

SUPPLEMENTAL ONLINE CONTENT

Lang JJ, Prince SA, Merucci K, et al. Cardiorespiratory fitness is a strong and consistent predictor of morbidity and mortality among adults: An overview of meta-analyses representing over 20 million data points from 191 unique cohort studies

eAppendix 1: Search strategy

eAppendix 2: Excluded articles after full-text review with reason

eTable 1: GRADE decision table

eTable 2: AMSTAR2 assessment

eTable 3 : Summary of findings

eFigure 1: Mortality outcomes by sex.

eFigure 2: Incident outcomes by sex

eMethods: Expanded method section

This supplement has been provided by the authors to give readers additional information about their work.

eAppendix 1: Search strategy

Ovid MEDLINE(R) ALL 1946 to November 18, 2022

#	Searches
1	*Cardiorespiratory fitness/
2	((cardiorespirator* or cardio respirator* or aerobic or cardiopulmonar* or cardio pulmonar* or cardiovascular* or cardio vascular* or physical* work* or cardiometaboli* or cardio metaboli*) adj4 (fitness or capacit* or endurance or perform* or health*).ti,kf. or ((cardiorespirator* or cardio respirator* or aerobic or cardiopulmonar* or cardio pulmonar* or cardiovascular* or cardio vascular* or physical* work* or cardiometaboli* or cardio metaboli*) adj4 (fitness or capacit* or endurance or perform* or health*).ab. /freq=2
3	(Cardiorespiratory fitness and CRF).ab.
4	(Cardiovascular Health Study and CHS).ab.
5	exp *exercise tests/
6	((minute or mile or distance or timed) adj3 run).ti,kf. or ((minute or mile or distance or timed) adj3 run).ab. /freq=2
7	((fitness or exercise or endurance or step or walk or run or beep or tread?mill or ergometry or eurofit or stress) adj3 test*).ti,kf. or ((fitness or exercise or endurance or step or walk or run or beep or tread?mill or ergometry or eurofit or stress) adj3 test*).ab. /freq=2
8	((functional or aerobic or exercise) adj3 (capacity or endurance)).ti,kf. or ((functional or aerobic or exercise) adj3 (capacity or endurance)).ab. /freq=2
9	((Submaximal or maximal or graded) adj3 (treadmill? or tread mill? or ergometer?)).ti,ab,kf.
10	(maxim* oxygen or peak oxygen or VO2*).ti,kf. or (maxim* oxygen or peak oxygen or VO2*).ab. /freq=2
11	or/1-10 [CARDIORESPIRATORY FITNESS]
12	(meta-analysis or systematic review).pt.
13	meta-analysis/ or systematic review/ or meta-analysis as topic/ or systematic review as topic/
14	((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf.
15	(cochrane review* or ((umbrella* or mapping or integrative or integrated) adj3 (review* or overview*))).ti,ab,kf.
16	((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview* or synthes*))).ti,ab,kf.
17	"review of reviews".ti,ab,kf,kw.
18	(meta analy* or metanaly* or meta synthes* or metasynthes* or meta ethnography).ti,ab,kf,kw.
19	(cochrane or evidence report).jw.
20	((search* or medline or pubmed or embase or Cochrane or scopus or "web of science" or "sources of information" or data sources or following databases) and (study selection or selection criteria or eligibility criteria or inclusion criteria or exclusion criteria)).ti,ab.

21	(systematic literature adj (research or search)).ti.
22	or/12-21 [SYSTEMATIC REVIEWS + META ANALYSES]
23	(letter or editorial or comment or case reports or historical article or report or protocol or protocols or retraction of publication or retracted publication or published erratum).pt. or retraction of publication as topic/ or reply.ti.
24	22 not 23 [adapted from "SR / MA / HTA / ITC - MEDLINE, Embase, PsycInfo. In: CADTH Search Filters Database. Ottawa: CADTH; 2022: https://searchfilters.cadth.ca/link/33 ." Accessed 2022-10-28. and "Salvador-Oliván JA, Marco-Cuenca G, Arquero-Avilés R. Development of an efficient search filter to retrieve systematic reviews from PubMed. J Med Libr Assoc. 2021 Oct 1;109(4):561-574. doi: 10.5195/jmla.2021.1223."]
25	11 and 24 [CRF + SYSTEMATIC REVIEWS + META ANALYSES]
26	(exp animals/ or exp animal experimentation/ or exp models, animal/) not (humans/ or exp human experimentation/ or exp persons/ or human*.ti.)
27	(animal* or ape or apes or chimpanzee* or gerbil* or guineapig* or guinea pig* or hamster? or hare or hares or macaque* or mammal* or mice or monkey* or mouse or primate* or rabbit* or rat or rats or rodent?).ti.
28	26 or 27 [ANIMAL STUDIES]
29	25 not 28
30	limit 29 to yr="2002-current"

