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Cardiorespiratory fitness and health in children and adolescents: an overview of systematic reviews with meta-analyses representing over 125 000 observations covering 33 health-related outcomes

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ABSTRACT

Objective To synthesise data on the associations between cardiorespiratory fitness (CRF) and health in children and adolescents, evaluate the certainty of evidence and identify knowledge gaps.

Design An overview of systematic reviews with meta-analyses. Results were pooled using forest plots and certainty of evidence evaluated with GRADE.

Data sources Medline, Embase, Scopus, CINAHL and SPORTDiscus were searched from January 2002 to March 2024.

Eligibility criteria for selected studies Systematic reviews with meta-analyses exploring CRF and health in children and adolescents aged <18 years.

Results From the 9062 records identified, 14 reviews were included. Meta-analysed data from 125 164 observations covering 33 health outcomes were compiled, showing favourable (n=26) or null (n=7) associations with CRF. Among general populations, the associations were weak-to-moderate, with favourable links between CRF and indicators of anthropometry and adiposity, cardiometabolic and vascular health, and mental health and well-being. Among clinical populations, CRF was lower in participants with a condition compared with healthy controls, with the largest difference for newly diagnosed cancer (mean difference=−19.6 mL/kg/min; 95% CI: −21.4,−17.8). Patients with cystic fibrosis had a greater risk for all-cause mortality when comparing low CRF vs. high (relative risk=4.9; 95% CI: 1.1, 22.1). The certainty of evidence ranged from very low to moderate.

Conclusion CRF shows promising links to numerous health outcomes in paediatric populations, though the low certainty of evidence calls for further research. High-quality longitudinal evidence is warranted to confirm the findings and investigate a predictive role of childhood CRF for future health.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Cardiorespiratory fitness (CRF) is an important health marker across the lifespan. However, no attempt has been made to synthesise meta-analysed evidence on CRF and health in paediatric populations.

WHAT THIS STUDY ADDS

⇒ This overview compiled refereed evidence for general and clinical paediatric populations, helping to demonstrate the scope of health outcomes linked to CRF, the certainty of current evidence and important knowledge gaps.
⇒ The study identified 14 systematic reviews with meta-analyses representing over 125 000 observations covering 33 health-related outcomes. CRF shows promising associations with numerous health outcomes in general and clinical populations of children and adolescents.
⇒ The certainty of current evidence is generally low, and the covered scope of health benefits of CRF is not exhaustive. High-quality longitudinal evidence is warranted to provide stronger support for the use of CRF as an indicator of children and adolescents' current and future health.

INTRODUCTION

Cardiorespiratory fitness (CRF) represents the ability of the body to deliver oxygen to skeletal muscles to generate the energy needed to perform sustained whole-body physical activity.[1 2] CRF is dependent on the integrated function of multiple organs and bodily systems (eg, pulmonary, circulatory)[2] and is influenced by several modifiable (eg, physical activity, sedentary time, environment) and non-modifiable (eg, genetics, sex, age) factors.[3] Previous research has identified CRF as an important marker of current and future health.[3–6] In addition, the American Heart Association released a scientific statement describing the importance of assessing CRF in clinical practice.[2 7]

CRF can be measured via maximal exercise testing with gas analysis, exercise-based estimated via maximal or submaximal exercise testing without gas analysis (using exercise prediction equations or exercise performance) or non-exercise estimated via non-exercise prediction equations. Objective measurements of CRF are performed in the field or laboratory/office settings, using a variety of tests (eg, cardiopulmonary exercise testing, 6 min walk, 20-metre shuttle run), protocols (eg, maximal exercise to volitional exhaustion, submaximal exercise) and modalities (eg, treadmill running/walking,

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stationary cycling, bench stepping). An individual's CRF is commonly reported as peak ($\dot{V}O_2$peak) or maximal oxygen uptake ($\dot{V}O_2$max) in litres per minute or scaled to body mass in millilitres per kilogram per minute (ml/kg/min) or as metabolic equivalents of task (METs) with 1 MET equal to 3.5 millilitres of oxygen consumed per kilogram of body mass per minute.[2 3] While each assessment method has pros and cons, both measured and estimated CRF have been shown to strongly predict health outcomes.[2 8]

Over recent decades, the association between CRF and morbidity[5 9–16] and mortality[5 17 18] among adults has been extensively addressed. Fewer systematic reviews with meta-analyses have synthesised the available evidence in paediatric populations, and most of them explored a single health-related outcome (eg, arterial stiffness,[19] glycated haemoglobin)[20] or several outcomes limited to a specific area (eg, mental health,[21] metabolic profile).[22] Certain outcomes, such as mortality, are less common in children and adolescents compared with adults, making it more challenging to quantify the associations with CRF; however, exploring the links between CRF and health in children and adolescents is equally important as it is for adults. To our knowledge, no attempt has been made to synthesise meta-analysed data on the associations between CRF and a wide range of health outcomes in paediatric populations into a single study. Moreover, CRF may be a useful health marker not only in healthy children and adolescents but also in those with chronic health conditions, which warrants a synthesis of evidence across the general and clinical populations. An overview of reviews design (also referred to as umbrella review in the literature)[23] was chosen to obtain a full picture of the extant evidence on this topic and identify knowledge gaps. The overview approach is considered a useful evidence-based practice to deal with the increasing number of systematic reviews when an overall picture is needed,[24 25] which has successfully been applied for addressing various health-related topics in the past.[26 27] Understanding the breadth and quality of available evidence using the overview of reviews approach will create a comprehensive view, helping to inform future directions for CRF use in clinical practice, public health surveillance, policy and research. Thus, this overview aims to synthesise the results of systematic reviews with meta-analyses that have examined the association between CRF and health among children and adolescents under 18 years of age from the general and clinical populations, assess the certainty of evidence for each outcome and identify current research gaps.

