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Longitudinal change in cardiorespiratory fitness and the association with cardiovascular disease and all-cause mortality in young Asian men: a cohort study

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ABSTRACT

Introduction Cardiorespiratory fitness (CRF) in young adulthood is a determinant of chronic disease risk. To better understand whether CRF might also behave as a modifiable risk factor, we examined the associations between longitudinal changes in 2.4 km run times and health outcomes in a cohort of healthy young men.

Methods Our dataset comprised individual run times and health outcomes captured in four national registries. Cox proportional hazards models were used to examine the association between baseline run times and relative hazards of first major adverse cardiovascular events (MACE) and all-cause mortality (ACM). Relative hazards associated with longitudinal change in run times were estimated using models that were adjusted for run-time at baseline.

Results The study sample comprised 148 825 healthy men ages 18–34 years who had undergone at least two routine fitness tests that were 5–9 years apart. During 1 294 778 person-years of follow-up, we observed 1275 first MACE and 764 ACM events occurring at mean ages of 43.2 (SD 6.0) years and 39.2 (SD 6.6) years, respectively. A 1% increase in run-time per annum was associated with a 1.13 (95% CI 1.10 to 1.16) times greater hazard of first MACE and a 1.06 (95% CI 1.02 to 1.10) times greater hazard of ACM. The association between longitudinal change in run times and first MACE was preserved in sensitivity analyses using models adjusted for body mass index at baseline.

Conclusion Among men under the age of 35 years, longitudinal change in run times was associated with the risk of cardiovascular disease two decades onwards.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ There is sufficient evidence to establish a positive association between cardiorespiratory fitness (CRF) in youth and future disease risk. Longitudinal changes in CRF are also associated with prospective health outcomes, but the literature on this association is mostly limited to older adults. We sought to understand whether these associations were evident in healthy men ages 18–34 years.

WHAT THIS STUDY ADDS

⇒ This study provides robust observational evidence for a strong association between longitudinal changes in CRF and the outcomes of cardiovascular disease incidence and all-cause mortality in young adult men.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our study lends weight to public health policy that promotes CRF among young men, regardless of their level of baseline fitness.

INTRODUCTION

Cardiorespiratory fitness (CRF) has been recognised as an intermediate risk factor on the causal pathway from leisure-time physical activity[1] and exercise[2] to cardiovascular (CV) morbidity and mortality.[3] It follows that low CRF contributes significantly to the global burden of disease.[4 5] Past meta-analyses have demonstrated that CRF consistently predicted the risks of CV events and all-cause mortality (ACM).[6–8] There are also high-quality observational studies[9 10] that show a strong association between longitudinal improvement in CRF and decreasing risk of morbidity and mortality. As a whole these studies suggest that CRF behaves as a modifiable predictor of premature mortality and ill health.[11–13] Past studies have, however, typically been conducted in smaller cohorts of older participants who had undergone two fitness tests in a clinical setting.[14–16] Moreover, the predominantly clinical nature of these studies, describing CRF as part of chronic disease management and cardiac rehabilitation, limits their generalisability to younger, healthier and fitter populations.

Studies in children and adolescents suggest that there is insufficient evidence to confidently link a high level of physical fitness to a healthier CV risk profile.[17] Among the small number of cohort studies that have been conducted in larger cohorts of younger adults,[18 19] analyses have typically involved only a single baseline measure of CRF. A recent scientific statement by the American Heart Association, however, has identified 'a need for continued collection of data to assess the impact of CRF in youth on cardiovascular disease (CVD) outcomes because currently (sic) longitudinal data are limited'.[20] We, therefore, undertook to examine the associations between baseline and longitudinal changes in CRF and CVD incidence and ACM in a large cohort of healthy young males.

METHODS

Study sample

Our study sample was drawn from the individual physical proficiency test (IPPT) records collated by the Singapore Armed Forces from 1 January 1993 to 31 December 2015. More details on our study population are available from a previous publication.[21] The inclusion criteria were as follows: male gender and had at least one valid fitness test result within a first time frame defined as ages 18–25 years. A participant was excluded if he did not have at least one valid fitness test result recorded within a second time frame defined as 5–9 years after the very first fitness test. The first and second time frames corresponded to periods of full-time military service and service with the reserve, respectively, thereby emulating the time frame of a previous cohort study.[22] All participants underwent routine medical assessments[23] that helped determine their state of health and continued eligibility to participate in the annual fitness test, meaning participants with significant health conditions were excluded ab initio. Of 481 585 potential participants, we excluded 294 165 participants (online supplemental figure 1) who did not meet inclusion criteria and another 38 595 participants who met exclusion criteria. The final dataset comprised 148 825 participants.