Ovid Embase 1974 to 2022 November 18

#	Searches
1	*Cardiorespiratory fitness/
2	((cardiorespirator* or cardio respirator* or aerobic or cardiopulmonar* or cardio pulmonar* or cardiovascular* or cardio vascular* or physical* work* or cardiometaboli* or cardio metaboli*) adj4 (fitness or capacit* or endurance or perform* or health*).ti,kf. or ((cardiorespirator* or cardio respirator* or aerobic or cardiopulmonar* or cardio pulmonar* or cardiovascular* or cardio vascular* or physical* work* or cardiometaboli* or cardio metaboli*) adj4 (fitness or capacit* or endurance or perform* or health*).ab. /freq=2
3	(Cardiorespiratory fitness and CRF).ab.
4	(Cardiovascular Health Study and CHS).ab.
5	exp *exercise test/
6	((minute or mile or distance or timed) adj3 run).ti,kf. or ((minute or mile or distance or timed) adj3 run).ab. /freq=2
7	((fitness or exercise or endurance or step or walk or run or beep or tread?mill or ergometry or eurofit or stress) adj3 test*).ti,kf. or ((fitness or exercise or endurance or step or walk or run or beep or tread?mill or ergometry or eurofit or stress) adj3 test*).ab. /freq=2

8	((functional or aerobic or exercise) adj3 (capacity or endurance)).ti,kf. or ((functional or aerobic or exercise) adj3 (capacity or endurance)).ab. /freq=2
9	((Submaximal or maximal or graded) adj3 (treadmill? or tread mill? or ergometer?)).ti,ab,kf.
10	(maxim* oxygen or peak oxygen or VO2*).ti,kf,kw. or (maxim* oxygen or peak oxygen or VO2*).ab. /freq=2
11	or/1-10 [CARDIORESPIRATORY FITNESS]
12	meta-analysis/ or systematic review/ or "meta analysis (topic)"/ or "systematic review (topic)"/
13	((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf.
14	(cochrane review* or ((umbrella* or mapping or integrative or integrated) adj3 (review* or overview*))).ti,ab,kf.
15	((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview* or synthes*))).ti,ab,kf.
16	"review of reviews".ti,ab,kf,kw.
17	(meta analy* or metanaly* or meta synthes* or metasynthes* or meta ethnography).ti,ab,kf,kw.
18	(cochrane or evidence report).jx.
19	((search* or medline or pubmed or embase or Cochrane or scopus or "web of science" or "sources of information" or data sources or following databases) and (study selection or selection criteria or eligibility criteria or inclusion criteria or exclusion criteria)).ti,ab.
20	(systematic literature adj (research or search)).ti.
21	or/12-20 [SYSTEMATIC REVIEWS + META ANALYSES]
22	(letter or editorial or conference abstract or note or short survey or erratum).pt. or reply.ti.
23	21 not 22 [adapted from "SR / MA / HTA / ITC - MEDLINE, Embase, PsycInfo. In: CADTH Search Filters Database. Ottawa: CADTH; 2022: https://searchfilters.cadth.ca/link/33 ." Accessed 2022-10-28. and "Salvador-Oliván JA, Marco-Cuenca G, Arquero-Avilés R. Development of an efficient search filter to retrieve systematic reviews from PubMed. J Med Libr Assoc. 2021 Oct 1;109(4):561-574. doi: 10.5195/jmla.2021.1223."]
24	11 and 23 [CRF + SYSTEMATIC REVIEWS + META ANALYSES]
25	(animals/ or exp animal experiment/ or exp animal model/) not (humans/ or exp human experiment/ or exp named groups of persons/ or human*.ti.)
26	(animal* or ape or apes or chimpanzee* or gerbil* or guineapig* or guinea pig* or hamster? or hare or hares or macaque* or mammal* or mice or monkey* or mouse or primate* or rabbit* or rat or rats or rodent?).ti.
27	25 or 26 [ANIMAL STUDIES]
28	24 not 27