METHODS

This overview of reviews was registered in the international prospective register of systematic reviews PROSPERO (#CRD42022370149) and adhered to the Preferred Reporting Items for Overviews of Reviews statement.[28] We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 for the abstracts checklist.[29] The study is a part of a large overview of reviews project exploring the associations between CRF and health across the lifespan. A sibling overview of meta-analytical evidence among adults (≥18 years) was reported elsewhere.[5]

Eligibility criteria

Study population: children and adolescents (mean age <18 years), including the general and clinical populations with diagnosed chronic health conditions.

Exposure: the primary exposure was CRF, assessed by any of the following conventional methods: (1) measured via maximal exercise testing with gas analysis (eg, $\dot{V}O_2$max, $\dot{V}O_2$peak), (2) exercise-based estimated via maximal or submaximal exercise testing without gas analysis (using exercise prediction equations or exercise performance) or (3) non-exercise estimated via non-exercise prediction equations.

Outcome: any health-related outcomes, including physical, mental and social well-being. Examples also include chronic health conditions and mortality.

Study design: systematic reviews with meta-analyses, which included a sample search strategy and a search of at least two bibliometric databases. The primary study designs included in reviews could include prospective or retrospective cohorts, case-control, cross-sectional or intervention studies.

Publication status and language restrictions: systematic reviews published in a peer-reviewed academic journal in English, French or Spanish (based on authors' language proficiency). Conference abstracts, commentaries, editorials, dissertations or grey literature were ineligible.

Timeframe: systematic reviews published after 1 January 2002 were included to capture the 20-year period from the initial search. The primary papers included in the reviews could have been published before the review date restriction.

Data sources and search strategy

The records from five databases (Medline (via OVID), Embase (via OVID), Scopus, CINAHL (via EBSCOhost) and SPORTDiscus (via EBSCOhost)) from 1 January 2002 to 18 November 2022 were considered for the initial search, which was later updated from 1 November 2022 to 8 March 2024. The search strategy was created by a research librarian (KM) in collaboration with the authorship team. Following the Peer Review of Electronic Search Strategies guidelines,[30] the final search was peer-reviewed by an independent research librarian. The search strategy was developed for a large overview of review project aimed to explore relationships between CRF and health across the lifespan and is provided in online supplemental eAppendix 1. In addition, the authors hand-searched the reference lists of eligible reviews.

Article screening and selection process

Removal of duplicates was conducted by automated and manual methods using RefWorks. Further de-duplication and record screening were performed in Covidence. Two of the following reviewers (ID, SAP, CC-S, J-PC, BJF, TM, BS, GRT and JJL) independently performed the title and abstract screening. The records that met the inclusion criteria or provided insufficient evidence in the abstract to make a final decision underwent full-text screening by two independent reviewers (ID, SAP, CC-S, J-PC, BJF, TM, BS, GRT and JJL). Disagreements at the screening and selection process were resolved by consensus-based discussion between two reviewers (SAP and JJL) or by a third reviewer (GRT).

Data extraction

Data extraction forms were piloted by the authors for accuracy and then completed in Covidence by two independent reviewers (ID, SAP, CC-S, J-PC, BJF, TM, BS, GRT and JJL) with conflicts resolved by a third reviewer (JJL). The forms included items covering demographic characteristics, study design characteristics, meta-analysed effect estimates and variance and details for quality assessment. Findings were grouped using an outcome-centric approach, detailed in Kho *et al*.[31]

Methodological quality assessment

The quality of the included systematic reviews was evaluated using the second edition of A MeaSurement Tool to Assess Systematic Reviews (AMSTAR 2) checklist[32] by two independent reviewers (ID, SAP, CC-S, J-PC, BJF, TM, BS, GRT and JJL), with conflict resolution by consensus or with the involvement of a third reviewer (JJL).

Overlap of primary studies between systematic reviews

For each outcome, the aim was to identify systematic reviews with non-overlapping primary studies to avoid double counting of evidence, which could result in giving data from certain primary studies a disproportionate influence. For those outcomes where more than one review was available, the corrected covered area (CCA) was calculated to measure the degree of overlap of primary publications, using the following formula: $CCA = (N - r) / ((r * c) - r)$, where N is the total number of the included primary studies in systematic reviews for the outcome (including double counting), r is the number of unique primary studies and c is the number of systematic reviews included for the outcome.[33] When the degree of overlap was high (11–15%) or very high (>15%),[33] the selection of reviews was critically assessed by the authors, and the lower quality and older systematic reviews were excluded.