Measures of CRF

As a part of the IPPT, participants performed the modified Cooper's test[24] running 2400 m on a 400 m track at the fastest speed possible. Run times were recorded by a fitness instructor and logged in the IPPT database along with personal details, age and test date. While each participant would have been required to complete at least one fitness test annually, individual participants may have registered multiple attempts to ensure they met the passing requirement or to improve their performance record. We selected the most favourable (shortest) run times within each time frame to consistently determine the most representative measure of CRF and avoid misclassification[25] of individual participants. This approach was deemed more suitable than deriving summary values owing to the onerous nature of CRF testing, where a participant is predominantly at risk of underperformance. The best results within the first and second time frames are hereafter referred to as baseline and interval results, respectively. We computed estimates of maximal aerobic capacity (eVO_2max) in mL/kg/min and corresponding metabolic equivalents of task (MET)[26] for purposes of comparing our results with measures of CRF described in other studies.

Outcome events

The primary outcome for our study was time to first major adverse cardiovascular event (MACE) defined as acute myocardial infarction (AMI), stroke, coronary revascularisation or CV mortality, whichever had been recorded earlier in national registries[27–29] from 1 January 2007 to 31 December 2018. The secondary outcome for our study was time to death of any cause from 1 January 2007 to 31 December 2018.

Study variables

The common identifier for all data points was Singapore's national identification card number. Data were collated from the respective databases and joined by data administrators in the National Registry of Diseases Office (NRDO) to maintain strict confidentiality. As event dates were coded according to month and year by the respective registries, we standardised time at event to reflect the 15th day of the respective month. The final deidentified dataset was hosted on a stand-alone terminal at the NRDO's data laboratory.

Descriptive analyses

The Spearman's ranked coefficient test was used to assess correlation between baseline and interval run times. The relative rate of longitudinal change in run-time, henceforth referred to a longitudinal change, was expressed as the percentage change from baseline to interval run-time divided by the time elapsed between tests expressed in years. The distribution of longitudinal change values was inspected graphically by means of a histogram. We also established three categories of longitudinal change: The first category was defined a priori as any participant who had experienced an improvement in run time, hence a rate of change less than 0.0% per annum comprising 24 409 (16.4 %) participants. By imposing a distribution of approximately 2:1, we set a second cut-off value at 3.0% change per annum. Hence, the second (reference) and third categories encompassed 83 300 (56.0%) and 41 116 (27.6%) participants, respectively. When reporting descriptive statistics, we described continuous variables using mean values and SD, ordinal data using medians and IQRs and outcome events using absolute counts. Crude incidence rates were expressed as number of events per 10 000 person-years.

Survival time analyses

Either 1 January 2007 or the date of the interval fitness test, whichever was later, was designated as the time of entry into the study period. Censoring events comprised:

Table 1 Baseline run-time decile, run-time characteristics, distribution, participant age and duration of follow-up for n=148 825 participants

Run-time decile	Range of baseline run times in seconds	Relative rate of longitudinal change					Mean age in years at time of entry into observation period in years (SD)	Mean duration of follow-up until MACE or censoring event in years (SD)
		Mean (SD) %pa	≤0.0% pa	0.1%–2.9% pa	≥3.0% pa	Total		
1st	454–565	+3.3 (2.4)	709	6508	7811	15 030	28.1 (3.0)	7.7 (3.1)
2nd	566–593	+3.2 (2.4)	655	7103	7185	14 947	28.2 (3.2)	7.4 (3.0)
3rd	594–622	+2.8 (2.4)	999	8676	5318	15 003	29.7 (4.3)	8.1 (3.1)
4th	623–648	+2.4 (2.5)	1302	9758	3724	14 794	30.0 (4.4)	8.2 (3.2)
5th	649–664	+2.2 (2.5)	1599	11 056	3654	16 317	30.5 (4.6)	8.6 (3.1)
6th	665–681	+2.0 (2.5)	2042	8618	2884	13 558	31.1 (4.7)	8.9 (3.1)
7th	682–702	+1.8 (2.5)	2669	9474	2981	15 144	31.7 (4.8)	9.2 (3.0)
8th	703–723	+1.5 (2.4)	3147	9044	2686	14 900	33.0 (4.8)	9.7 (2.9)
9th	724–756	+1.2 (2.3)	4460	7424	2379	14 294	34.2 (4.9)	10.0 (2.8)
10th	757–1200	+0.6 (2.5)	6788	5534	2484	14 838	33.3 (4.8)	9.3 (3.1)
Overall	451–1200	+2.1 (2.6)	24 370	83 195	41 106	148 825	31.0 (4.8)	8.7 (3.0)

MACE, major adverse cardiovascular event; pa, per annum.

non-CV cause of death, missing causes of death or being alive at end of study period (ie, 31 December 2018) without occurrence of MACE during follow-up. Onset of ACM was specified as the event of interest in secondary analyses with censoring event defined as being alive at the end of study period regardless of prior MACE. The full study period concluded on 31 December 2018. HRs for the outcomes first MACE and ACM were estimated using Cox proportional hazards models with the first decile of run times serving as referent. The relationships between run-time deciles and hazards of first MACE and ACM were described graphically using dot and whiskers plots of HRs that were adjusted for age at time of entry into study period. Subsequent models treated longitudinal change first as a continuous and then as a categorical variable and were adjusted for baseline run-time decile, age at time of entry into study period and time elapsed between tests. The adequacy of the proportional hazards assumption was assessed using the global goodness-of-fit test proposed by Schoenfeld.[30]

Sensitivity analyses

The mean rate of longitudinal change among participants from the 10th run-time decile was +0.6% pa (SD 2.5). This was a sharp departure from the eighth (+1.5% per annum (SD 2.4)) and ninth (+1.2% per annum (SD 2.3)) deciles (table 1) that might have biased our results in the direction of no effect. Therefore, to assess the robustness of our estimates we ran additional models that omitted the 10th run-time decile. Furthermore, a narrow reference category (first run-time decile) may have increased the risk of erroneous findings. We therefore combined the 1st, 2nd and 3rd deciles to form a new reference tertile, grouping 4th, 5th and 6th and 7th, 8th and 9th into second and third tertiles, respectively, omitting the 10th decile as mentioned above. Finally, we ran additional models with body mass index (BMI) at baseline in a subset of 100 846 (67.8%) of participants for whom data was available. MS Excel 2016 (Microsoft Corporation) and STATA V.13 (StataCorp) were used to conduct all statistical analyses. Findings with $p<0.05$ were considered as statistically significant. We used the Strengthening the Reporting of Observational Studies in Epidemiology[31] checklist and the Checklist for statistical Assessment of Medical Papers[32] statement to ensure the completeness of our reporting.

Equity, diversity and inclusion statement

Our study involved a population of young men undergoing national service in a multicultural country located in Southeast Asia (Singapore). The research team comprised six men and one woman (third author), who are mid-career (two) and advanced career (five) clinician scientists. The authors' disciplines include public health, physiotherapy and medicine (preventive medicine, sports medicine and cardiology). All the authors are from high-income countries (Singapore and Germany). We acknowledge that this cohort excluded women and participants with pre-existing medical conditions, thus limiting the generalisability of our findings.

RESULTS

Within the first time frame, the median participant underwent 3 (IQR 2–3) tests. Mean baseline run-time (table 1) was 667 s (SD 84) and mean age at time of test was 22.9 years (SD 2.8). Within the second time frame, the median participant underwent 4 (IQR 3–7) rounds of testing. Mean interval run-time was 751 s (SD 117) and mean age was 29.3 years (SD 2.7). Ranked correlation between baseline and interval run times was assessed as modest (r=0.502). Mean baseline run times corresponded to eVO_2max values of 46.9 mL/kg/min and 13.4 METs.

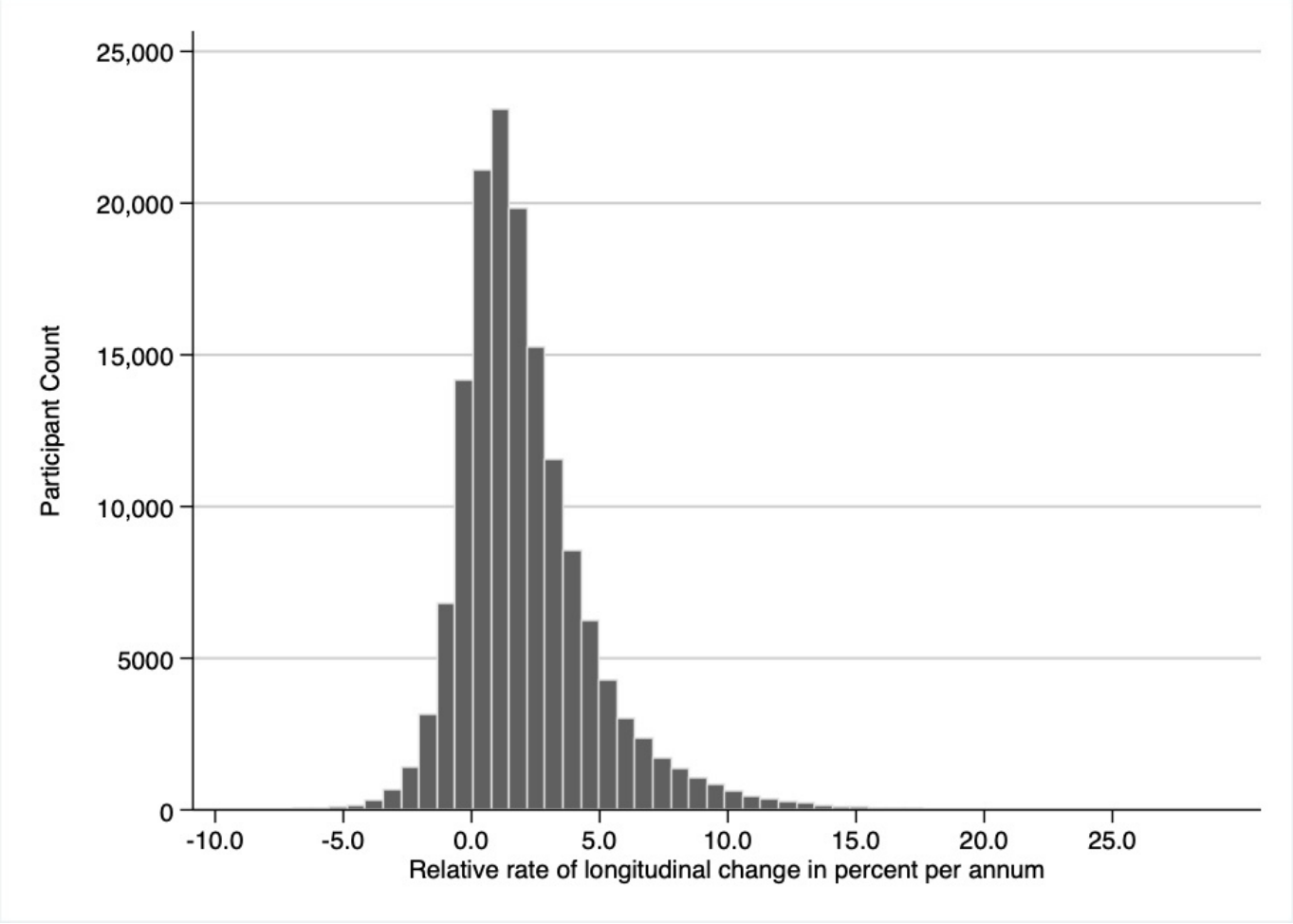

Figure 1 Distribution of relative rates of longitudinal change within the study sample (n=148 825).

Mean interval run times corresponded to 42.1 mL/kg/min and 12.0 METs.

The average time elapsed between tests, that is, the duration between baseline and interval tests, was 6.4 years (SD 1.0). Visual inspection of relative rates of longitudinal change (figure 1) showed an approximately normal distribution with a mean rate of 2.1% per annum (SD 2.6). We identified that 39 083 (26%) participants entered the study in 2007 and the remainder entered between 2008 to 2015. Mean age at year of entry into follow-up period was 31.0 years (SD 3.7). Overall, 1 294 778 person-years of follow-up were recorded until time of censoring or first MACE. The study population (table 2) registered 1591 MACE comprising 652 (41%) AMI events, 384 (24%) acute stroke events, 263 PCI (17%) procedures, 63 (4%) coronary artery bypass grafting procedures and 229 (14%) deaths attributable to CV causes. Overall, 1275 participants within the sample experienced a first MACE at a crude rate of 9.4 events per 10 000 person-years of follow-up. Mean age at time of first MACE was 42.4 years (SD 6.2). There were 764 deaths due to all causes until time of censoring or death. Of these, 535 (70%) deaths were categorised as 'non-CV death' or 'missing cause of death' resulting in a crude mortality rate of 5.9 deaths per 10 000 person-years. Average age at time of death was 39.2 years (SD 6.6). Across baseline run-time deciles (table 1), participants with shorter run times were generally younger, had shorter duration of follow-up and experienced greater longitudinal change. Each incremental run-time decile (table 2) also saw a greater number of first MACE and ACM events. More detailed information on outcome events can be found in online supplemental table 1.

Associations between baseline 2.4 km run times, longitudinal change and hazards for first MACE and ACM

In comparison with the reference first decile, hazards of first MACE were significantly elevated from eighth decile of baseline run-time onwards (table 3, figure 2). Test for linear trend in HRs was also significant (p<0.001). Relative hazard of ACM was significantly elevated from the ninth decile onwards with a significant test for linear trend (p=0.011). These associations were maintained in models that included longitudinal change expressed as a continuous variable. Adjusted models showed that each additional percentage point of relative increase in run-time per annum was associated with a 1.13 (95% CI 1.10 to 1.16; p<0.001) times greater hazard of first MACE and a 1.06 (95% CI 1.02 to 1.10; p=0.001) times greater hazard of ACM. When longitudinal change was coded

Table 2 Number of outcome events by baseline run-time decile and category of longitudinal change for n=148 825 participants

Run-time Decile	First MACE					ACM				
	Relative rate of longitudinal change			Total	Mean age in years (SD)	Relative rate of longitudinal change			Total	Mean age in years (SD)
	≤0.0% pa	0.1%–2.9% pa	≥3.0% pa	n		≤0.0% pa	0.1%–2.9% pa	≥3.0% pa	n	
1st	<5	15	21	–	39.5 (6.9)	<5	17	19	–	33.8 (6.4)
2nd	<5	16	16	–	39.4 (7.0)	<5	15	15	–	34.1 (5.7)
3rd	<5	36	30	–	42.1 (6.9)	<5	25	14	–	39.0 (7.0)
4th	10	55	14	79	41.9 (6.5)	7	43	6	56	37.2 (6.7)
5th	12	67	19	98	41.7 (6.3)	7	41	15	63	39.5 (7.3)
6th	16	73	13	102	44.2 (5.7)	9	40	12	61	41.1 (8.3)
7th	17	98	20	135	42.4 (6.1)	20	73	22	115	41.0 (6.8)
8th	34	145	21	200	43.6 (5.3)	18	70	13	101	41.3 (6.1)
9th	50	166	33	249	44.5 (5.4)	30	84	22	136	42.0 (6.5)
10th	119	129	26	274	44.0 (5.6)	53	61	7	121	42.6 (6.0)
Overall	262	800	213	1275	43.2 (6.0)	150	469	145	764	39.2 (6.6)

ACM, all-cause mortality; MACE, major adverse cardiovascular event; pa, per annum; SD, standard deviation.

as a categorical variable, a decrease in run-time (<0.0% per annum) was associated with a 0.72 (95% CI 0.62 to 0.83; p<0.001) times lower hazard of first MACE and a 0.80 (95% CI 0.66 to 0.97; p=0.025) times lower hazard of ACM than the reference category. Increased run-time (>3.0% per annum) was associated with a 1.54 (95% CI 1.31 to 1.81; p<0.001) times greater hazard of first MACE and a 1.29 (95% CI 1.06 to 1.58; p<0.012) times greater hazard of ACM.

Sensitivity analyses

Associations of longitudinal change with hazards of first MACE and ACM were largely preserved in models that excluded the tenth run-time decile and categorised run times as terciles (online supplemental tables 2 and 3). Finally, we counted 231 first MACE and 90 ACM events in a subgroup of participants whose BMI information was available at baseline. Adjusted HRs were significant for first MACE but not for ACM (online supplemental table 4).

DISCUSSION

Using a national registry data, we compiled a large survival-time dataset that comprised 2.4 km run times assessed at multiple time points and key health outcomes from a population of young Asian males. There was an overall increase in run times over the 6-year interval between tests with a fair degree of correlation between baseline and interval measures. More importantly, we were able to demonstrate that hazards of first MACE and ACM were significantly associated with baseline and longitudinal change in 2.4 km run-time.

Baseline CRF, CVD incidence and ACM

In pooled analyses conducted as a part of a systematic review of past clinical cohorts, participants from the low CRF category (≤7.9 MET) had a 1.56 times (95% CI 1.39 to 1.75) higher risk for CVD events than participants in the high CRF category (≥10.9 METs).[6] By comparison, participants in our study were two decades younger and fitter on baseline and interval tests. Nonetheless, our analyses involving run-time tertiles (online supplemental table 3) produced a remarkably similar relative hazard of first MACE for the least fit tertile. In a study on CVD disability in 1 078 685 Swedish military conscripts,[18] participants in the least fit reference quintile experienced a 9.10 (95% CI 3.45 to 20.0) times greater hazard of AMI relative to the fittest quintile after four decades of follow-up. Our sample saw a much more conservative estimate for the relative hazard of first MACE in the ninth and tenth deciles, likely due to the shorter duration of follow-up. A second study in 169 989 working adults in Sweden, however, reported relative risk estimates of CVD incidence that were closer to our own.[19] Concerning the hazards of ACM, our estimates resembled the associations reported by Kodama *et al*[6] and generally fell within the limits of estimates described among Swedish adults[19] and US veterans.[33] A past review of Cooper Center Longitudinal Study participants[34] identified that the risk of ACM was only elevated after 10–20 years of follow-up. Our study provides evidence to the contrary, indicating that the differentiation of ACM hazards by CRF category might occur earlier than previously documented.

Longitudinal change in CRF, CVD incidence and ACM

The correlation between baseline and follow-up run times was more modest in our cohort than what has been described in past studies.[35–37] We suspect that our baseline measures may have been influenced by the highly structured environment found in a military setting. As a result, the likelihood of run times and, therefore, estimated

Table 3 Cox proportional hazards for first MACE and ACM in n=148 825 participants in analysis of baseline 2.4 km run times and longitudinal change in run times adjusted for age at time of entry into study period and time elapsed between tests

	MACE						ACM					
	Model 1a		Model 1b*		Model 1c†		Model 2a		Model 2b*		Model 2c†	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Baseline Run-time Decile												
1st	1.00 (referent)	–	1.00 (referent)	–	1.00 (referent)	–	1.00 (referent)	–	1.00 (referent)	–	1.00 (referent)	–
2nd	0.92 (0.57 to 1.49)	0.736	0.95 (0.59 to 1.53)	0.819	0.95 (0.59 to 1.53)	0.818	0.91 (0.57 to 1.46)	0.709	0.93 (0.58 to 1.48)	0.747	0.93 (0.58 to 1.49)	0.759
3rd	1.11 (0.74 to 1.68)	0.616	1.18 (0.78 to 1.79)	0.424	1.19 (0.79 to 1.80)	0.399	0.78 (0.50 to 1.23)	0.290	0.81 (0.51 to 1.27)	0.350	0.82 (0.52 to 1.29)	0.391
4th	1.22 (0.81 to 1.82)	0.341	1.37 (0.92 to 2.06)	0.125	1.38 (0.92 to 2.07)	0.122	1.07 (0.70 to 1.63)	0.747	1.13 (0.74 to 1.72)	0.565	1.16 (0.76 to 1.77)	0.496
5th	1.24 (0.84 to 1.83)	0.279	1.43 (0.97 to 2.12)	0.072	1.43 (0.96 to 2.12)	0.075	0.98 (0.65 to 1.48)	0.940	1.05 (0.69 to 1.58)	0.828	1.07 (0.71 to 1.62)	0.748
6th	1.30 (0.88 to 1.92)	0.189	1.53 (1.03 to 2.26)	0.035	1.53 (1.03 to 2.93)	0.034	1.03 (0.68 to 1.56)	0.901	1.10 (0.72 to 1.67)	0.654	1.13 (0.74 to 1.73)	0.559
7th	1.39 (0.95 to 2.03)	0.091	1.68 (1.15 to 2.46)	0.008	1.66 (1.13 to 2.44)	0.009	1.60 (1.10 to 2.34)	0.015	1.74 (1.19 to 2.55)	0.004	1.78 (1.21 to 2.62)	0.003
8th	1.67 (1.16 to 2.41)	0.006	2.07 (1.43 to 2.99)	<0.001	2.02 (1.39 to 2.93)	<0.001	1.22 (0.83 to 1.79)	0.324	1.33 (0.90 to 1.97)	0.153	1.36 (0.92 to 2.01)	0.128
9th	1.85 (1.29 to 2.67)	0.001	2.35 (1.63 to 3.39)	<0.001	2.32 (1.60 to 3.35)	<0.001	1.48 (1.02 to 2.16)	0.040	1.64 (1.12 to 2.41)	0.011	1.70 (1.15 to 2.50)	0.007
10th	2.27 (1.58 to 3.26)	<0.001	3.07 (2.13 to 4.43)	<0.001	2.98 (2.07 to 4.31)	<0.001	1.46 (1.00 to 2.14)	0.049	1.67 (1.13 to 2.47)	0.009	1.73 (1.17 to 2.56)	0.006
Age at entry into study period in years	1.15 (1.14 to 1.17)	<0.001	1.17 (1.15 to 1.19)	<0.001	1.16 (1.15 to 1.18)	<0.001	1.06 (1.02 to 1.09)	<0.001	1.07 (1.03 to 1.10)	<0.001	1.07 (1.03 to 1.10)	<0.001
Time elapsed between tests in years	–	–	1.06 (1.00 to 1.13)	0.050	1.05 (0.99 to 1.11)	0.992	–	–	0.99 (0.92 to 1.07)	0.822	0.99 (0.91 to 1.07)	0.800
Longitudinal change in run-time per annum												
Continuous variable												
1.0% pa	–	–	1.13 (1.10 to 1.16)	<0.001	–	–	–	–	1.06 (1.02 to 1.10)	0.001	–	–
Categorical variable												
<0.0% pa	–	–	–	–	0.72 (0.62 to 0.83)	<0.001	–	–	–	–	0.80 (0.66 to 0.97)	0.025
0.0%–3.0% pa	–	–	–	–	1.00 (referent)	–	–	–	–	–	1.00 (referent)	–
>3.0% pa	–	–	–	–	1.54 (1.31 to 1.81)	<0.001	–	–	–	–	1.29 (1.06 to 1.58)	0.012
PH assumption	0.242		0.209		0.234		0.325		0.318		0.398	

*Model treats longitudinal change as a continuous variable.
†Model treats longitudinal change as a categorical variable.
ACM, all-cause mortality; CI, confidence interval; MACE, major adverse cardiovascular event; pa, per annum; PH, proportional hazards.

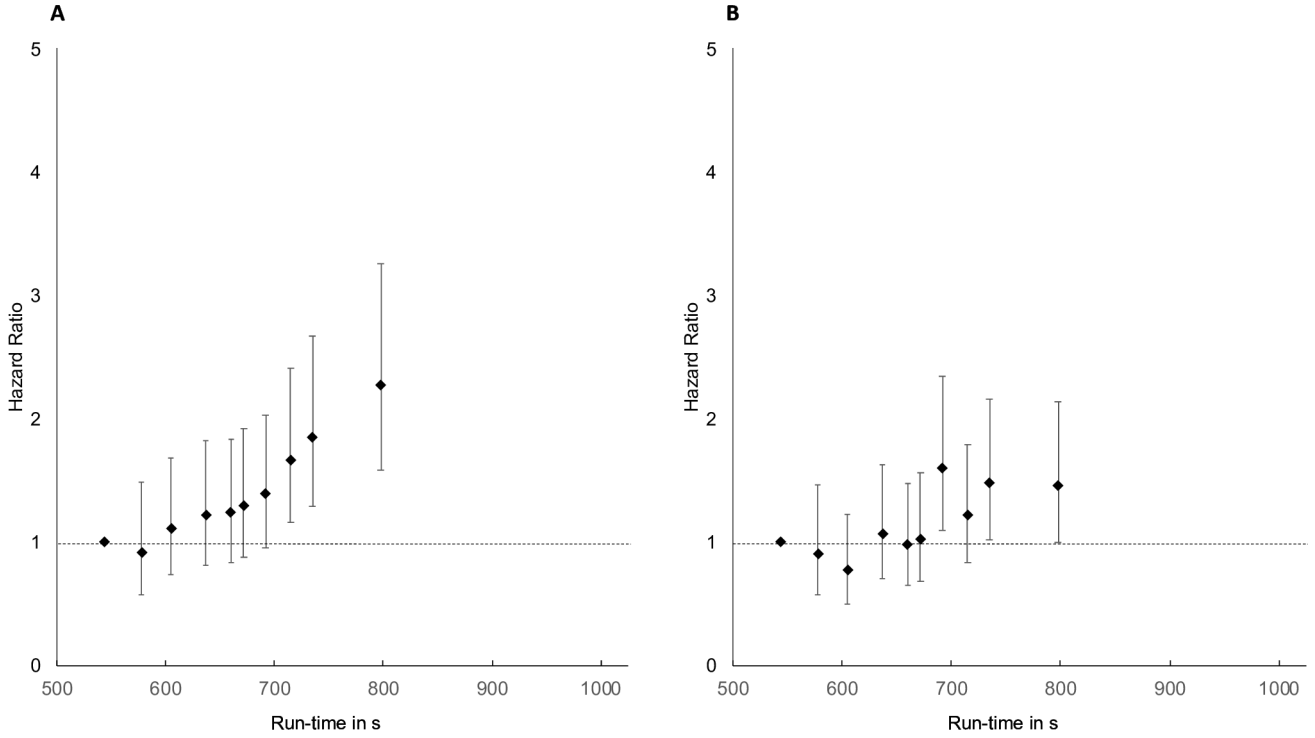

Figure 2 HRs with 95% CIs for first MACE (A) and ACM (B) by baseline run-time decile adjusted for age at time of entry into study period (n=148 825). ACM, all-cause mortality; MACE, major adverse cardiovascular event.

CRF tracking consistently across time and into civilian life might have been reduced. Our analyses on the associations between longitudinal change in run times and hazards of CVD and ACM are nevertheless consistent with the associations reported in older populations, who typically registered lower levels of CRF,[9 38] and smaller changes in absolute CRF.[15 39–41] In the Coronary Artery Risk Development in Young Adults (CARDIA) study, which involved a cohort of 5115 participants aged 18–30 years,[22 42 43] a 1 min reduction in performance on a modified Balke treadmill test protocol over an intervening period of 7 years was associated with a 20% increase in hazards of CVD and a 21% increase in hazards of ACM. Notwithstanding differences in test protocols, baseline fitness levels among CARDIA participants[44] (13.8 METs and 13.0 METs in white and black men, respectively) were remarkably similar to those observed in our study. The findings from our cohort, which was followed over a shorter time, indicate that the differentiation in hazards associated with a relative decline in fitness might already manifest at a relatively young age.

Strengths and limitations

Participants' high level of familiarity with the test protocol[45] should have contributed to a relatively low risk of measurement error. Our study also minimised misclassification bias[25] by selecting the best run times for respective life course periods.

One key limitation of our study was the inability to fully eliminate reverse causality bias. A past study on physical activity and health outcomes has recommended that incident cases occurring within 2 years of follow-up are removed from the analytical dataset.[46] However, we do not suspect a high risk of reverse causality bias for two reasons. First, by virtue of data availability, we were unable to register the earliest outcome events among participants who entered follow-up before 2007. Second, sensitivity analyses which excluded the 10th decile, hence the longest run times and, therefore, the participants most likely to introduce reverse causality, did not meaningfully alter our study's conclusions. Nevertheless, our hazard estimates for ACM need to be interpreted with caution given that subclinical cardiomyopathy may have affected 2.4 km run times and mortality risk simultaneously. Another key limitation was the inability to adjust estimates for important time-varying factors such as alcohol consumption, BMI and smoking[47] and account for how rising obesity and falling smoking prevalence[48 49] may have interacted with longitudinal changes in 2.4 km run times. Moreover, participants had been screened for underlying risk factors and chronic disease ab initio, thus limiting the generalisability of our findings to healthy individuals. Finally, our approach of selecting the best run times in each of the two time frames meant that we could not further explore how the shape of longitudinal trajectories might have affected our estimates.

Public health implications

Our observational findings on the propensity for health risks to be associated with both baseline and longitudinal changes in CRF estimates provide robust evidence in support of public health messaging that targets all levels

of fitness in young males. Moreover, our study indicates that where available, routine 2.4km run times could be monitored as an individual-level or population-level risk indicator for CVD incidence.

CONCLUSION

CRF, as estimated by 2.4km run times, among young Asian males was strongly associated with the risks of CVD. Additionally, a net decline in individual CRF was associated with elevated risk of CVD even after accounting for CRF and BMI at baseline. Our findings reiterate the importance of CRF as a modifiable risk factor for chronic disease and a priority for public health action in young Asian males.

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