29	limit 28 to yr="2002-current"
----	-------------------------------

Scopus

(((TITLE ((cardiorespirator* OR "cardio respirator*" OR aerobic OR cardiopulmonar* OR "cardio pulmonar*" OR cardiovascular* OR "cardio vascular*" OR "physical* work*" OR cardiometaboli* OR "cardio metaboli*") W/4 (fitness OR capacit* OR endurance OR perform* OR health*)) OR KEY ((cardiorespirator* OR "cardio respirator*" OR aerobic OR cardiopulmonar* OR "cardio pulmonar*" OR cardiovascular* OR "cardio vascular*" OR "physical* work*" OR cardiometaboli* OR "cardio metaboli*") W/4 (fitness OR capacit* OR endurance OR perform* OR health*)) OR ABS ("Cardiorespiratory fitness" AND "CRF") OR ABS ("Cardiovascular Health Study" AND "CHS") OR TITLE ((minute OR mile OR distance OR timed) W/3 run) OR ABS ((minute OR mile OR distance OR timed) W/3 run) OR TITLE ((fitness OR exercise OR endurance OR step OR walk OR run OR beep OR "tread*mill" OR ergometry OR eurofit OR stress) W/3 test*) OR ABS ((fitness OR exercise OR endurance OR step OR walk OR run OR beep OR "tread*mill" OR ergometry OR eurofit OR stress) W/3 test*) OR TITLE ((functional OR aerobic OR exercise) W/3 (capacity OR endurance)) OR KEY ((functional OR aerobic OR exercise) W/3 (capacity OR endurance)) OR TITLE-ABS-KEY ((submaximal OR maximal OR graded) W/3 (treadmill* OR "tread mill*" OR ergometer*)) OR TITLE ("maxim* oxygen" OR "peak oxygen" OR vo2*) OR KEY ("maxim* oxygen" OR "peak oxygen" OR vo2*)) AND ((INDEXTERMS (meta-analysis) OR INDEXTERMS ("systematic review") OR INDEXTERMS ("meta analysis (topic)") OR INDEXTERMS ("systematic review (topic)") OR INDEXTERMS ("meta-analysis as topic") OR INDEXTERMS ("systematic review as topic") OR TITLE-ABS-KEY ((systematic* W/3 (review* OR overview*)) OR (methodologic* W/3 (review* OR overview*))) OR TITLE-ABS-KEY ("cochrane review*" OR ((umbrella* OR mapping OR integrative OR integrated) W/3 (review* OR overview*))) OR TITLE-ABS-KEY ((quantitative W/3 (review* OR overview* OR synthes*)) OR (research W/3 (integrati* OR overview* OR synthes*))) OR TITLE-ABS-KEY ("review of reviews") OR TITLE-ABS-KEY ("meta analy*" OR metanaly* OR "meta synthes*" OR metasynthes* OR "meta ethnography") OR SRCTITLE (cochrane OR "evidence report") OR TITLE-ABS ((search* OR medline OR pubmed OR embase OR cochrane OR scopus OR "web of science" OR "sources of information" OR "data sources" OR "following databases") AND ("study selection" OR "selection criteria" OR "eligibility criteria" OR "inclusion criteria" OR "exclusion criteria")) OR TITLE ("systematic literature" W/1 (research OR search)) AND NOT (SRCTYPE (p OR n OR r) OR DOCTYPE ("cp" OR "ed" OR "er" OR "le" OR "no" OR "rp") OR TITLE (reply))) AND (PUBYEAR > 2001)) AND NOT ((INDEXTERMS (animal OR animals OR "animal experiment" OR "animal experimentation" OR "animal model" OR "models, animal") AND NOT (INDEXTERMS (humans OR "human experiment" OR "human experimentation" OR "named groups of persons" OR persons) OR TITLE (human*))))

CINAHL via EBSCOhost	Query	Limiters/Expanders
----------------------	-------	--------------------

(1981 to present)#		
S28	S22 NOT S27	Limiters - Published Date: 20020101-
S27	S25 OR S26	
S26	TI animal* or ape or apes or chimpanzee* or gerbil* or guineapig* or guinea pig* or hamster# or hare or hares or macaque* or mammal* or mice or monkey* or mouse or primate* or rabbit* or rat or rats or rodent#	
S25	S23 NOT 24	
S24	MH "human" OR TI human*	
S23	MH "animals+" OR MH "animal studies" OR MH "Models, Biological"	
S22	S8 AND S21	
S21	S19 NOT S20	
S20	PT (letter or editorial or commentary or case study or historical material or protocol or response) OR MH "Scientific Misconduct" OR TI reply	
S19	S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18	
S18	TI (systematic literature N1 (research or search))	
S17	TI (((search* or medline or pubmed or embase or Cochrane or scopus or "web of science" or "sources of information" or data sources or following databases) and (study selection or selection criteria or eligibility criteria or inclusion criteria or exclusion criteria)) OR AB (((search* or medline or pubmed or embase or Cochrane or scopus or "web of science" or "sources of information" or data sources or following databases) and (study selection or selection criteria or eligibility criteria or inclusion criteria or exclusion criteria)))	
S16	SO (cochrane or evidence report)	
S15	TI ((meta analy* or metanaly* or meta synthes* or metasynthes* or meta ethnography)) OR AB ((meta analy* or metanaly* or meta synthes* or metasynthes* or meta ethnography))	
S14	TI "review of reviews" OR AB "review of reviews"	
S13	TI (((quantitative N3 (review* or overview* or synthes*)) or (research N3 (integrati* or overview* or synthes*)))) OR AB (((quantitative N3 (review* or overview* or synthes*)) or (research N3 (integrati* or overview* or synthes*))))	

