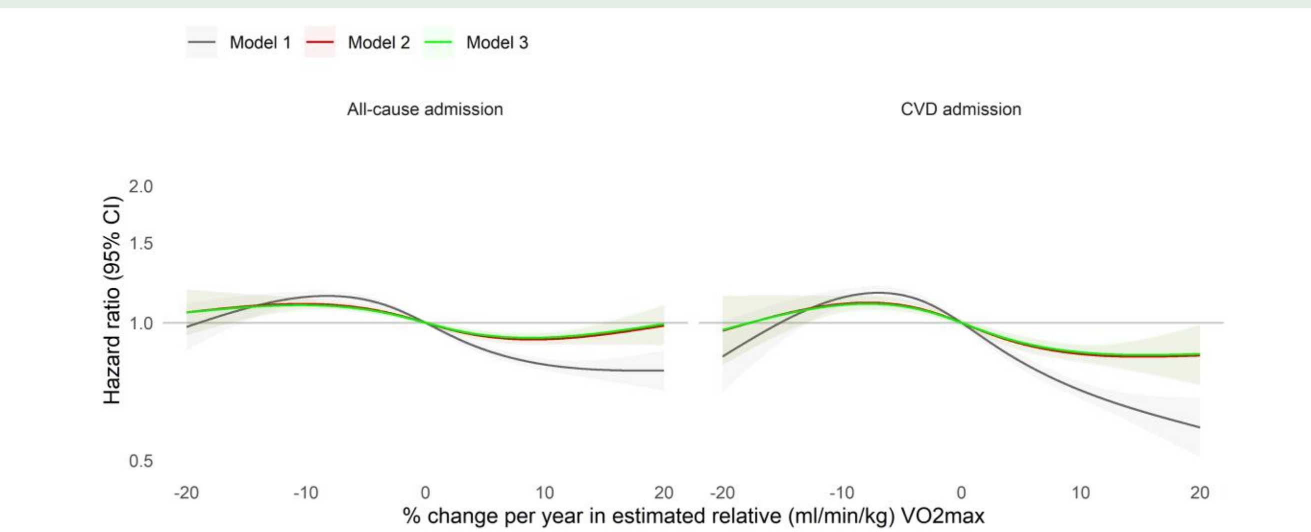

Figure 1 Natural cubic spline regressions with hazard ratio (95% confidence interval) for the association between annual percentage change in estimated relative (mL/min/kg) cardiorespiratory fitness and all-cause and cardiovascular disease-related hospital admission. Reference level is set to 0% and knots to −3% and 3%. Model 1 adjusted for prior hospital admission and baseline cardiorespiratory fitness, Model 2 additionally adjusted for sex and age at the second screening, and Model 3 additionally adjusted for change in smoking, diet, and stress between the first and second screening. CI, confidence interval; CVD, cardiovascular disease.

all-cause admission, in comparison with a decline in CRF (*Table 3*). But an increase of an initially low CRF level was associated with reduced risk of both CVD [HR = 0.86 (0.79–0.93)] and all-cause admissions [HR = 0.91 (0.86–0.97)]. For participants with an average baseline CRF, maintenance of CRF was associated with a risk reduction of CVD admission [HR = 0.87 (0.77–0.98)], and an increase in CRF lowered the risk of both CVD [HR = 0.87 (0.79–0.95)] and all-cause admissions [HR = 0.90 (0.85–0.96)]. For participants with high CRF at baseline,

Table 2 Hazard ratios (95% confidence interval) of hospital admission in relation to annual percentage change in mL/min/kg

	Decliners (≤1%)	Maintainers (−1% to 1%)	Increasers (>1%)	Omnibus tests of model coefficient Overall (score)
CVD hospital admission				
Model 1	1.00 (ref)	0.97 (0.91–1.04) ($P = 0.534$)	0.84 (0.80–0.89) ($P < 0.001$)***	<0.001
Model 2	1.00 (ref)	0.91 (0.84–0.97) ($P = 0.009$)*	0.86 (0.81–0.90) ($P < 0.001$)***	<0.001
Model 3	1.00 (ref)	0.91 (0.85–0.98) ($P = 0.014$)*	0.87 (0.82–0.92) ($P < 0.001$)***	<0.001
All-cause hospital admission				
Model 1	1.00 (ref)	0.97 (0.92–1.02) ($P = 0.299$)	0.88 (0.84–0.91) ($P < 0.001$)***	<0.001
Model 2	1.00 (ref)	0.93 (0.88–0.97) ($P = 0.004$)*	0.88 (0.85–0.92) ($P < 0.001$)***	<0.001
Model 3	1.00 (ref)	0.93 (0.89–0.98) ($P = 0.008$)*	0.89 (0.86–0.93) ($P < 0.001$)***	<0.001

Model 1 adjusted for prior hospital admission and baseline CRF.
Model 2 additionally adjusted for sex and age at the second screening.
Model 3 additionally adjusted for change in smoking, diet, and stress between the first and second screening.
*$P < 0.05$.
***$P < 0.001$.

maintenance of CRF was not associated with any significant risk reduction in comparison with a decline. An increase of an already high CRF level was, however, associated with reduced risk of both CVD [HR = 0.88 (0.79–0.99)] and all-cause admissions [HR = 0.85 (0.79–0.91)].

Prior hospital admission

Among participants with a history of prior hospital admission, maintenance of CRF was associated with a significantly lower risk of CVD admission [HR = 0.86 (0.74–0.99)] and an increase in CRF was associated with even greater risk reduction of both CVD [HR = 0.80 (0.72–0.90)] and all-cause admissions [HR = 0.86 (0.80–0.93)], in comparison with a decline (*Table 4*). For participants with no prior hospital admission, maintenance of CRF was associated with a slight but significant risk reduction of all-cause admission [HR = 0.94 (0.89–0.99)], whereas an increase in CRF was associated with risk reduction of both CVD [HR = 0.89 (0.83–0.95)] and all-cause admissions [HR = 0.90 (0.87–0.94)].

Prevented fraction for the population

Prevented fraction for the population ranged from 1% to 5% for CVD admission and from 1% to 4% for all-cause admission (*Figure 2*). This means that the burden of CVD hospital admissions was 1% lower thanks to maintenance of CRF and 5% lower thanks to increase in CRF, than if the whole population had experienced a decline in CRF between screenings. The equivalent burden of all-cause admissions was 1% and 4%, respectively. By adding up these percentages (6% for CVD and 5% for all-cause admission), the estimated total number of admissions that would have been observed if all participants would have had a decline in CRF was 7137 and 14,934, respectively. With regard to the observed number of admissions in the cohort (6709 CVD admissions and 14 188 all-cause admissions), an estimated 428 CVD admissions and 746 all-cause admissions were potentially avoided. Applying the same estimation in the total Swedish population resulted in potentially avoided admissions of approximately 10 800 and 61,100, respectively (there are approximately 170 000 CVD-related and 1 160 000 all-cause-related yearly admissions in the Swedish population).[26]

To further elucidate potential cost savings from the hypothetical number of avoided admissions, we used the average healthcare cost of a CVD-related admission in Sweden [SEK ≍ 95.000 (EUR ≍ 8.000)] and the equivalent cost of an all-cause admission [SEK ≍ 80.000 (EUR ≍ 6.700)].[26] In the cohort, maintenance of or increase in CRF hence potentially saved roughly SEK ≍ 40 million (EUR ≍ 3.3 million) in direct healthcare costs of CVD admissions and SEK ≍ 60 million (EUR ≍ 5 million) in all-cause admissions. In the total Swedish population, theoretical calculations resulted in savings of SEK ≍ 1 billion (EUR ≍ 84 million) in CVD admissions and SEK ≍ 5 billion (EUR ≍ 400 million) in all-cause admissions.

Discussion

In this prospective study on a large cohort of Swedish women and men, maintenance of CRF (−1% to 1% annual change) was associated with a lower risk of both CVD-related and all-cause hospital admissions, in comparison with a decline in CRF (≤1% annual change). Due to the expected age associated, and accelerating decline in CRF over time, maintenance of a stable CRF likely requires a physically active lifestyle, and potentially even behavioural change, and can therefore be considered an improvement in CRF. An increase in CRF (>1% annual change) was associated with even greater risk reduction, especially for participants with a history of prior hospital admission. The associations remained after adjustment for prior admission, baseline CRF, sex, age, and change in smoking, diet, and stress. These associations are as important in women as in men, as there was no interaction with sex.

These results are in line with prior research. For instance, a recent study on the HPA cohort demonstrated that in comparison with the maintenance of CRF, an increase in absolute CRF (≥3% per year) reduced the odds (odds ratio [ORs]) of hypertension with 11%, which is a key risk factor for CVD,[20] whereas a decline in CRF with −1 to ≤3% and ≥−3% increased the risk with 21% and 25%, respectively.[20] Another study found that both maintenance of and increase in CRF lowered the risk of hypertension, metabolic syndrome, and hypercholesterolaemia after 6-year follow-up, in both women and men.[17] The current study extends on these findings by demonstrating that in addition to its effects on known risk factors for CVD, change in CRF is related also to subsequent hospital admission, which has relevant clinical implications.

Along the lines of the findings in the present paper, a prospective study from 2018 on middle-aged men found that in comparison with individuals who 'became unfit', maintenance of high CRF ('remained fit') (HR = 0.43) and increase in CRF ('became fit') (HR = 0.34) were associated with lower risk of stroke, over a mean 23-year follow-up.[27] Another study that instead measured CRF at a single time point found

Table 3 Hazard ratios (95% confidence interval) of hospital admission in relation to annual percentage change in mL/min/kg, stratified for baseline cardiorespiratory fitness

	Low baseline CRF			Average baseline CRF			High baseline CRF		
	Decliners (≤1%)	Maintainers (−1% to 1%)	Increasers (>1%)	Decliners (≤1%)	Maintainers (−1% to 1%)	Increasers (>1%)	Decliners (≤1%)	Maintainers (−1% ; 1%)	Increasers (>1%)
CVD hospital admission									
Model 1	1.00 (ref)	1.02 (0.91–1.14)	0.83 (0.76–0.90)***	1.00 (ref)	0.92 (0.82–1.04)	0.85 (0.77–0.93)***	1.00 (ref)	0.96 (0.83–1.10)	0.88 (0.78–0.98)*
Model 2	1.00 (ref)	0.93 (0.83–1.04)	0.84 (0.78–0.92)***	1.00 (ref)	0.86 (0.77–0.98)*	0.86 (0.78–0.94)*	1.00 (ref)	0.92 (0.80–1.06)	0.88 (0.79–0.99)*
Model 3	1.00 (ref)	0.93 (0.83–1.04)	0.86 (0.79–0.93)***	1.00 (ref)	0.87 (0.77–0.98)*	0.87 (0.79–0.95)*	1.00 (ref)	0.93 (0.81–1.07)	0.88 (0.79–0.99)*
All-cause hospital admission									
Model 1	1.00 (ref)	0.99 (0.91–1.07)	0.90 (0.84–0.95)***	1.00 (ref)	0.95 (0.88–1.03)	0.88 (0.83–0.94)***	1.00 (ref)	0.98 (0.90–1.07)	0.84 (0.78–0.90)***
Model 2	1.00 (ref)	0.93 (0.85–1.01)	0.90 (0.85–0.96)*	1.00 (ref)	0.91 (0.84–0.99)*	0.89 (0.83–0.95)***	1.00 (ref)	0.95 (0.87–1.04)	0.84 (0.78–0.90)***
Model 3	1.00 (ref)	0.93 (0.85–1.01)	0.91 (0.86–0.97)*	1.00 (ref)	0.92 (0.85–1.00)	0.90 (0.85–0.96)*	1.00 (ref)	0.96 (0.88–1.05)	0.85 (0.79–0.91)***

Model 1 adjusted for prior hospital admission.
Model 2 additionally adjusted for sex and age at the second screening.
Model 3 additionally adjusted for change in smoking, diet, and stress between the first and second screening.
*$P < 0.05$.
***$P < 0.001$.

that among 19 485 individuals, higher mid-life CRF was associated with a lower risk of heart-failure hospitalization after the age of 65.[23] Higher relative CRF, defined as one metabolic equivalent increment in VO_2peak measured at a single time point, has also been associated with lower risk of fatal coronary events among healthy (relative risk [RR] = 0.82) and unhealthy (RR = 0.72) middle-aged men.[12] However, none of these studies evaluated hospital care utilization as in the present study.

Here, participants with a history of prior hospital admission or with the lowest baseline CRF level experienced the greatest risk reduction of CVD-related admissions from an increase in CRF between screenings. Similarly, higher relative CRF (measured at a single time point) has been associated with a lower risk of fatal coronary events among men, over a 13-year follow-up, and those who were least fit with the most unfavourable risk profiles benefited the most.[12] Having low CRF has also been associated with a higher incidence rate of CVD morbidity.[11] In total, people with worse risk profiles might have the most to gain from sufficient physical activity levels and improved CRF, when it comes to CVD risk prevention.

The findings in the present paper are in agreement also with studies on mortality as the primary outcome. For example, one prospective study that followed 579 middle-aged men over a median of 11 years found that one unit increase in relative VO_2max was associated with 9% (HR = 0.91) reduced risk of all-cause mortality.[22] Another study on 14 345 men found that both maintenance of (HR = 0.70; HR = 0.73) and increase in (HR = 0.61; HR = 0.58) CRF lowered the risk of all-cause and CVD mortality over a 6-year follow-up, in comparison with a decline in CRF.[28] The present study adds to this knowledge by analysing the joint risk of a number of CVD-related diagnoses as well as all-cause hospital admission, in a large cohort that includes adult women and men of varying ages.

Clinical implications for hospital planning

As demonstrated in this paper, intra-individual maintenance of or increase in CRF during adulthood is associated with a lower risk of future hospital admission. This adds new, clinically relevant knowledge about the effects of change in CRF on hospital utilization and provides an indication of associated costs for hospital planning and societal health economy alike. Further, the PFP estimated that maintenance of or increase in CRF might have averted 6% and 5% of CVD and all-cause hospital admissions, respectively, with projected large hypothetical direct cost savings for the healthcare system. In 2019, the total cost for CVDs in Sweden was estimated to SEK 60.2 billion (EUR ≍ 5 billion), of which nearly half included healthcare costs.[29] Contrary, however, the expected age-associated decline in CRF instead forecasts an increase in healthcare utilization and costs, wherefore efforts to prevent or lessen the decline in CRF are clinically essential.

Cardiorespiratory fitness may be maintained or improved by engaging in regular physical activity of sufficient intensity, frequency, and duration. General guidelines recommend vigorous intensity (at least 60% of VO_2max), 15–15 min/session, and 3–5 days/week to improve CRF.[30] The more intensive activity, the lower the requirement for duration and frequency. Also, more muscles involved will have greater aerobic challenge on the cardiovascular system. Hence, activities that involve the lower body, or more preferably both arms, legs, and trunks, are recommended for more significant effect. Also, health benefits may be reached with increased levels of physical activity, even though CRF is not increased.

Strengths and limitations

The primary strength of this paper is the large cohort of both women and men of varying ages from the working population, whereas most prior knowledge is based on findings from male, middle-aged cohorts. Most prior studies assess CRF at a single time point. Using a single

Table 4 Hazard ratios (95% confidence interval) of hospital admission in relation to annual percentage change in mL/min/kg, stratified for prior hospital admission

	Prior hospital admission			No prior hospital admission		
	Decliners (≤1%)	Maintainers (−1% to 1%)	Increasers (>1%)	Decliners (≤1%)	Maintainers (−1% to 1%)	Increasers (>1%)
CVD hospital admission						
Model 1	1.00 (ref)	0.87 (0.75–1.01)	0.79 (0.71–0.88)***	1.00 (ref)	1.01 (0.93–1.09)	0.86 (0.81–0.92)***
Model 2	1.00 (ref)	0.85 (0.73–0.98)*	0.80 (0.72–0.89)***	1.00 (ref)	0.92 (0.85–0.99)*	0.88 (0.82–0.93)***
Model 3	1.00 (ref)	0.86 (0.74–0.99)*	0.80 (0.72–0.90)***	1.00 (ref)	0.92 (0.85–1.00)	0.89 (0.83–0.95)***
All-cause hospital admission						
Model 1	1.00 (ref)	0.92 (0.83–1.02)	0.84 (0.78–0.91)***	1.00 (ref)	0.99 (0.93–1.04)	0.89 (0.85–0.93)***
Model 2	1.00 (ref)	0.91 (0.82–1.01)	0.85 (0.79–0.92)***	1.00 (ref)	0.93 (0.88–0.98)*	0.89 (0.85–0.93)***
Model 3	1.00 (ref)	0.92 (0.83–1.02)	0.86 (0.80–0.93)***	1.00 (ref)	0.94 (0.89–0.99)*	0.90 (0.87–0.94)***

Model 1 adjusted for baseline CRF.
Model 2 additionally adjusted for sex and age at the second screening.
Model 3 additionally adjusted for change in smoking, diet, and stress between the first and second screening.
*$P < 0.05$.
***$P < 0.001$.

Prevented fraction for the population for CVD- and all-cause hospital admission

	[a]Decliners (<-1%)	[a]Maintainers (-1% ; 1%)	[a]Increasers (>1%)
CVD hospital admission			
[b]Hazard Ratio (95% CI)	1 (ref)	0.91 (0.85-0.98)	0.87 (0.82-0.92)
PFP (%)	1 (ref)	1%	5%
All-cause hospital admission			
[b]Hazard Ratio (95% CI)	1 (ref)	0.93 (0.89-0.98)	0.89 (0.86-0.93)
PFP (%)	1 (ref)	1%	4%

[a]Annual percentage change in relative CRF ($mL^{*}min^{-1}{}^{*}kg^{-1}$)
[b]Hazard Ratios are based on adjustment model 3 (95% CI)

Figure 2 Prevented fraction for the population for cardiovascular disease-related and all-cause hospital admission, in relation to annual percentage change in estimated relative (mL/min/kg) cardiorespiratory fitness. Adjusted for prior hospital admission, baseline cardiorespiratory fitness, sex, age at the second screening, and change in smoking, diet, and stress between the first and second screening. CI, confidence interval; CVD, cardiovascular disease; PFP, prevented fraction for the population.

assessment conveys a risk to incorrectly estimate the true effects of long-term exposure if the participants change their activity habits. Another strength of the present study is therefore the two standardized objective measurements of CRF at separate time points.

Including multiple time points do however contribute to potential selection biases. Participants were collected based on whether they had attended two HPAs, and individuals who chose to perform multiple HPAs likely differ from those who did not return for a second visit (possibly more active and potentially healthier). Conversely, however, this might indicate that the observed effects on hospital admissions from maintenance of or increase in CRF are even larger in the population. Moreover, performing a HPA is voluntary, which might further contribute to this selection bias and influence the representability of the study findings. The high proportion of having high educational level in this cohort might indicate a selection bias. Further, the self-report questions have not been externally validated. In addition, it is possible that regression to the mean may influence some of the results, i.e. that individuals in the high and low CRF groups more likely change towards the mean of the sample at the subsequent measure, while individuals in the moderate CRF group may have the potential to change in both directions. However, similar trends in the associations between maintenance and increase in CRF and hospital admission were observed, indicating that regression to the mean may not have had a substantial impact on the results.

The PFP and subsequent calculations of hypothetical healthcare costs provide an indication of the potential savings from maintenance of or increase in CRF. However, the estimations should be communicated with caution, as these are theoretical calculations. Lastly, submaximal testing to estimate VO_2max is not as exact as directly measured VO_2max using gas exchange. The submaximal estimated Åstrand protocol has, however, been validated against directly measured VO_2max (during treadmill running) in an adult population sample with small but non-significant systematic error.[31] It is not considered feasible to conduct direct VO_2max measurements on large population-based cohorts.

Conclusions

Maintenance of CRF over time, which in itself can be seen as an improvement since a decline in CRF with age is expected, was associated with a lower risk of future hospital admission after adjustment for multiple confounders and change in other lifestyle habits. An increase in CRF was associated with even greater risk reduction, with the most beneficial outcomes for participants with a history of prior hospital admission. The results can in turn be used to estimate hypothetical savings in healthcare costs. In total, these findings emphasize that preventing or lessening the age-associated decline in CRF is important for CVD prevention as well as for reducing overall healthcare utilization and costs, regardless of change in other lifestyle-related risk factors. Efforts to maintain or increase CRF in the population, and, as an important modifiable factor, adding a measurement of CRF in clinical practice, could improve risk stratification for future hospital admissions and strengthen disease-preventive work.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

Author contributions

All authors contributed substantially to the conception and design, equation of data, or analysis and interpretation. F.G. drafted the article, and E.E.-B., D.A., S.P., and M.B. critically revised the paper. All authors gave final approval, and all agreed to be held accountable for all aspects of the work to ensure accuracy and integrity.

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Data availability

Data are available after decent request to the corresponding author.

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