Data synthesis

A narrative synthesis was used to summarise findings across all reviews. The results were reported as described by the authors of systematic reviews, grouped by health outcome and presented separately for general (apparently healthy) and clinical populations. For each health outcome, the meta-analysis effect estimates along with the 95% CIs, the number of included primary studies, total sample size and heterogeneity statistics were extracted and synthesised in the summary of findings table. With regard to effect measures, correlation coefficient (r), mean difference (MD), standardised mean difference (SMD), effect size (ES), OR and relative risk (RR) were extracted, summarised and discussed. The r values were interpreted as weak (≤ 0.10), moderate (0.10–0.37) or large (≥ 0.37) based on the McGrath and Meyer classification[34] used in the included systematic reviews,[20 35] which informed the majority of associations across the presented outcomes. A two-sided p value <0.05 was statistically significant. Outcomes with the same measure of effect were illustrated in forest plots to allow for easy comparison between findings.

Risk of bias (RoB) and certainty of evidence assessment

The RoB assessments for primary studies were extracted from included systematic reviews, where available. The assessment tools varied across reviews and included Newcastle–Ottawa Scale,[36] National Institutes of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies,[37] the Strengthening the Reporting of OBservational studies in Epidemiology checklist,[38] Quality Assessment Tool for Quantitative Studies of the Effective Public Health Practice Project,[39] an Appraisal Tool for Cross-sectional Studies[40] or a modified Checklist for Reporting on Observational Longitudinal Research.[41] The RoB assessment was not reported in one review[42]; thus, a new assessment was conducted and verified by two reviewers (SAP and JJL) using the Joanna Briggs Institute Critical Appraisal Checklist for Cross-Sectional Studies.[43]

The evidence informing each outcome was evaluated using a modified Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach[44] by one reviewer (ID) with verification for accuracy by a second reviewer (SAP or JJL). Disagreements were resolved through discussion and consensus among the reviewers. To better suit the context of the overview and minimise the challenges associated with using a standard GRADE approach in public health research,[45 46] the authorship team made the following modifications to the GRADE framework: (1) the initial rating for evidence coming from studies of longitudinal design started at a 'high' grade as the higher-quality evidence (ie, randomised controlled trials) was deemed not feasible for this overview's research question, (2) if more than one review was available for a single outcome, the GRADE assessment was based on the highest quality evidence (eg, solely on longitudinal evidence, where both longitudinal and cross-sectional evidence was available) to ensure the findings supported by stronger evidence are appropriately recognised and communicated and (3) the numerical scale for downgrading was adjusted to 0, 0.5 and 1 point to reduce the risk of being severely penalised for features inherent to observational study design and to allow for a more granular evaluation and differentiation between levels of certainty. The certainty was downgraded due to concerns in the standard five domains (RoB, inconsistency of results, indirectness of evidence, imprecision and publication bias).[44] Other considerations, such as large magnitude of an estimated effect, the presence of a dose-response gradient and accounting for plausible confounding factors could upgrade the certainty if there were no serious concerns in other domains.[44] The detailed GRADE decision rules are presented in online supplemental eTable 1.

Patient and public involvement statement

Patients and the public were not involved in the design or conduct of this study.

Equity, diversity and inclusion statement

The authorship team included diversity across genders and career stages, bringing varied perspectives and experiences. Limited stratification by sex in the included reviews did not allow authors to stratify the results of the overview by sex; however, the global representation and gender balance of study populations were integrated into the GRADE analysis for the assessment of the indirectness of the results.

RESULTS

Search results and study characteristics

The search identified 9062 potentially relevant records after the removal of duplicates. Following title and abstract screening, 199 papers were accessed for full-text review. Of these, 14 systematic reviews with meta-analyses[19–22 35 42 47–54] were deemed eligible for inclusion in the overview. A detailed PRISMA flow diagram of the literature search and screening process is presented in figure 1.

The included papers were published between 2014 and 2024, with the most (79%, n=11) published within the last 5 years. The median number of primary studies included specifically in CRF-related meta-analyses was 7.2 (range: 2 to 22), and the median number of participants was 3381 (range: 137 to 13289). A detailed summary of characteristics of included systematic reviews can be found in table 1.

Methodological quality of included studies

Study quality using AMSTAR 2 ranged from 'critically low' (n=8) to 'high' (n=4), with details provided in online supplemental eTable 2.

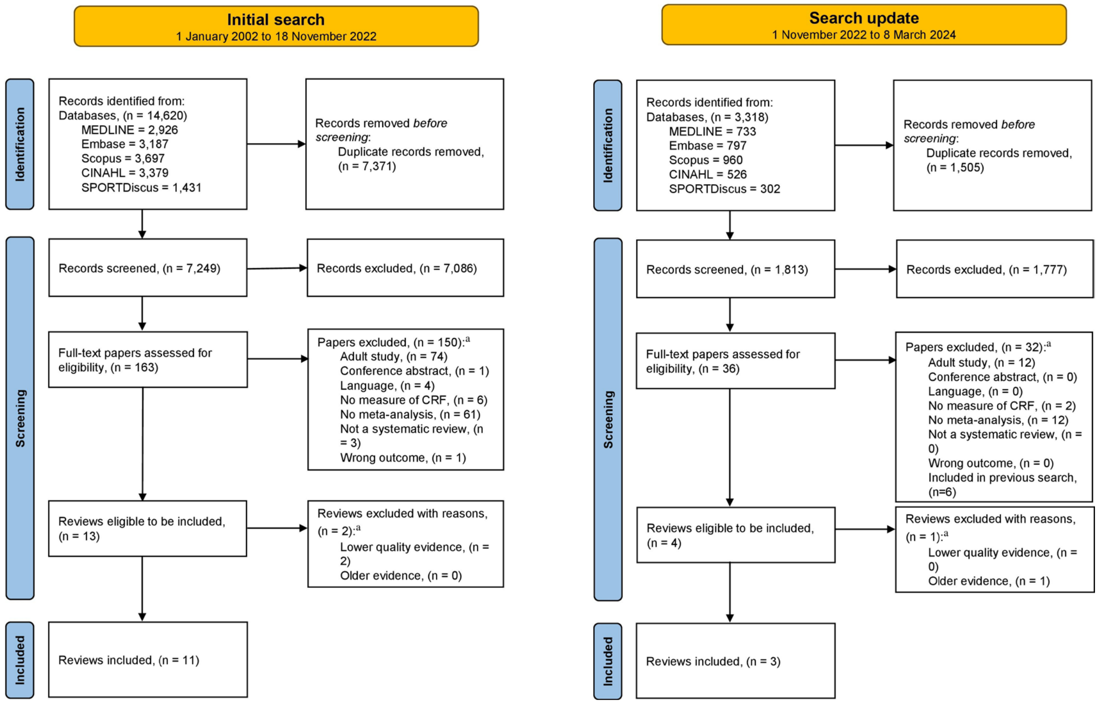

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart illustrating the number of articles identified, screened and included in the overview. *Notes:* [a]A list of excluded articles with reasons is provided in online supplemental eAppendix 2.

Meta-analyses of observational studies

Overall, 14 included reviews meta-analysed data from 125 164 observations covering 33 health-related outcomes, including indicators of cardiovascular health, metabolic health and mental health and well-being. Each outcome was informed by evidence from one (n=28) or two (n=5) systematic reviews and was examined in the general population of children and adolescents (n=25), a clinical population (n=7) or both (n=1).

Outcome data in the general population

Among children and adolescents from the general population, there were favourable links between CRF and (1) anthropometric and adiposity indicators (eg, skinfold thickness, waist circumference, body mass index (BMI)),[35] (2) cardiometabolic and vascular health indicators (eg, metabolic syndrome, fasting insulin, homeostatic model assessment for insulin resistance, total cholesterol, high-density lipoprotein cholesterol, total cholesterol to high-density lipoprotein cholesterol ratio, triglycerides, central pulse wave velocity)[19 35] and (3) mental health and well-being outcomes (eg, depression, self-concept, self-esteem, self-perception, well-being, and health-related quality of life).[21] Out of 14 included reviews, four studies reported a correlation coefficient value to demonstrate the strength and direction of the associations. The strength of the associations ranged from weak to moderate and included favourable (positive) values for high-density lipoprotein cholesterol[35] and indicators of mental well-being[21] and favourable (negative) values for all other outcomes. Figure 2 provides a visual representation of all correlation coefficients with 95% CIs. The strongest associations were for CRF and skinfold thickness (r=−0.34; 95% CI: −0.41 to –0.26),[35] waist circumference (r=−0.29; 95% CI: −0.42 to –0.14)[35] and self-perception (r=0.27; 95% CI: 0.20, 0.34).[21] Across all outcomes, no unfavourable associations were reported, though several results did not reach statistical significance (eg, body weight, fasting glucose, low-density lipoprotein cholesterol, systolic and diastolic blood pressure, anxiety)[35 42] or were inconsistent in terms of statistical significance in longitudinal vs cross-sectional evidence (eg, body fat percentage statistically significant only in cross-sectional evidence,[42] waist circumference statistically significant only in longitudinal evidence).[35] Table 2 summarises findings for additional health outcomes, where results were expressed using other statistical measures (eg, OR, ES, RR).

Outcome data in clinical populations

Among clinical populations, CRF was substantially lower in children and adolescents with a disease compared with healthy controls (figure 3). The largest MDs were for patients with newly diagnosed cancer (MD=−19.6 mL/kg/min; 95% CI: -21.4 to –17.8)[53] and congenital heart disease (MD=−7.9 mL/kg/min; 95% CI: −9.9 to –5.8)[54] compared with healthy controls. Among children and adolescents with type 1 diabetes, a moderate negative (favourable) relationship was found between CRF and glycated haemoglobin levels (r=−0.31; 95% CI: −0.44 to –0.19)[20] (figure 2). Among patients diagnosed with cystic fibrosis, those with lower CRF had a notably higher risk of all-cause mortality than their peers with higher CRF (RR=4.9; 95% CI: 1.1, 22.1)[47] (table 2).

Certainty of evidence

The certainty of the evidence across all outcomes ranged from very low (n=18) to moderate (n=2) and was most often downgraded due to RoB, inconsistency and imprecision. A summary of the certainty of evidence assessment is presented in online supplemental eTable 3.

DISCUSSION

This overview of 14 systematic reviews evaluated meta-analysed data from 125 164 observations covering 33 health-related outcomes among children and adolescents from general and

Table 1 Characteristics of included systematic reviews

First author, year	Population description*	Exposure description	Study design(s)*	Range of follow-up*	Outcome(s)	Total number of studies*	Total sample size*	AMSTAR 2 rating†
General population								
Bermejo-Cantarero, 2021[48]	General populations of children and adolescents (under 18 years of age)	CRF‡	Cross-sectional (12)	NA	HRQoL	12	10 712	Critically low
Cadenas-Sanchez, 2021[21]	General populations of children and adolescents (6–18 years of age)	CRF‡	Cross-sectional (52§), longitudinal (4), interventions (4)	1–8 years	Well-being, self-concept, self-esteem, self-perception, anxiety, depression	58	33 616	High
De Oliveira, 2016[22]	Apparently healthy adolescents (10–19 years of age)	Low vs high VO_2max	Cross-sectional (20), longitudinal (1)	7 years	MetS	21	NR	Critically low
Garcia-Hermoso, 2020[35]	General healthy children and adolescents (mean age of 3 to 18 years)	CRF‡	Longitudinal (55)	1–27 years	Skinfold thickness, BF%, BMI, obesity, WC TC, HDL-C, TC:HDL-C, LDL-C, TGL, fasting glucose, fasting insulin, HOMA-IR, SBP, DBP and MetS	55	37 452	Critically low
Gonçalves, 2021[42]	Apparently healthy adolescents (10–19 years of age)	VO_2max	Cross-sectional (23)	NA	BF%, BMI, WC, body weight	23	17 604	Critically low
Lona, 2022[19]	Children and adolescents without medication for CV risk factors (3–18 years of age)	CRF‡	Cross-sectional (5)	NA	cPWV	5	2760	Critically low
Clinical populations								
De Medeiros, 2021[49]	Healthy adolescents and those living with HIV (13–18 years of age)	VO_2max	Cross-sectional (5)	NR	HIV	5	197 with HIV and 185 healthy controls	Critically low
De Visser, 2024[50]	Adolescents with T1D and T2D and healthy controls (median age of 14 to 15 years)	VO_2max	Cross-sectional (NR), longitudinal (NR)	NR	T1D and T2D	55	1018 with T1D and 1064 healthy controls, 286 with T2D and 469 healthy controls (for CRF exposure)	Low
Hansen, 2014[51]	Obese and lean adolescents (12–18 years of age)	VO_2 peak	NR	NR	Obesity	9	333 with obesity and 145 lean	Critically low
Huerta-Uribe, 2023[20]	Children and adolescents with T1D (mean age of 3 to 18 years)	CRF‡ (largely VO_2peak/max)	NR	NR	HbA1c	13	34 863	Critically low
Pella, 2023[52]	Adolescents with JIA and healthy controls (mean age of 11 to 17 years)	VO_2 peak	Cross-sectional studies (NR), case-control (NR), longitudinal (NR)	NR	JIA	8	538	High
Schmidt-Andersen, 2024[53]	Children and adolescents with newly diagnosed cancer and healthy controls (1–18 years of age)	CRF‡	Longitudinal (5), RCT (4), quasi-experimental (3), cross-sectional (1), but based on the research question all scored as cross-sectional	NR	Cancer	13	594 within 1 month of cancer diagnosis and 3674 healthy controls	High
Vendrusculo, 2019[47]	Patients with cystic fibrosis (mean age of 10 to 30 years)	VO_2 peak	Longitudinal (6)	8 years	All-cause mortality in cystic fibrosis patients	6	551	Low
Villaseca-Rojas, 2022[54]	Children and adolescents with CHD and healthy controls (5–17 years of age)	VO_2peak, W max, HR max, VE/CO_2 slope	Cross-sectional (20), RCT (1)	NA	CHD	21	1540 with CHD and 1248 healthy controls	High

Continued

Table 1 Continued

First author, year	Population description*	Exposure description	Study design(s)*	Range of follow-up*	Outcome(s)	Total number of studies*	Total sample size*	AMSTAR 2 rating†

AMSTAR 2 is a critical appraisal tool for systematic reviews.[31]
*Data presented are for all the papers included in the systematic reviews and may include exposures other than CRF and/or participants aged >18 years.
†Details on the AMSTAR 2 quality assessment are available in online supplemental eTable 2.
‡CRF includes different measures of CRF, but all have been included under the bucket of CRF.
§One study was classified as including both cross-sectional and longitudinal design elements, and one study was classified as being both cross-sectional and interventional.
BF%, body fat percentage; BMI, body mass index; CHD, congenital heart disease; cPWV, central pulse wave velocity; CRF, cardiorespiratory fitness; CV, cardiovascular; DBP, diastolic blood pressure; HbA1c, glycated haemoglobin; HDL-C, high-density lipoprotein cholesterol; HIV, human immunodeficiency virus; HOMA-IR, homeostatic model assessment for insulin resistance; HRmax, maximum heart rate; HRQoL, health-related quality of life; JIA, juvenile idiopathic arthritis; LDL-C, low-density lipoprotein cholesterol; MetS, metabolic syndrome; NA, not applicable; NR, not reported; RCT, randomised controlled trial; SBP, systolic blood pressure; TC, total cholesterol; TC:HDL, total cholesterol to high-density lipoprotein-cholesterol ratio; T1D, type 1 diabetes; T2D, type 2 diabetes ; TG, triglycerides; VE/CO_2, ventilatory equivalent; VO_2max, maximal oxygen consumption; VO_2peak, peak oxygen consumption; WC, waist circumference; Wmax, maximal workload.

clinical populations. The results demonstrated favourable links between CRF and a wide range of health-related indicators (in the domains of adiposity, cardiometabolic and vascular health, mental health and well-being and mortality), as well as lower levels of CRF in patients with chronic diseases compared with healthy controls. However, the certainty of the evidence across all outcomes ranged from very low to moderate.

General population

Among the general population of children and adolescents, higher CRF levels were associated with better health, as suggested by favourable findings across 17 health-related outcomes: adiposity (skinfold thickness, waist circumference, body mass index), metabolic and vascular health (metabolic syndrome, fasting insulin, homeostatic model assessment for insulin resistance, total cholesterol, triglycerides, high-density lipoprotein cholesterol, total cholesterol to high-density lipoprotein cholesterol ratio, central pulse wave velocity) and mental health and well-being (depression, self-concept, self-esteem, self-perception, well-being, health-related quality of life). Results for seven outcomes (anxiety, body fat percentage, body weight, fasting glucose, low-density lipoprotein cholesterol, systolic and diastolic blood pressure) were not statistically significant, suggesting no association in the general population. This is largely in agreement with a previous systematic review, reporting favourable longitudinal associations of CRF in childhood and adolescence with lower body mass index, waist circumference, prevalence of metabolic syndrome, mental health, self-esteem and quality of life.[55] Regarding blood pressure, lipid profile and glucose homeostasis, no significant association in paediatric populations was observed by previous research,[55] which is also consistent with our findings. Immediate associations with certain health markers could be harder to detect in part due to the limited variability of the health measures (eg, blood pressure, lipids) among children. There is little room for an effect in generally healthy children; however, among children with

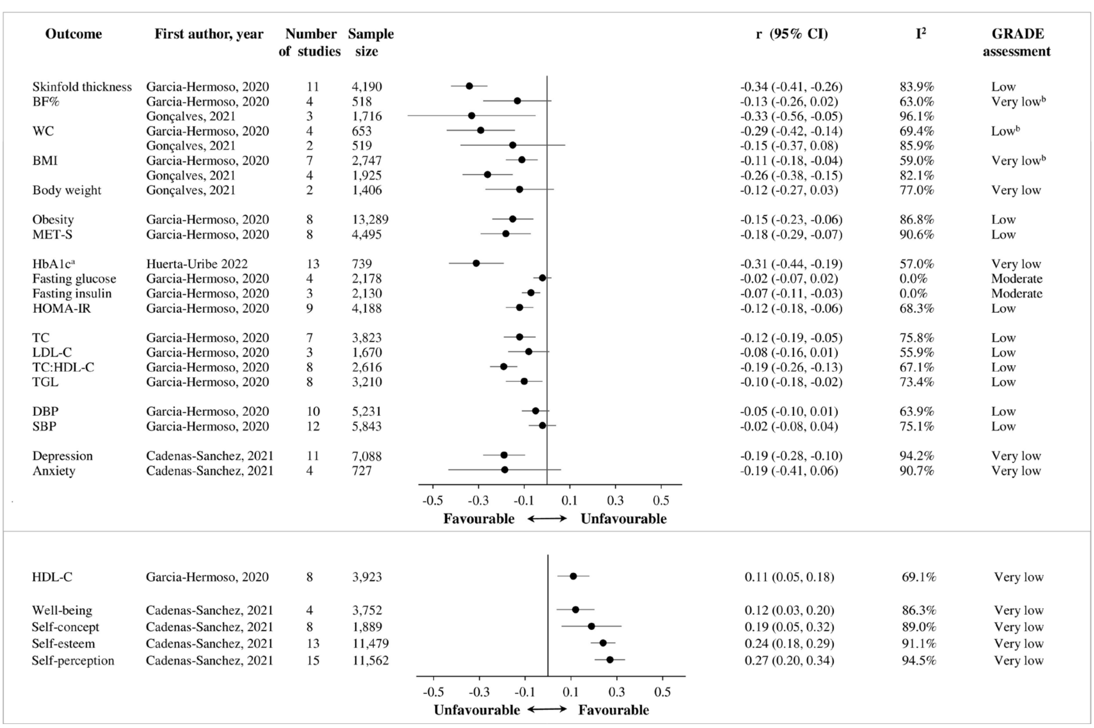

Figure 2 Linear correlations between cardiorespiratory fitness and health outcomes in children and adolescents. *Notes:* all outcomes are presented for the general population, except HbA1c. [a]Data are for the clinical population of children and adolescents with type 1 diabetes. [b]Longitudinal evidence was prioritised over cross-sectional for GRADE assessment. BF%, body fat percentage; BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; HbA1c, glycated haemoglobin; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; I^2, heterogeneity index; LDL-C, low-density lipoprotein cholesterol; MetS, metabolic syndrome; r, correlation coefficient; SBP, systolic blood pressure; TC, total cholesterol; TC:HDL, total cholesterol to HDL-C ratio; WC, waist circumference.

Table 2 Relationships between cardiorespiratory fitness and health outcomes, expressed using statistical measures other than correlation coefficient or mean difference

Outcome	First author, year	Number of studies	Sample size total (with a disease)	Comparisons	Effect measures (95% CI)	I^2	GRADE assessment
General population							
MetS	De Oliveira, 2016[22]	5	5231	Health outcome in participants with low CRF vs high	OR=4.05 (95% CI: 2.09, 7.87)	78%	Very low
cPWV	Lona, 2022[19]	2	1744	Association of CRF with health outcomes	ES=−0.03 (95% CI: −0.05, −0.01)	67%	Very low
HRQoL	Bermejo-Cantarero, 2021[48]	6	7368		ES=0.20 (95% CI: 0.12, 0.28)	69%	Very low
Clinical populations							
T1D	De Visser, 2024[50]	22	2082 (1,018 T1D)	CRF in participants with disease vs healthy controls	SMD=−0.39 (95% CI: −0.7, −0.09)	89%	Very low
T2D	De Visser, 2024[50]	9	755 (286 T2D)		SMD=−1.06 (95% CI: −1.57, −0.56)	84%	Very low
Cystic fibrosis	Vendrusculo, 2019[47]	2	137	Mortality in patients with low CRF vs high	RR=4.90 (95% CI: 1.09, 22.07)	32%	Very low

CI, confidence interval; cPWV, central pulse wave velocity; CRF, cardiorespiratory fitness; ES, effect size; HRQoL, health-related quality of life; MetS, metabolic syndrome; OR, odds ratio; RR, relative risk; SMD, standardised mean difference; T1D, type 1 diabetes; T2D, type 2 diabetes.

a more deleterious health status (eg, obesity class II-III), CRF shows a larger effect.[56] Overall, multiple important outcomes were covered by the extracted meta-analysed data, adding to the limited research available in this area. Future research should extend beyond adiposity, cardiometabolic profile and mental health. Other clinical outcomes (eg, immune protection,[57] nephrological conditions)[58] could potentially contribute to a more comprehensive understanding of the role of CRF as a summative indicator of the overall health status of children and adolescents.

Clinical populations

Among clinical populations, children and adolescents with cystic fibrosis were at considerably lower mortality risk when they had higher levels of CRF compared with lower levels.[47] In participants with type 1 diabetes, higher CRF was associated with better glucose control (ie, lower glycated haemoglobin levels).[20] Although the evidence is limited to only two health outcomes, these findings suggest that CRF may be a useful health marker not only in generally healthy populations of children and adolescents but also in clinical paediatric populations. Extensive data are available in this research area for adults, illustrating that CRF is a strong and consistent health-related marker in persons with and without chronic disease.[5 59] However, more research in this area is needed for children and adolescents.

Additionally, lower levels of CRF were found in patients with a chronic disease (juvenile idiopathic arthritis, HIV infection, newly diagnosed cancer, type 1 and type 2 diabetes) compared with their healthy peers. This could suggest that clinical populations are at a higher risk of unfavourable health outcomes. However, in the case of obesity, findings of this overview showed that participants with lower CRF had a higher risk of obesity among general populations, while no statistically significant difference was identified for CRF levels between adolescents with and without obesity. This result could be related to differences in the measurement of CRF, or it may further highlight the complexity of the CRF-obesity relationship previously discussed in the literature.[60 61] Collectively, these findings further contribute to the existing evidence, highlighting CRF as a valuable objective indicator of health status.[3 7] Further investigation into CRF across a wider variety of chronic health conditions (eg, asthma,[62] chronic kidney disease,[58] attention deficit hyperactivity disorder)[63] in paediatric populations could yield valuable insights, supporting the inclusion of CRF assessment in clinical practice and public health surveillance.

Implications for translational impact

Despite the widespread recognition of CRF for improved health earlier in life, most paediatric populations do not present with a healthy CRF level.[7] Poor CRF levels elevate the risk for paediatric health conditions, such as diabetes,[50] while also increasing risk for adverse health outcomes later in life,[35] which has economic and workforce implications.[64] Although guidelines to improve CRF through health-related behaviours, such as physical activity

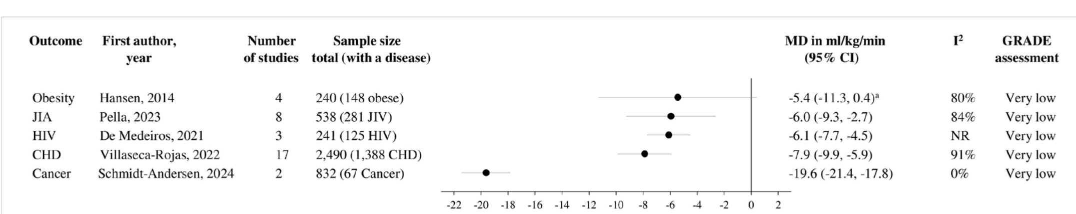

Figure 3 Mean differences between cardiorespiratory fitness in clinical populations of children and adolescents vs healthy controls. *Notes:* [a]Measured by VO_2peak corrected for lean tissue mass. CHD, congenital heart disease; CI, confidence interval; HIV, human immunodeficiency virus; JIA, juvenile idiopathic arthritis; I^2, heterogeneity index; MD, mean difference; NR, not reported.

participation, have been generated,[65 66] ongoing advocacy efforts are needed to scale physical activity programming in youth.[67] Our findings support CRF for health in paediatric populations. Routine screenings of CRF for generally healthy children and adolescents may help in preventing future chronic conditions. Moreover, assessing CRF in clinical paediatric populations may help guide secondary and tertiary interventions. Nonetheless, CRF remains a crucial lifespan health indicator across age demographics, and monitoring CRF in children and adolescents may contribute to long-term health benefits.

Certainty of evidence and knowledge gaps

Using a comprehensive search strategy and a modified GRADE approach allowed us to assess the scope and certainty of existing evidence and helped identify important knowledge gaps.

1) Little-to-no evidence of moderate and high certainty. The current meta-analysed evidence is predominantly of very low or low certainty, which reduced our confidence in estimates. The downgrading of evidence was largely due to a lack of representativeness of samples in primary studies, lack of global representation of primary studies in the reviews, relatively small sample sizes (<4000), and considerable heterogeneity (>50%). An absence of high certainty in estimates across all outcomes highlights the need for robust research designs, diverse geographical representation, larger sample sizes, better control of confounding factors and a deeper exploration of potential causes of heterogeneity.

2) Limited longitudinal evidence. The available meta-analytical evidence predominantly comprised cross-sectional studies, which limits the ability to establish causation and understand the long-term effects or changes over time. Only two of the included 14 systematic reviews focused exclusively on cohort studies,[35 47] and the spectrum of outcomes covered was limited to cardiometabolic profiles in the general population[35] and mortality in a clinical population of children and adolescents with cystic fibrosis.[47] More studies of longitudinal design are needed to explore CRF beyond its role as a marker of current health status in paediatric populations. Future research should focus on linking CRF in childhood and adolescence with long-term health outcomes to establish its potential as a predictor of disease risk later in life.

3) Limited scope of health outcomes and clinical populations. Although we were able to compile data on a broad range of health outcomes, the covered areas were limited to indicators of adiposity, cardiometabolic and vascular health, mental health and well-being. Much more extensive evidence exists for adults, covering a wider variety of chronic conditions (eg, chronic kidney disease, site-specific cancers, arrhythmia) and mortality outcomes (eg, all-cause mortality, all cancer mortality, cardiovascular mortality).[5] Evidence on additional health outcomes in paediatric populations (eg, within neurology, nephrology, immunology areas) and among various clinical populations (eg, patients with asthma, chronic kidney disease, attention deficit hyperactivity disorder) would provide a more comprehensive understanding of the relationships between childhood CRF and overall health.

Strengths and limitations

This overview has several strengths, including the development of a comprehensive search strategy with the involvement of experts in the field, the use of the AMSTAR 2 tool to evaluate review quality and the application of a modified GRADE approach to evaluate the certainty of the evidence. Although modifications to the GRADE approach could affect the comparability of the evidence assessment with other literature, the adjustments were deemed necessary due to the nature of the evidence and the context of the overview. The GRADE approach has been modified in various ways in previous studies[68–70] to allow for a more tailored assessment and to enhance its applicability in guiding evidence-based decisions.

This study provides important insights and identifies meaningful research gaps; however, there are several limitations to this overview that should be considered. The range of health outcomes and the quality of data was limited to the included reviews. Included reviews differed in the designs of primary studies (eg, longitudinal, cross-sectional), study populations (eg, clinical populations, general populations, exclusively adolescents) and other characteristics (eg, CRF measures, effect measures), limiting comparability and generalisability of the findings. Several included systematic reviews received critically low confidence ratings on AMSTAR 2, impacting the robustness of our conclusions. When evaluated against the GRADE criteria, most meta-analyses scored very low to low, even though the certainty of evidence assessment for each outcome was based on the available data of the highest quality (ie, where available, longitudinal evidence was prioritised above cross-sectional). Finally, the cross-sectional nature of the evidence in the included reviews did not allow us to establish temporal sequence in the reported relationships, highlighting the need for more high-quality longitudinal evidence[71] in this research area.

Perspective

CRF demonstrates potential as a predictive tool in paediatric populations. In 2020, the American Heart Association published a scientific statement highlighting protective relationships between CRF and health (eg, cardiovascular health, mental health), aiming to raise clinicians' attention to the value of CRF as a marker of current and future health in otherwise healthy children and adolescents.[7] This overview supports and extends these findings, summarising the data on a broad spectrum of health outcomes and demonstrating the potential of CRF in monitoring and predicting health beyond general populations, including children and adolescents with various clinical conditions. However, as identified by this overview, there are notable methodological limitations of evidence in this field. Low certainty of evidence may potentially lead to some associations being over- or underestimated, less reliable or less generalisable. Therefore, more work is needed to confirm the findings and examine the power of CRF as a predictive health indicator in children and adolescents to provide stronger support for the inclusion of CRF in clinical practice recommendations and surveillance programmes for paediatric populations.

CONCLUSIONS

This overview synthesised meta-analysed data on a wide range of health outcomes associated with CRF in general and clinical paediatric populations. Several promising links between CRF and health-related outcomes were identified, but the certainty in estimates was generally low, predominantly due to potential RoB, inconsistency and imprecision. More evidence, in particular, high-quality longitudinal studies, studies with larger sample sizes and studies focusing on underrepresented clinical populations are warranted to improve confidence in CRF as a health marker, as it relates to the strength of the effect, direction and causality. Better adherence to AMSTAR 2 guidelines is recommended for future studies to improve the methodological quality. Such evidence would provide stronger support for the use of children and adolescents' CRF as an indicator of their health status and a predictor of future disease burden, helping to inform and prepare the public health sector and clinical practices for future healthcare needs.

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