S12	TI ((cochrane review* or ((umbrella* or mapping or integrative or integrated) N3 (review* or overview*)))) OR AB ((cochrane review* or ((umbrella* or mapping or integrative or integrated) N3 (review* or overview*))))	
S11	TI (((systematic* N3 (review* or overview*)) or (methodologic* N3 (review* or overview*)))) OR AB (((systematic* N3 (review* or overview*)) or (methodologic* N3 (review* or overview*))))	
S10	MH "meta analysis" OR MH "systematic review"	
S9	PT "systematic review" OR PT "meta analysis"	
S8	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7	
S7	TI (maxim* oxygen or peak oxygen or VO2*) OR AB (maxim* oxygen or peak oxygen or VO2*)	
S6	TI ((Submaximal or maximal or graded) N3 (treadmill# or tread mill# or ergometer#)) OR AB ((Submaximal or maximal or graded) N3 (treadmill# or tread mill# or ergometer#))	
S5	TI ((functional or aerobic or exercise) N3 (capacity or endurance)) OR AB ((functional or aerobic or exercise) N3 (capacity or endurance))	
S4	TI ((fitness or exercise or endurance or step or walk or run or beep or tread#mill or ergometry or eurofit or stress) N3 test*) OR AB ((fitness or exercise or endurance or step or walk or run or beep or tread#mill or ergometry or eurofit or stress) N3 test*)	
S3	TI ((minute or mile or distance or timed) N3 run) OR AB ((minute or mile or distance or timed) N3 run)	
S2	TI ((cardiorespirator* or cardio respirator* or aerobic or cardiopulmonar* or cardio pulmonar* or cardiovascular* or cardio vascular* or physical* work* or cardiometaboli* or cardio metaboli*) N4 (fitness or capacit* or endurance or perform* or health*)) OR AB ((cardiorespirator* or cardio respirator* or aerobic or cardiopulmonar* or cardio pulmonar* or cardiovascular* or cardio vascular* or physical* work* or cardiometaboli* or cardio metaboli*) N4 (fitness or capacit* or endurance or perform* or health*))	
S1	(MM "Cardiorespiratory Fitness") or (MM "Exercise Test+")	

SPORTDiscus with Full Text via EBSCOhost (1930 to present)

#	Query	Limiters/Expanders
---	-------	--------------------

S23	S21 NOT S22	Limiters - Published Date: 20020101-
S22	TI animal* or ape or apes or chimpanzee* or gerbil* or guineapig* or guinea pig* or hamster# or hare or hares or macaque* or mammal* or mice or monkey* or mouse or primate* or rabbit* or rat or rats or rodent#	
S21	S9 AND S20	
S20	S18 NOT S19	
S19	TI reply	
S18	S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17	
S17	TI (systematic literature N1 (research or search))	
S16	TI (((search* or medline or pubmed or embase or Cochrane or scopus or "web of science" or "sources of information" or data sources or following databases) and (study selection or selection criteria or eligibility criteria or inclusion criteria or exclusion criteria))) OR AB (((search* or medline or pubmed or embase or Cochrane or scopus or "web of science" or "sources of information" or data sources or following databases) and (study selection or selection criteria or eligibility criteria or inclusion criteria or exclusion criteria)))	
S15	TI ((meta analy* or metanaly* or meta synthes* or metasynthes* or meta ethnography)) OR AB ((meta analy* or metanaly* or meta synthes* or metasynthes* or meta ethnography))	
S14	TI "review of reviews" OR AB "review of reviews"	
S13	TI ((quantitative N3 (review* or overview* or synthes*)) or (research N3 (integrati* or overview* or synthes*))) OR AB ((quantitative N3 (review* or overview* or synthes*)) or (research N3 (integrati* or overview* or synthes*)))	
S12	TI (cochrane review* or ((umbrella* or mapping or integrative or integrated) N3 (review* or overview*))) OR AB (cochrane review* or ((umbrella* or mapping or integrative or integrated) N3 (review* or overview*)))	
S11	TI ((systematic* N3 (review* or overview*)) or (methodologic* N3 (review* or overview*))) OR AB ((systematic* N3 (review* or overview*)) or (methodologic* N3 (review* or overview*)))	
S10	PT review	
S9	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8	

S8	TI (maxim* oxygen or peak oxygen or VO2*) OR AB (maxim* oxygen or peak oxygen or VO2*)	
S7	TI ((Submaximal or maximal or graded) N3 (treadmill# or tread mill# or ergometer#)) OR AB ((Submaximal or maximal or graded) N3 (treadmill# or tread mill# or ergometer#))	
S6	TI ((functional or aerobic or exercise) N3 (capacity or endurance)) OR AB ((functional or aerobic or exercise) N3 (capacity or endurance))	
S5	TI ((fitness or exercise or endurance or step or walk or run or beep or tread#mill or ergometry or eurofit or stress) N3 test*) OR AB ((fitness or exercise or endurance or step or walk or run or beep or tread#mill or ergometry or eurofit or stress) N3 test*)	
S4	TI ((minute or mile or distance or timed) N3 run) OR AB ((minute or mile or distance or timed) N3 run) TI ((fitness or exercise or endurance or step or walk or run or beep or tread#mill or ergometry or eurofit or stress) N3 test*) OR AB ((fitness or exercise or endurance or step or walk or run or beep or tread#mill or ergometry or eurofit or stress) N3 test*)	
S3	DE "EXERCISE tests" OR DE "STRESS echocardiography" OR DE "TREADMILL exercise tests"	
S2	TI ((cardiorespirator* or cardio respirator* or aerobic or cardiopulmonar* or cardio pulmonar* or cardiovascular* or cardio vascular* or physical* work* or cardiometaboli* or cardio metaboli*) N4 (fitness or capacit* or endurance or perform* or health*)) OR AB ((cardiorespirator* or cardio respirator* or aerobic or cardiopulmonar* or cardio pulmonar* or cardiovascular* or cardio vascular* or physical* work* or cardiometaboli* or cardio metaboli*) N4 (fitness or capacit* or endurance or perform* or health*))	
S1	DE "CARDIOVASCULAR fitness" OR DE "CARDIOPULMONARY fitness"	

eAppendix 2: References excluded at full-text screening with reasons.

1. Agostinis-Sobrinho, C., Ramirez-Velez, R., Garcia-Hermoso, A., Rosario, R., Moreira, C., Lopes, L., Martinkenas, A., Mota, J., & Santos, R. (2019). The combined association of adherence to Mediterranean diet, muscular and cardiorespiratory fitness on low-grade inflammation in adolescents: a pooled analysis. *European Journal of Nutrition*, 58(7), 2649-2656.
 - Not a systematic review
2. Al-Huda, F., Shapiro, G. D., Davenport, M. H., Bertagnolli, M., & Dayan, N. (2022). Association between Cardiorespiratory Fitness and Hypertensive Disorders of Pregnancy: A Systematic Review and Meta-Analysis. *Journal of Clinical Medicine*, 11(15).
 - Surgical, disease at birth, or pregnant population
3. Alexandrou, M. E., P. Theodorakopoulou, M., Boutou, A., Pella, E., Boulmpou, A., Papadopoulos, C. E., Zafeiridis, A., Papagianni, A., & Sarafidis, P. (2021). Cardiorespiratory fitness assessed by cardiopulmonary exercise testing between different stages of pre-dialysis chronic kidney disease: A systematic review and meta-analysis. *Nephrology*, 26(12), 972-980.
 - Surgical, disease at birth, or pregnant population
4. Alvarez-Bueno, C., Hillman, C. H., Cavero-Redondo, I., Sanchez-Lopez, M., Pozuelo-Carrascosa, D. P., & Martinez-Vizcaino, V. (2020). Aerobic fitness and academic achievement: A systematic review and meta-analysis. *Journal of sports sciences*, 38(5), 582-589.
 - Child and youth population
5. Alves, D. J. F., Bartholomeu-Neto, J., JÚNior, E. R., Zarricueta, B. S. R., NÓBrega, O. T., & CÓRdova, C. (2017). Walking speed, risk factors, and cardiovascular events in older adults--systematic review. *Journal of Strength & Conditioning Research*, 31(11), 3235-3244.
 - No meta-analysis
6. Alves Donato, A. N., Waclawovsky, A. J., Tonello, L., Firth, J., Smith, L., Stubbs, B., Schuch, F. B., & Boullosa, D. (2021). Association between cardiorespiratory fitness and depressive symptoms in children and adolescents: A systematic review and meta-analysis. *Journal of Affective Disorders*, 282, 1234-1240.
 - Child and youth population
7. Andrade Lima, C., Dornelas de Andrade, A., Campos, S. L., Brandao, D. C., Mourato, I. P., & Britto, M. C. A. d. (2018). Six-minute walk test as a determinant of the functional capacity of children and adolescents with cystic fibrosis: A systematic review. *Respiratory Medicine*, 137, 83-88.
 - No meta-analysis

8. Andrade, R. D. A., de Menezes, B. A., Vieira, L. L., Daniele, T. M. C., & de Sousa, N. J. F. (2019). Association between physical fitness and cardiovascular risk in young university students: Systematic review. *Motricidade, 15*(2-3), 75-84.
 - No meta-analysis
9. Aneni, E. C., Crippa, A., Osondu, C. U., Valero-Elizondo, J., Younus, A., Nasir, K., & Veledar, E. (2017). Estimates of Mortality Benefit From Ideal Cardiovascular Health Metrics: A Dose Response Meta-Analysis. *Journal of the American Heart Association, 6*(12).
 - No measure of CRF
10. Arena, R., Myers, J., & Guazzi, M. (2008). The clinical and research applications of aerobic capacity and ventilatory efficiency in heart failure: an evidence-based review. *Heart failure reviews, 13*(2), 245-269.
 - No meta-analysis
11. Baillot, A., Audet, M., Baillargeon, J. P., Dionne, I. J., Valiquette, L., Rosa-Fortin, M. M., Abou Chakra, C. N., Comeau, E., & Langlois, M. F. (2014). Impact of physical activity and fitness in class II and III obese individuals: A systematic review. *Obesity Reviews, 15*(9), 721-739.
 - No meta-analysis
12. Banerjee, A., Newman, D. R., Van den Bruel, A., & Heneghan, C. (2012). Diagnostic accuracy of exercise stress testing for coronary artery disease: a systematic review and meta-analysis of prospective studies. *International journal of clinical practice, 66*(5), 477-492.
 - meta-regression or meta-analysis of screening study
13. Barbosa Guedes, M., Sousa Rodrigues, T., & Ribeiro, J. M. (2013). Correlation between hypertension and functional capacity in older adults: a literature review. *Revista de Atencao Primaria a Saude, 16*(4), 455-459.
 - Language exclusion
14. Barratt, S. L., Davis, R., Sharp, C., & Pauling, J. D. (2020). The prognostic value of cardiopulmonary exercise testing in interstitial lung disease: a systematic review. *ERJ Open Research, 6*(3).
 - No meta-analysis
15. Bauters, C., & Lemesle, G. (2016). Screening for asymptomatic coronary artery disease in patients with diabetes mellitus: A systematic review and meta-analysis of randomized trials. *BMC Cardiovascular Disorders, 16*, 90.
 - Wrong meta-analysis type – cross-sectional data
16. Bayonas-Ruiz, A., Munoz-Franco, F. M., Ferrer, V., Perez-Caballero, C., Sabater-Molina, M., Tome-Esteban, M. T., & Bonacasa, B. (2021). Cardiopulmonary Exercise

Test in Patients with Hypertrophic Cardiomyopathy: A Systematic Review and Meta-Analysis. *Journal of Clinical Medicine*, 10(11).

- Wrong meta-analysis type – cross-sectional data

17. Behrens, G., Niedermaier, T., Berneburg, M., Schmid, D., & Leitzmann, M. F. (2018). Physical activity, cardiorespiratory fitness and risk of cutaneous malignant melanoma: Systematic review and meta-analysis. *PLoS ONE*, 13(10), e0206087.

- No meta-analysis

18. Bell, M., Fotheringham, I., Puneekar, Y. S., Riley, J. H., Cockle, S., & Singh, S. J. (2015). Systematic Review of the Association Between Laboratory- and Field-Based Exercise Tests and Lung Function in Patients with Chronic Obstructive Pulmonary Disease. *Chronic obstructive pulmonary diseases (Miami, Fla.)*, 2(4), 321-342.

- No meta-analysis

19. Bermejo-Cantarero, A., Alvarez-Bueno, C., Martinez-Vizcaino, V., Redondo-Tebar, A., Pozuelo-Carrascosa, D. P., & Sanchez-Lopez, M. (2021). Relationship between both cardiorespiratory and muscular fitness and health-related quality of life in children and adolescents: a systematic review and meta-analysis of observational studies. *Health and Quality of Life Outcomes*, 19(1), 127.

- Child and youth population

20. But-Hadzic, J., Dervisevic, M., Karpljuk, D., Videmsek, M., Dervisevic, E., Paravlic, A., Hadzic, V., & Tomazin, K. (2021). Six-minute walk distance in breast cancer survivors—a systematic review with meta-analysis. *International Journal of Environmental Research and Public Health*, 18(5), 1-13.

- Wrong meta-analysis type – cross-sectional data

21. Cadenas-Sanchez, C., Mena-Molina, A., Torres-Lopez, L. V., Migueles, J. H., Rodriguez-Ayllon, M., Lubans, D. R., & Ortega, F. B. (2021). Healthier Minds in Fitter Bodies: A Systematic Review and Meta-Analysis of the Association between Physical Fitness and Mental Health in Youth. *Sports medicine (Auckland, N.Z.)*, 51(12), 2571-2605.

- Child and youth population

22. Cahalin, L. P., Chase, P., Arena, R., Myers, J., Bensimhon, D., Peberdy, M. A., Ashley, E., West, E., Forman, D. E., Pinkstaff, S., Lavie, C. J., Guazzi, M., Cahalin, L. P., Chase, P., Arena, R., Myers, J., Bensimhon, D., Peberdy, M. A., Ashley, E., & West, E. (2013). A meta-analysis of the prognostic significance of cardiopulmonary exercise testing in patients with heart failure. *Heart failure reviews*, 18(1), 79-94.

- meta-regression or meta-analysis of screening study

23. Carrard, J., Guerini, C., Appenzeller-Herzog, C., Infanger, D., Konigstein, K., Streese, L., Hinrichs, T., Hanssen, H., Gallart-Ayala, H., Ivanisevic, J., & Schmidt-Trucksass, A. (2022). The Metabolic Signature of Cardiorespiratory Fitness: A Systematic Review. *Sports medicine (Auckland, N.Z.)*, 52(3), 527-546.

- No meta-analysis
24. Cederberg, K. L. J., Sikes, E. M., Bartolucci, A. A., & Motl, R. W. (2019). Walking endurance in multiple sclerosis: Meta-analysis of six-minute walk test performance. *Gait & posture*, 73, 147-153.
 - Wrong meta-analysis type – cross-sectional data
 25. Colcombe, S., & Kramer, A. F. (2003). Fitness Effects on the Cognitive Function of Older Adults: A Meta-Analytic Study. *Psychological Science (0956-7976)*, 14(2), 125-130.
 - No measure of CRF
 26. Copetti Rodriguez, C., de Camargo, E. M., Rodriguez-Añez, C. R., & Siqueira Reis, R. (2020). Physical activity, physical fitness and academic achievement in adolescents: a systematic review. / actividad física, aptitud física y desempeño académico en adolescentes: una revisión sistemática. *Revista Brasileira de Medicina do Esporte*, 26(5), 441-448.
 - No meta-analysis
 27. Cota, B. C., Suhett, L. G., Leite, N. N., Pereira, P. F., Ribeiro, S. A. V., & Franceschini, S. d. C. C. (2021). Cardiometabolic risk and health behaviours in adolescents with normal-weight obesity: a systematic review. *Public health nutrition*, 24(5), 870-881.
 - No meta-analysis
 28. Cruz-Montecinos, C., Nunez-Cortes, R., Vasconcello-Castillo, L., Solis-Navarro, L., Carrasco-Alonso, B., Calatayud, J., Perez-Alenda, S., & Torres-Castro, R. (2022). Exercise capacity in people with haemophilia: A systematic review. *Haemophilia : the official journal of the World Federation of Hemophilia*, 28(6), 891-901.
 - No meta-analysis
 29. da Silva Cunha de Medeiros, R. C., Dos Santos, I. K., de Oliveira, A. L. V., de Goes, C. J. D., de Medeiros, J. A., da Silva, T. A. L., de Souza Araujo, J., de Alcantara Varela, P. W., Cobucci, R. N., de Araujo Tinoco Cabral, B. G., & Dantas, P. M. S. (2021). Comparison of Muscle Strength, Aerobic Capacity and Body Composition between Healthy Adolescents and Those Living with HIV: A Systematic Review and Meta-Analysis. *International Journal of Environmental Research and Public Health*, 18(11).
 - Child and youth population
 30. de Andrade Goncalves, E. C., Augusto Santos Silva, D., & Gimenes Nunes, H. E. (2015). Prevalence and Factors Associated With Low Aerobic Performance Levels in Adolescents: A Systematic Review. *Current pediatric reviews*, 11(1), 56-70.
 - No meta-analysis
 31. de la Motte, S. J., Gribbin, T. C., Lisman, P., Murphy, K., & Deuster, P. A. (2017). Systematic Review of the Association Between Physical Fitness and Musculoskeletal

Injury Risk: Part 2-Muscular Endurance and Muscular Strength. *Journal of strength and conditioning research*, 31(11), 3218-3234.

- No meta-analysis
32. De Oliveira, R. G., & Guedes, D. P. (2016). Physical activity, sedentary behavior, cardiorespiratory fitness and metabolic syndrome in adolescents: Systematic review and meta-analysis of observational evidence. *PLoS ONE*, 11(12).
- Child and youth population
33. Dulfer, K., Helbing, W. A., Duppen, N., & Utens, E. M. W. J. (2014). Associations between exercise capacity, physical activity, and psychosocial functioning in children with congenital heart disease: a systematic review. *European Journal of Preventive Cardiology*, 21(10), 1200-1215.
- No meta-analysis
34. Dun, Y., Wu, S., Cui, N., Thomas, R. J., Olson, T. P., Zhou, N., Li, Q., & Liu, S. (2021). Screening for Asymptomatic Coronary Artery Disease via Exercise Stress Testing in Patients With Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Frontiers in cardiovascular medicine*, 8, 770648.
- meta-regression or meta-analysis of screening study
35. Durstenfeld, M. S., Sun, K., Tahir, P., Peluso, M. J., Deeks, S. G., Aras, M. A., Grandis, D. J., Long, C. S., Beatty, A., & Hsue, P. Y. (2022). Use of Cardiopulmonary Exercise Testing to Evaluate Long COVID-19 Symptoms in Adults: A Systematic Review and Meta-analysis. *JAMA Network Open*, 5(10), e2236057.
- Wrong meta-analysis type – cross-sectional data
36. Eckstein, M. L., Aberer, F., Dobler, F. J. R., Aziz, F., Heise, T., Sourij, H., & Moser, O. (2022). Association of HbA1c with VO2max in Individuals with Type 1 Diabetes: A Systematic Review and Meta-Analysis. *Metabolites*, 12(11).
- Wrong meta-analysis type – cross-sectional data
37. Etnier, J. L., Nowell, P. M., Landers, D. M., & Sibley, B. A. (2006). A meta-regression to examine the relationship between aerobic fitness and cognitive performance. *Brain research reviews*, 52(1), 119-130.
- meta-regression or meta-analysis of screening study
38. Fang, N., Jiang, M., & Fan, Y. (2016). Ideal cardiovascular health metrics and risk of cardiovascular disease or mortality: A meta-analysis. *International Journal of Cardiology*, 214, 279-283.
- No measure of CRF
39. Fernandes Csengeri, L., de Souza, M. K., Soares de Almeida, S., Vanerson Passos Neves, R., de Luca Corrêa, H., Rocha de Moraes, M., Almeida, W. M., de Moraes, M., Gustavo Simões, H., Prestes, J., & dos Santos Rosa, T. (2020). O papel da aptidão aeróbia sobre o paradoxo da obesidade: uma revisão sistemática. / the role of physical fitness in obesity

paradox: a systematic review. *Revista Brasileira de Ciência e Movimento: RBCM*, 28(3), 205-229.

- Language exclusion

40. Fernandes M. de Sousa, A., Medeiros, A. R., Del Rosso, S., Stults-Kolehmainen, M., & Boullousa, D. A. (2019). The influence of exercise and physical fitness status on attention: a systematic review. *International Review of Sport & Exercise Psychology*, 12(1), 202-234.

- No meta-analysis

41. Fogelholm, M. (2010). Physical activity, fitness and fatness: relations to mortality, morbidity and disease risk factors. A systematic review. *Obesity reviews : an official journal of the International Association for the Study of Obesity*, 11(3), 202-221.

- No meta-analysis

42. Franklin, J. D., Atkinson, G., Atkinson, J. M., & Batterham, A. M. (2019). Peak Oxygen Uptake in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis: A Meta-Analysis. *International journal of sports medicine*, 40(2), 77-87.

- Wrong meta-analysis type – cross-sectional data

43. Franklin, J. D., & Graham, M. (2022). Repeated maximal exercise tests of peak oxygen consumption in people with myalgic encephalomyelitis/chronic fatigue syndrome: a systematic review and meta-analysis. *Fatigue: Biomedicine, Health and Behavior*, 10(3), 119-135.

- Wrong meta-analysis type – cross-sectional data

44. Garcia-Hermoso, A., Ramirez-Velez, R., Garcia-Alonso, Y., Alonso-Martinez, A. M., & Izquierdo, M. (2020). Association of Cardiorespiratory Fitness Levels During Youth With Health Risk Later in Life: A Systematic Review and Meta-analysis. *JAMA pediatrics*, 174(10), 952-960.

- Child and youth population

45. Glue, C., Haveron, R., Smith, M. L., Thiagarajan, P., Edwards, H., Mulligan, H., & Wilkinson, A. (2020). Six-minute walk test values for people with and without long-term conditions in relation to the Walk Score®: a scoping review. *Physical Therapy Reviews*, 25(5-6), 411-421.

- No meta-analysis

46. Gomes-Neto, M., Rodriguez, I., Ledo, A. P., Vieira, J. P. B., & Brites, C. (2018). Muscle Strength and Aerobic Capacity in HIV-Infected Patients: A Systematic Review and Meta-Analysis. *Journal of acquired immune deficiency syndromes (1999)*, 79(4), 491-500.

- Wrong meta-analysis type – cross-sectional data

47. Gonçalves, E. C. A., Fernandes, R., Alves Junior, C. A. S., Silva, D. A. S., & Trindade, E. B. S. M. (2021). Oxygen uptake and indicators of obesity: Meta-analysis including 17,604 adolescents. *Revista Brasileira de Medicina do Esporte*, 27(6), 621-626.

- Child and youth population
48. González Valero, G., Zurita Ortega, F., Román Mata, S. S., Pérez Cortés, A. J., Puertas Molero, P., & Chacón Cuberos, R. (2018). Análisis de la capacidad aeróbica como cualidad esencial de la condición física de los estudiantes: Una revisión sistemática. / Analysis of aerobic capacity as an essential quality of students' physical condition: A systematic review. *Retos: Nuevas Perspectivas de Educación Física, Deporte y Recreación*, 34, 395-402.
- No meta-analysis
49. Gottarde, L. A. F., Vitor, G. B. B., Martini, F. A. N., & de Oliveira, R. G. (2021). Atividade física, aptidão física e dor lombar em adultos jovens: revisão sistemática de evidências observacionais. *Fisioterapia Brasil*, 22(6), 931-950. <https://doi.org/10.33233/fb.v22i6.4817>
- Language exclusion
50. Grao-Cruces, A., Ruiz-Ariza, A., De La Torre-Cruz, M. J., & Martínez-López, E. J. (2018). Students with excess weight obtain lower physical fitness test scores in physical education than normal weight pairs: Myth or reality? *Journal of Physical Education and Sport*, 18(3), 1562-1571.
- No meta-analysis
51. Grässler, B., Hökelmann, A., & Cabral, R. H. (2020). RESTING HEART RATE VARIABILITY AS A POSSIBLE MARKER OF COGNITIVE DECLINE. *Kinesiology*, 52(1), 72-84.
- No meta-analysis
52. Guo, L., & Zhang, S. (2017). Association between ideal cardiovascular health metrics and risk of cardiovascular events or mortality: A meta-analysis of prospective studies. *Clinical cardiology*, 40(12), 1339-1346.
- No measure of CRF
53. Hansen, D., Marinus, N., Remans, M., Courtois, I., Cools, F., Calsius, J., Massa, G., & Takken, T. (2014). Exercise tolerance in obese vs. lean adolescents: a systematic review and meta-analysis. *Obesity reviews : an official journal of the International Association for the Study of Obesity*, 15(11), 894-904.
- Child and youth population
54. Heggelund, J., Vancampfort, D., Tacchi, M. J., Morken, G., & Scott, J. (2020). Is there an association between cardiorespiratory fitness and stage of illness in psychotic disorders? A systematic review and meta-analysis. *Acta psychiatrica Scandinavica*, 141(3), 190-205.
- Wrong meta-analysis type – cross-sectional data

55. Hou, Y., Yan, L., Mao, J., Wang, X., Li, L., Zhong, C., Liu, H., & Zhao, Z. (2018). The application value of 6-minute walking test in clinical evaluation of chronic heart failure. *Chinese Journal of Evidence-Based Medicine*, 18(9), 907-917.
- Language exclusion
56. Huerta-Uribe, N., Ramirez-Velez, R., