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# Combinations of BMI and cardiorespiratory fitness categories: trends between 1995 and 2020 and associations with CVD incidence and mortality and all-cause mortality in 471 216 adults

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## Aims

To describe time trends in combinations of cardiorespiratory fitness (CRF) and body mass index (BMI) status, and to analyse their associations with cardiovascular disease (CVD) incidence and mortality and all-cause mortality.

## Methods and results

Prospective cohort study with data from occupational health screenings in Swedish employees, including  $n = 471\,216$  (aged 18–74 years) between 1995 and 2020, and  $n = 169\,989$  in risk analyses. Cardiorespiratory fitness was estimated from a submaximal cycle test. High CRF was defined as top quartile, and low CRF as bottom quartile. Body mass index was used to define normal weight (18.5–24.9 kg/m<sup>2</sup>), overweight (25.0–29.9 kg/m<sup>2</sup>), and obesity ( $\geq 30$  kg/m<sup>2</sup>). Outcome data (CVD incidence and mortality, all-cause mortality) were obtained from national registers. From 1995 to 2020, the combination of obesity + low CRF increased from 2.1% to 5.3% (relative increase 154%) whereas the combination of normal weight + high CRF decreased from 13.2% to 9.3% (–30%) (both  $P < 0.001$ ). Negative changes were more pronounced in men, younger ages, and non-university educated. At the end of the period, prevalence of obesity + low CRF were higher in men vs. women (3.1% vs. 2.2%), older vs. younger (3.7% vs. 1.7%), and in non-university vs. university educated (5.0% vs. 0.3%), all  $P$ -value  $< 0.001$ . Having a high CRF attenuated the risk of all three outcomes in all BMI categories, especially in individuals with obesity (hazard ratio 3.90 vs. 6.67 for CVD mortality). Both a low BMI and a high CRF prolonged age of onset for all three outcomes.

## Conclusions

The combination of obesity with low CRF has increased markedly since the mid-90s, with clear implications for increased CVD morbidity and mortality, and all-cause mortality.

## Keywords

BMI • Cardiorespiratory fitness • Cardiovascular disease • Mortality • Obesity

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## Introduction

Obesity and low cardiorespiratory fitness (CRF) are two main risk factors for multiple morbidities, including cardiovascular disease (CVD) and associated mortality.<sup>1</sup> The prevalence of obesity has increased in most Western countries, including Sweden, commonly following a socioeconomic gradient.<sup>2–4</sup> While trend analyses on cardiorespiratory CRF are less common, levels of CRF (or proxies thereof) appear to be in general decline.<sup>5–7</sup>

It is less clear how combinations of CRF and body mass index (BMI) status have developed in recent years. Some research has elucidated the combined contribution of these two common risk predictors to excessive morbidity and mortality,<sup>8–10</sup> larger population-based samples are lacking with potential to study any variation in time trends or effects on different outcomes between genders, age groups, and socioeconomic status. Since obesity remains largely resistant to conventional treatment,<sup>11,12</sup> due to such factors as prolonged alterations in metabolism and appetite,<sup>13–15</sup> there is a need to understand and clarify how CRF may potentially attenuate the excess health risks in individuals with obesity.<sup>8,16–18</sup> Prevention of obesity has likewise proven to be a considerable challenge, meaning that health promotion strategies for individuals with existing obesity are a clear priority.<sup>19,20</sup> Along with dietary changes, an increase in physical activity (commonly resulting in increased CRF) is one of the main strategies.

We aimed to quantify time trends for combinations of normal weight, overweight, and obesity with high or low CRF in a large population-based sample of the Swedish working population from 1995 to 2020. We also describe the same trends in gender, age, and education level categories. Finally, we analysed how combinations of BMI and CRF status were associated with CVD morbidity and mortality, and all-cause mortality in the same gender, age, and education level categories.

## Methods

This study used data from the Health Profile Assessment (HPA) database, managed by the HPI Health Profile Institute (HPI, Stockholm, Sweden). Health Profile Assessment is an interdisciplinary method<sup>21</sup> comprised by a questionnaire with data on current lifestyles, previous and current physical activity habits, perceived health, and overall stress; anthropometry testing with data on body weight and height; a submaximal ergometer CRF test; and an in-depth interview with a HPA coach regarding the collected data. Participation is optional and free of charge for the individual and offered to all employees working for a company or organization connected to occupational or other health services. The Health Profile Institute was responsible for standardization of methods, education of data collection staff, and administration of the central database.

### Study population—time trend analyses

From October 1982 until November 2020, data from a total of 559 927 men and women were registered and stored in a central database. The annual inclusion rate was substantially lower in the formative years (1982:  $n = 1$ , 1994:  $n = 891$ ), compared to more recent years (1995:  $n = 1350$ , last full year of data 2019:  $n = 29\,839$ ). We therefore restricted our analysis to include only the years 1995–2020 ( $N = 558\,372$ ). Of these,  $n = 471\,216$  (aged 18–74 years) provided

valid data for CRF, BMI, gender, and educational level and were included in the time trend analyses.

### Study population—risk analyses

For the risk analyses, we included all participants in the HPA database with valid data from a HPA since 1982 on BMI and CRF ( $n = 472\,771$ ), within the age span 18–74 years (excluding  $n = 122$ ), with valid data on the covariates included in the multi-adjusted analyses (excluding  $n = 125\,834$ ), with data on outcomes from national registers until 31 December 2019 (excluding  $n = 6691$  who performed their HPA after that date) and with no previous history of CVD (excluding  $n = 1700$  with previous CVD). Hence, we had data from  $n = 338\,424$  participants for the risk analyses. As only high vs. low CRF were included in risk analyses,  $n = 169\,989$  participants are included (see Statistics below).

### Assessment and categorization of obesity and cardiorespiratory fitness

Body mass was assessed with a calibrated scale in light-weight clothing to the nearest 0.5 kg. Body height was measured to the nearest 0.5 cm using a stadiometer. Body mass index ( $\text{kg}/\text{m}^2$ ) was subsequently calculated. We defined normal weight as a BMI 18.5–24.9  $\text{kg}/\text{m}^2$ , overweight as BMI 25.0–29.9  $\text{kg}/\text{m}^2$ , and obesity as BMI  $\geq 30.0$   $\text{kg}/\text{m}^2$ .

$\text{VO}_2\text{max}$  was estimated from the standardized submaximal Åstrand cycle ergometer test in  $\text{L}/\text{min}$ ,<sup>22</sup> and expressed in relation to height squared to minimize influence of body size ( $\text{L}/\text{min}/\text{m}^2$ ). To minimize well-known errors with submaximal testing, participants were requested to refrain from vigorous activity the day before the test, consuming a heavy meal 3 h and smoking/snuff use 1 h before the test, and avoiding stress. Previous validation studies on adult population samples show small and non-significant mean differences on group level [ $-0.07$   $\text{L}/\text{min}$  95% confidence interval (CI)  $-0.21$  to  $0.06$ ] between estimated  $\text{VO}_2\text{max}$  using the Åstrand protocol and direct measured  $\text{VO}_2\text{max}$  during treadmill running with an absolute error and coefficient of variance similar to other submaximal tests (Standard error of estimate =  $0.48$   $\text{L}/\text{min}$ , coefficient of variation = 18.1%).<sup>23</sup> We used bottom quartile (cut-off 25th percentile,  $<0.777$   $\text{L}/\text{min}/\text{m}^2$  for men and  $<0.727$  for women) to define low CRF and the top quartile (cut-off 75th percentile,  $>1.080$   $\text{L}/\text{min}/\text{m}^2$  for men and  $>1.010$  for women) as high CRF. The quartile cut-offs were derived from the entire sampling period (i.e. 1995–2020).

### Assessment of covariates

Highest educational attainment at the time for the HPA was obtained from Statistics Sweden, by linking the participant personal identity number and defined as non-university and university attainment. Current exercise, smoking, diet, and overall stress were all self-reported using the following statements; *I exercise for the purpose of maintaining/improving my physical fitness, health and well-being...* with the alternatives *Never, Sometimes, 1–2 times/week, 3–5 times/week, or At least 6 times/week; I smoke...* with the alternatives *At least 20 cig/day, 11–19 cig/day, 1–10 cig/day, Occasionally, or Never; I consider my diet, regarding both meal frequency and nutritional content to be...* with the alternatives *Very poor, Poor, Neither good nor bad, Good, or Very good; and I perceive stress in my life, both in my private life and at work...* with the alternatives *Very often, Often, Sometimes, Rarely, or Never*.

### Cardiovascular disease and mortality events

All participants were followed from their health assessment test to the first CVD event, death or until 31 December 2019. Incident cases of first-time CVD event prior (for exclusion) and after the health assessment

test (ICD10 codes I20, I21, I25, I46, I63, I64, I65, I66) and death from any cause were ascertained through the Swedish national cause of death registry and the national in-hospital registry. For cause-specific mortality analyses, the same ICD codes as for incident cases were used to define CVD as the main underlying cause of death.

## Ethical standards

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Stockholm Ethics Committee (Dnr 2015/1864-31/2 and 2016/9-32).

## Statistics

For trend analyses, we calculated six main categories: (i) normal weight + high CRF, (ii) normal weight + low CRF, (iii) overweight + high CRF, (iv) overweight + low CRF, (v) obesity + high CRF, and (vi) obesity + low CRF. All performed years of HPA were grouped into 2-year periods (except the first period where we used 5 years) for reduced sampling variations and increased power: 1995–2000, 2001–02, 2003–04, 2005–06, 2007–08, 2009–10, 2011–12, 2013–14, 2015–16, 2017–18, and 2019–20. In cases where participants had data from more than one time period, only data from the first measurement were used. Direct standardization was used to acquire CRF rates adjusted by gender, age, and education level for each year group to the level of the population of aged 18–74 years in Sweden ( $n = 6\,991\,720$ ) (data from national register data, www.scb.se). Logistic regression models adjusted for gender, age, and educational level were applied to study significant changes of each of the six risk categories over time. To study interaction between subgroups, an interaction term (2-year group  $\times$  sub-group) was introduced, and significant interaction(s) were defined as  $P$ -value  $< 0.05$  for the interaction term.

For the risk analyses, first we used Cox regression to quantify hazard ratios (HRs) and 95% CI for quantification of the strength of association between our six risk categories and our outcome variables (CVD incidence, CVD mortality, and all-cause mortality). The proportionality assumption was examined using scaled Schoenfeld residuals, detecting zero slopes for the scaled Schoenfeld residuals on functions of time for outcomes. Two adjustment models were used, model 1 including adjustment for gender, age, and performed year of the HPA, and model 2 including additional adjustment for educational level, exercise habits, smoking, diet, and perceived overall stress. We performed additional sensitivity analyses excluding the first 2 years of follow-up, to minimize the potential influence of reverse causation. To study interaction between subgroups, an interaction term (performed year  $\times$  sub-group) was introduced in the Cox regression analyses. Significant interaction(s) were defined as  $P$ -value  $< 0.05$  for the interaction term. Population attributable risk (PAR) was calculated (assuming causality) from the risk category-specific HR estimate and the prevalence of the factor, using the equation  $PAR = \% \text{ of cases exposed to the factor} \times 100 \times (HR - 1)/HR$ . Age at event and death was calculated as estimated marginal means adjusting for gender and age at testing using general linear modelling. The statistical analyses were conducted using IBM SPSS (Statistical Package for the Social Sciences for Windows), version 27.0.0, 2019, SPSS Inc., Chicago, IL, USA and R version 4.0.5 with the package suite Tidverse.

## Results

### Cohort characteristics

The proportion of men and women varied across sampling periods, with increasingly more men participating in HPAs

(Supplementary material online, Table S1). Participation rates by age group (18–49 and 50–74 years) were similar across sampling periods, but with a continuous trend of more participants with university, and fewer with non-university, educational level from inception to 2019–20.

### Trends in obesity and cardiorespiratory fitness combination categories

In the trend analyses (Table 1 and Figure 1), two distinct patterns were evident: a reduction of the normal weight + high CRF category (from 13.2% to 9.3%, relative change  $-30\%$ ), and a concomitant increase in the overweight + low CRF (8.6–11.5%, relative change  $+34\%$ ) and obesity + low CRF (2.1–5.3%, relative change  $+154\%$ ) categories, respectively.

Men and participants with non-university education had a steeper increase in obesity + low CRF prevalence compared to women and participants with university education ( $P = 0.070$  and  $P = 0.019$  for interaction), with similar trends seen for overweight + low CRF in younger compared to older participants ( $P < 0.001$ ) (Figure 2 and Supplementary material online, Table S2). All above had a steeper decrease in normal weight + high CRF ( $P < 0.001$ ) compared to their counterparts. At the end of the study period (year 2019–20), the standardized prevalence of obesity + low CRF was higher in men compared to women (3.1% vs. 2.2%), older compared to younger (3.7% vs. 1.7%), and in non-university compared to university educated (5.0% vs. 0.3%).

### Impact of body mass index and cardiorespiratory fitness categories on cardiovascular disease incidence, cardiovascular disease mortality, and all-cause mortality

A total of 7141 cases of first-time CVD, 536 CVD deaths, and 5744 deaths due to all causes occurred over mean follow-up time of 9.8 years [standard deviation (SD) 5.5] and 9.9 years (SD 5.5), respectively.

Our main analyses of the associations between the six categories of BMI and CRF with our three outcome variables (incident CVD, CVD mortality, and all-cause mortality) are shown in Table 2 and Figure 3. Compared with our reference category (normal weight + high CRF) there were significant differences in HRs both in terms of increasing BMI (independent of CRF) and with low CRF (independent of BMI) for all three outcomes. Hazard ratios were particularly high for CVD mortality for the obesity + low CRF category (6.67, 95% CI 2.94–15.13).

There were significant interactions between the combined CRF and BMI categories and age groups ( $P < 0.001$ ) for CVD incidence (younger age group experiences greater risk increase) and all-cause mortality (older age group experiences greater risk increase). Borderline or non-significant interactions were seen for gender ( $P = 0.73$  for CVD incidence,  $P = 0.09$  for all-cause mortality) and for educational level ( $P = 0.07$  for CVD incidence,  $P = 0.48$  for all-cause mortality) and the combined CRF and BMI categories.

**Table 1** Participant characteristics across the different sampling periods for the trend analyses ( $n = 471\,216$ ), and for the main risk analyses ( $n = 169\,989$ )

Years	Normal weight		Overweight		Obesity		Total N
	High CRF	Low CRF	High CRF	Low CRF	High CRF	Low CRF	
Trend analysis							
1995–2000	14.6%	12.4%	10.4%	7.3%	2.7%	1.8%	17 532
2001–2002	14.1%	12.9%	10.5%	7.4%	2.9%	2.2%	16 242
2003–2004	12.5%	15.0%	8.9%	8.7%	2.5%	2.2%	31 854
2005–2006	12.1%	13.8%	9.5%	9.0%	2.9%	2.6%	39 944
2007–2008	11.9%	13.1%	9.8%	9.0%	3.3%	2.8%	44 792
2009–2010	12.9%	12.0%	10.1%	8.8%	3.5%	2.9%	38 411
2011–2012	12.9%	12.1%	10.2%	9.1%	3.2%	3.1%	58 648
2013–2014	12.0%	12.6%	9.7%	10.0%	3.1%	3.6%	69 613
2015–2016	10.6%	12.6%	9.6%	10.4%	3.2%	4.0%	58 151
2017–2018	10.9%	11.4%	9.5%	9.3%	3.5%	4.1%	56 738
2019–2020	11.0%	10.7%	9.9%	9.7%	3.6%	4.3%	39 291
Relative change	–24.5%	–14.0%	–4.7%	33.2%	29.9%	138.0%	
Risk analysis							
N (% women)	42 420 (54%)	43 085 (57%)	33 279 (33%)	30 235 (37%)	10 812 (47%)	10 158 (38%)	
Age (years)	35.5 (9.4)	46.6 (11.1)	38.3 (9.7)	49.9 (9.6)	39.0 (9.4)	48.5 (9.9)	
No regular exercise	15%	43%	20%	48%	32%	57%	
Daily smoker	6%	14%	7%	13%	10%	13%	
Poor diet	4%	5%	7%	6%	13%	12%	
University degree	41%	25%	28%	17%	19%	14%	
Often perceived stress	16%	14%	14%	11%	16%	13%	
CVD incidence							
n (%)	279 (0.7%)	1166 (2.7%)	464 (1.4%)	1298 (4.3%)	176 (1.6%)	409 (4.0%)	
Follow-up years	10.1 (5.6)	10.0 (5.4)	9.9 (5.4)	9.3 (5.3)	9.4 (5.3)	8.4 (5.2)	
Incidence rate	6.5	27.0	14.1	46.4	17.4	48.0	
Mortality							
CVD, n (%)	7 (0.02%)	95 (0.2%)	30 (0.1%)	107 (0.4%)	10 (0.1%)	48 (0.5%)	
Follow-up years	10.2 (5.6)	10.2 (5.5)	9.9 (5.5)	9.5 (5.3)	9.4 (5.3)	8.6 (5.3)	
Incidence rate	0.2	2.2	0.9	3.7	1.0	5.5	
All-cause, n (%)	255 (0.6%)	1192 (2.8%)	290 (0.9%)	970 (3.2%)	131 (1.2%)	325 (3.2%)	
Incidence rate	5.9	27.2	8.8	33.7	12.8	37.1	

Data are presented as % or mean (SD). Incidence rate presented as cases per 10 000 person-years. CRF, cardiorespiratory fitness; CVD, cardiovascular disease; SD, standard deviation.

## Populations attributable risks and age at event

Population attributable risks (compared to our reference category of normal weight + high CRF) ranged from 2% to 14% for CVD incidence, 3% to 26% for CVD mortality, and 1% to 21% for all-cause mortality (Table 3). The overweight + low CRF category had a higher PAR (14%, 26%, and 20% for CVD incidence, CVD mortality, and all-cause mortality, respectively) compared to the obesity + low CRF category (6%, 14%, and 10%, respectively), mainly due to the higher prevalence of overweight + low CRF compared to obesity + low CRF. Obesity + low CRF category was in general 1.0–1.6 years younger at CVD onset compared to normal weight categories and overweight + high CRF ( $P < 0.05$ ).

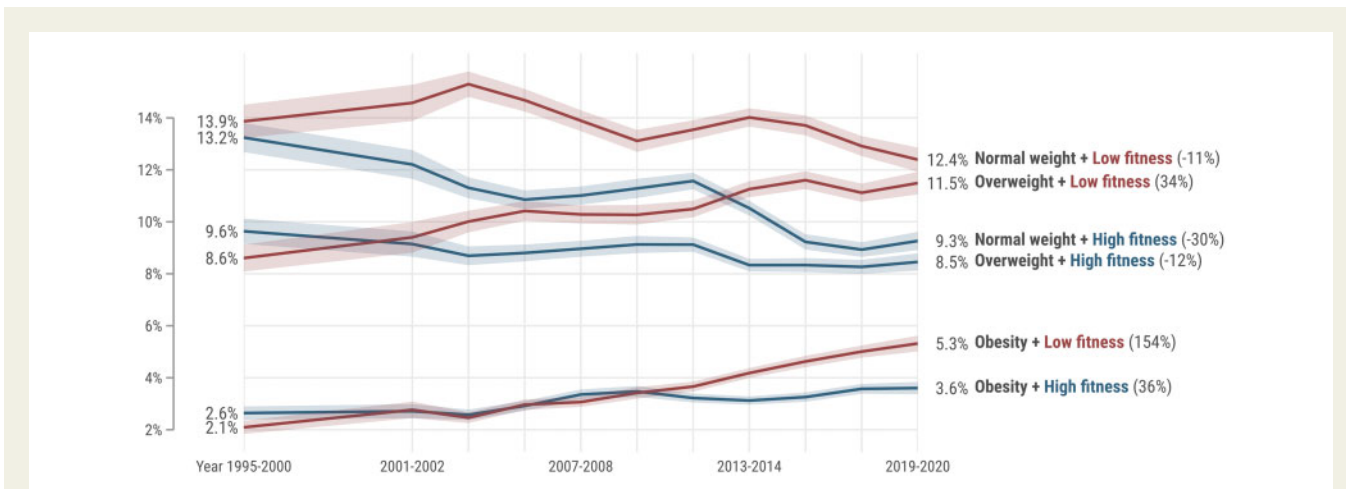
## Sensitivity analyses

To minimize potential bias from reverse causation, we performed a sensitivity analysis where we excluded the first 2 years of follow-up (see Table 2). Hazard ratios were generally somewhat attenuated, although not sufficiently to materially alter our initial main findings.

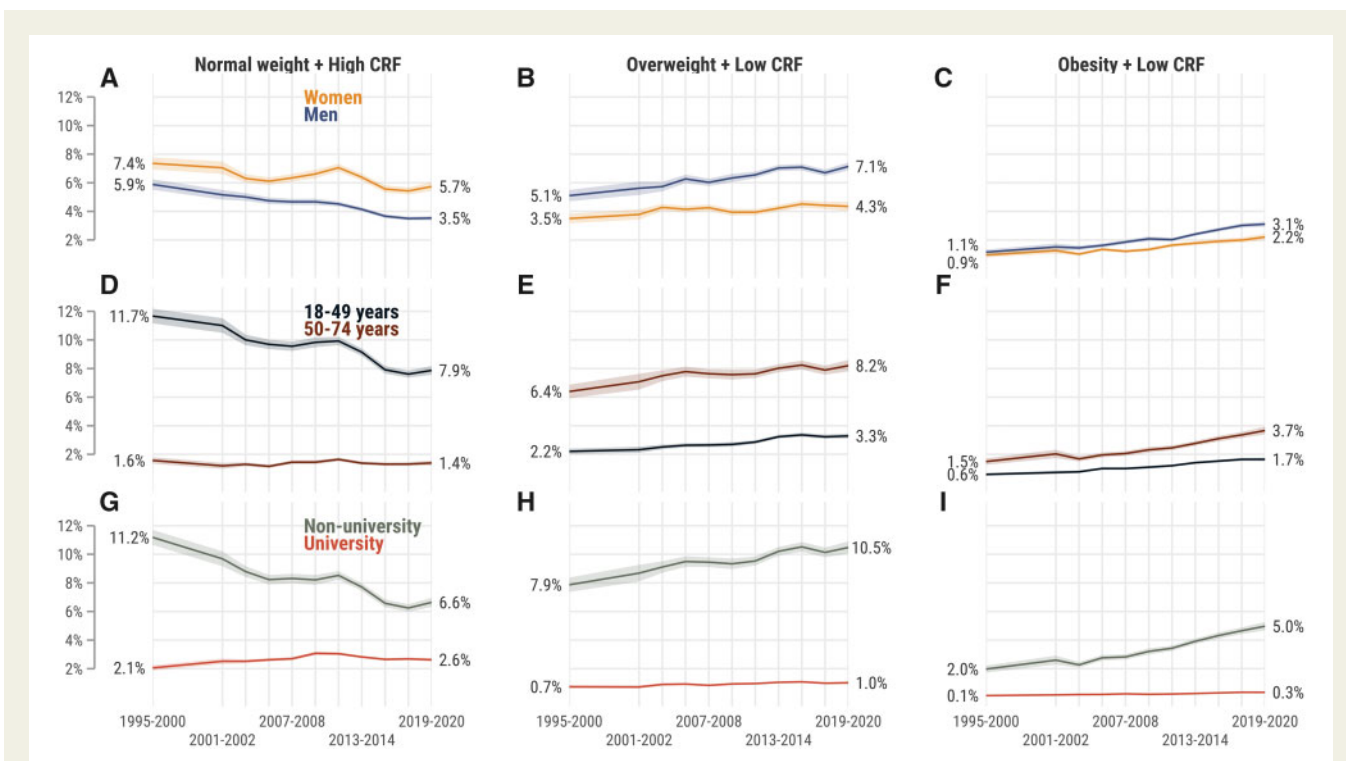
## Discussion

### Main findings

In this large cohort of Swedish employed adults, including both men and women with a wide range in age and education levels, with objective measurements of BMI and CRF spanning 25 years, we noted a consistent and marked increase in the combination of both



**Figure 1** Time trends in prevalence of combinations of cardiorespiratory fitness (low: first quartile, high: fourth quartile) and body mass index status (normal weight: body mass index <25 kg/m<sup>2</sup>, overweight: body mass index ≥25 to <30 kg/m<sup>2</sup>, and obesity: body mass index ≥30 kg/m<sup>2</sup>) in Swedish adults (n = 471 216), 1995–2020. All data are standardized across time periods to minimize the influence of sampling variations in gender, age, and educational level. Shaded areas indicate 95% confidence intervals.



**Figure 2** Time trends in prevalence of combinations of cardiorespiratory fitness (low: first quartile, high: fourth quartile) and body mass index status (normal weight: body mass index 18.5–24.9 kg/m<sup>2</sup>, overweight: body mass index 25–29.9 kg/m<sup>2</sup>, and obesity: body mass index ≥30 kg/m<sup>2</sup>) in Swedish adults (n = 471 216), across gender (A–C), age (D–F), and educational level (G–I), 1995–2020. All data are standardized across time periods to minimize the influence of sampling variations in gender, age, and educational level. CRF, cardiorespiratory fitness. Shaded areas indicate 95% confidence intervals.

overweight + low CRF and obesity + low CRF. There was also a significant reduction in the prevalence of the normal weight + high CRF combination. These changes were more pronounced in men, age <50 years and in non-university educated individuals. Taken together,

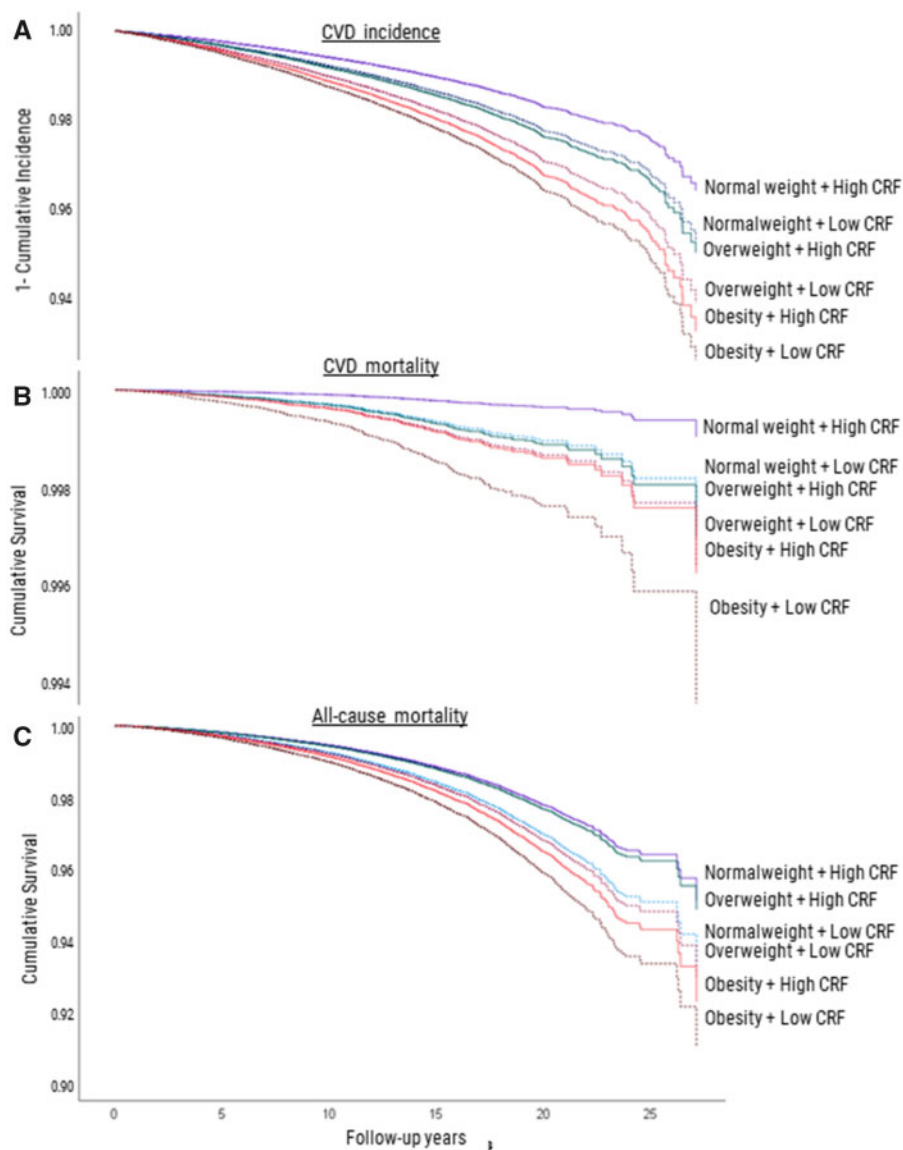
this clearly demonstrates that there has been a considerable decline in the physical health status of the adult population.

When comparing risks between fit/unfit individuals with overweight and obesity, high CRF was generally associated with a reduced

**Table 2** Risk (hazard ratio with 95% confidence interval) of cardiovascular disease incidence, cardiovascular disease mortality, and all-cause mortality in relation to body mass index and cardiorespiratory fitness categories ( $n = 169\ 989$ , no cardiovascular disease at baseline)

	N	Cases	Normal weight + high CRF	Normal weight + low CRF	Overweight + high CRF	Overweight + low CRF	Obesity + high CRF	Obesity + low CRF
CVD incidence								
Total sample, Model 1	169 989	3792	1.00 (ref)	1.51 (1.32–1.73)	1.44 (1.24–1.67)	1.94 (1.69–2.23)	2.05 (1.70–2.47)	2.39 (2.04–2.79)
Total sample, Model 2	169 989	3792	1.00 (ref)	1.32 (1.15–1.52)	1.40 (1.20–1.62)	1.73 (1.50–1.99)	1.91 (1.58–2.31)	2.12 (1.80–2.50)
Events <2 years excluded	169 539	3342	1.00 (ref)	1.28 (1.11–1.48)	1.42 (1.21–1.65)	1.66 (1.43–1.92)	1.95 (1.60–2.37)	2.01 (1.69–2.39)
Women	78 555	1119	1.00 (ref)	1.35 (1.06–1.70)	1.51 (1.14–2.00)	1.73 (1.34–2.21)	1.87 (1.34–2.62)	2.16 (1.61–2.90)
Men	91 434	2673	1.00 (ref)	1.33 (1.12–1.59)	1.37 (1.14–1.63)	1.75 (1.47–2.08)	1.92 (1.53–2.43)	2.13 (1.75–2.609)
18–49 years	117 742	1148	1.00 (ref)	1.37 (1.11–1.68)	1.48 (1.22–1.80)	1.71 (1.38–2.11)	2.28 (1.79–2.89)	2.66 (2.06–3.43)
50–74 years	52 247	2644	1.00 (ref)	1.19 (0.97–1.46)	1.24 (0.98–1.57)	1.55 (1.27–1.90)	1.36 (0.98–1.88)	1.77 (1.41–2.21)
Non-university	123 729	3213	1.00 (ref)	1.39 (1.19–1.64)	1.44 (1.21–1.71)	1.73 (1.47–2.04)	1.88 (1.52–2.33)	2.17 (1.81–2.61)
University	46 260	579	1.00 (ref)	1.04 (0.77–1.40)	1.29 (0.95–1.76)	1.85 (1.37–2.49)	2.31 (1.48–3.61)	1.96 (1.29–2.98)
CVD mortality								
Model 1	169 989	297	1.00 (ref)	4.00 (1.83–8.74)	3.33 (1.46–7.60)	4.86 (2.22–10.63)	4.52 (1.72–11.87)	8.94 (3.99–20.04)
Model 2	169 989	297	1.00 (ref)	2.93 (1.33–6.45)	3.14 (1.37–7.16)	3.73 (1.69–8.22)	3.90 (1.48–10.29)	6.67 (2.94–15.13)
Deaths <2 years excluded	169 971	279	1.00 (ref)	2.72 (1.23–6.02)	3.05 (1.33–6.99)	3.68 (1.67–8.13)	3.94 (1.49–10.41)	6.16 (2.70–14.08)
All-cause mortality								
Model 1	169 989	3163	1.00 (ref)	1.61 (1.39–1.86)	1.08 (0.91–1.28)	1.66 (1.43–1.92)	1.72 (1.40–2.13)	2.15 (1.81–2.55)
Model 2	169 989	3163	1.00 (ref)	1.38 (1.19–1.60)	1.05 (0.89–1.25)	1.46 (1.25–1.69)	1.60 (1.29–1.98)	1.88 (1.58–2.24)
Deaths <2 years excluded	169 798	2972	1.00 (ref)	1.37 (1.18–1.60)	1.08 (0.90–1.29)	1.47 (1.26–1.72)	1.69 (1.36–2.11)	1.84 (1.53–2.21)
Women	78 555	1373	1.00 (ref)	1.32 (1.08–1.62)	1.06 (0.82–1.38)	1.43 (1.15–1.78)	1.29 (0.93–1.80)	1.74 (1.33–2.26)
Men	91 434	1790	1.00 (ref)	1.46 (1.18–1.80)	1.09 (0.86–1.36)	1.51 (1.22–1.87)	1.90 (1.43–2.52)	2.01 (1.58–2.56)
18–49 years	117 742	910	1.00 (ref)	1.28 (1.04–1.57)	0.95 (0.77–1.18)	1.61 (1.28–2.02)	1.71 (1.32–2.21)	1.73 (1.28–2.35)
50–74 years	52 247	2253	1.00 (ref)	1.65 (1.29–2.12)	1.37 (1.02–1.84)	1.67 (1.30–2.15)	1.56 (1.05–2.31)	2.26 (1.72–2.979)
Non-university	123 729	2674	1.00 (ref)	1.42 (1.20–1.68)	1.06 (0.87–1.29)	1.46 (1.23–1.74)	1.66 (1.32–2.10)	1.88 (1.55–2.29)
University	46 260	489	1.00 (ref)	1.22 (0.90–1.66)	1.05 (0.73–1.50)	1.50 (1.08–2.09)	1.31 (0.74–2.34)	2.03 (1.31–3.15)

Model 1 covariates: gender, age and performed year; Model 2 covariates: as model 1 + educational level, exercise habits, smoking, diet, and perceived overall stress. CRF, cardiorespiratory fitness; CVD, cardiovascular disease.



**Figure 3** Combinations of cardiorespiratory fitness and body mass index status with (A) cumulative cardiovascular disease incidence, (B) cardiovascular disease mortality, and (C) all-cause mortality in ( $n = 169\,989$ ). Adjusted according to model 2. CRF, cardiorespiratory fitness; CVD, cardiovascular disease.

risk for all three outcomes, with a more pronounced positive contribution of high CRF on CVD mortality. When teasing out the relative contribution of obesity and low CRF on health, our data indicate that obesity was a more potent driver of CVD incidence and all-cause mortality than low CRF, independently of other known risk factors including smoking and stress, whereas low CRF appeared to be approximately equal with obesity for determining the risk of CVD mortality. The generally lower risks noticed in individuals with normal weight or overweight and high CRF (compared to obesity and low CRF) translated to 1.5 years delay in CVD onset and 1.3–3.3 more years of life expectancy (for CVD mortality).

Moreover, these findings were seen across important subgroups, such as men and women, older and younger individuals, and across educational levels. Removing the first 2 years of follow-up, to

minimize the risk of bias from reverse causation, did not materially alter our findings.

### Previous studies

Previous trend studies have reported a decrease in CRF and an increase in BMI,<sup>4,5,7</sup> however, trend analyses of combinations in CRF and BMI status is lacking. In a previous paper, we have reported a general decrease in relative CRF (assessed as estimated  $\text{VO}_2\text{max}$  in  $\text{mL}/\text{min}/\text{kg}$ ) between 1995 and 2017 by 10.8% in the same study population (with fewer participants),<sup>5</sup> which was later confirmed in compiled international data from eight different high- and upper-middle-income countries between 1967 and 2016.<sup>7</sup> Decreases were defined in both papers to be more pronounced in men and younger ages, and in the previous paper also in low/middle educational level.



**Table 3** Combinations of cardiorespiratory fitness and body mass index status on age at onset/death as well as population attributable risks for cardiovascular disease incidence and mortality, and all-cause mortality (n = 169 989)

	Normal weight + high CRF	Normal weight + low CRF	Overweight + high CRF	Overweight + low CRF	Obesity + high CRF	Obesity + low CRF
CVD incidence						
Age at onset, mean years (SEE) <sup>a</sup>	61.2 (0.30) <sup>b</sup>	60.9 (0.15) <sup>b</sup>	61.5 (0.24) <sup>b,c</sup>	60.4 (0.14)	60.4 (0.38)	59.9 (0.24)
Population attributable risk (%)		7	3	14	2	6
CVD mortality						
Age at death, mean years (SEE) <sup>a</sup>	65.3 (2.01)	63.1 (0.54)	63.3 (0.95)	62.9 (0.49)	62.7 (1.63)	62.0 (0.74)
Population attributable risk (%)		21	7	26	3	14
All-cause mortality						
Age at death, mean years (SEE) <sup>a</sup>	62.0 (0.34)	62.5 (0.15)	62.5 (0.31)	62.3 (0.17)	62.9 (0.46)	61.8 (0.29)
Population attributable risk (%)		21	1	20	3	10

CRF, cardiorespiratory fitness; CVD, cardiovascular disease; HPA, Health Profile Assessment; SEE, standard error of estimate.

<sup>a</sup>Estimated marginal means, adjusting for gender and age at the time point for HPA.

<sup>b</sup>Significantly different from the obesity + low fitness category after adjustment for multiple testing.

<sup>c</sup>Significantly different from overweight + low CRF after adjustment for multiple testing.

An increase in obesity (+86%) and severe obesity (+153%) during the last decades have also been observed in Sweden,<sup>4</sup> with a steeper increase in BMI and levels of obesity in rural parts and in those with lower education levels.<sup>24,25</sup>

Several investigations have been carried out on the contribution of CRF and BMI on chronic disease and mortality.<sup>8–10,16,18,26,27</sup> One of the first was by Wei *et al.*<sup>1</sup> who studied the association between normal weight, overweight, and obesity in fit and unfit well-educated men. Men with obesity had a three-fold overall risk of CVD, but with considerable differences in risk depending on CRF (Relative risk (RR): 1.6 vs. 5.0 for high vs. low CRF). Men with obesity had a two-fold risk of all-cause mortality, which again varied greatly depending on CRF (RR: 1.1 vs. 3.1 for high vs. low CRF). Indeed, the risks of low CRF were approximately similar to the risks of other CVD and all-cause mortality predictors, such as diabetes mellitus type 2, smoking, hypertension, and high cholesterol, but considerably lower than pre-existing CVD.

A meta-analysis,<sup>9</sup> including mainly US studies, found that the risk of all-cause mortality in individuals with obesity varied considerably by CRF (RR: 1.2 vs. 2.5 in fit vs. unfit). Indeed the risk in individuals with obesity or overweight and high CRF did not differ from normal weight and fit individuals. In addition, the risk of low CRF in normal weight individuals was similar to the excess risk seen in overweight and obesity categories (RR: 2.4).

Although our study confirmed an important role of CRF, especially for CVD mortality, the overall effects were less pronounced than these earlier studies. This was unlikely to have been due to our study having both men and women, since risks from both obesity and low CRF were similar in men and women. Another reason for why results differed between studies may be that, unlike obesity, there is no widely accepted definition of high and low CRF. Having a higher cut-off for high CRF, for example, is likely to lead to larger effects and vice versa.

### Implications for public health

This decline in physical health, here exemplified by the increase in the combination of overweight and obesity with low CRF, along with its

notable effects on excessive morbidity and mortality, highlights a need to fully understand the underlying causes, which are likely overlapping. Changing lifestyles (a poor diet and physical inactivity) and social factors, such as poverty and inequality, are clearly implicated. While obesity prevention has been on the public health agenda for several decades in Sweden, there are few implemented policy measures to counter the epidemic. Low CRF also carries an important weight in terms of public health, particularly for CVD mortality, but there is similarly a shortage of measures to promote physical activity and CRF.

### Strengths and limitations

Limitations include a sample consisting of adults with employment, meaning that the sample was likely biased towards individuals with higher education and socioeconomic position.<sup>4,5</sup> Our analysis on the associations between obesity and CRF with CVD mortality was compromised by a lack of statistical power, owing to few cases in some of the BMI/CRF categories. This meant that we could only perform an overall analysis of associations, not for important subgroups. There was also a lack of data on known risk factors for CVD and mortality, including those taken from blood samples such as blood glucose and lipids.

Strengths included a large and varied sample, including both men and women. The data collection period spanned 25 years, and included measured (not self-reported) data on body weight and cardiorespiratory CRF through a validated test.<sup>2</sup> We were also able to use nationwide databases for access to data on obtained educational level, as well as using the same databases for standardizing the values from each sampling period, meaning that our findings were unlikely to be biased by yearly variations in the gender, age, education, and geographic region of the included individuals. Outcome variables were also collected from nationwide national quality control registers.

### Conclusion

Since the mid-90 s, there has been a marked increase in the combination of obesity and low CRF. At the same time the proportion of

individuals with a normal weight BMI and high CRF combination was reduced by about a third. The negative changes were more pronounced in men, younger ages, and non-university educated groups. This represents a clear general decline in physical health.

The combination of obesity and low CRF was strongly associated with CVD incidence, CVD mortality, and all-cause mortality, independent of other established risk factors, and across important subgroups such as both men and women. The role of obesity appeared to be more pronounced than low fitness for determining CVD incidence and all-cause mortality, whereas low fitness was at least similar to obesity in determining the risk of CVD mortality. An important take-home message is the key role of exercise training and physical activity to increase CRF as well as contribute to healthy weight loss for lower CVD morbidity and mortality, particularly among high-risk individuals.<sup>28,29</sup>

## Supplementary material

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

## Data availability statement

The data underlying the findings in our study are not publicly available because the original approval by the regional ethic's board and the informed consent from the subjects participating in the studies did not include such a direct, free access. Data are owned by and can be requested from the HPI Health Profile Institute at support@hpihealth.se.

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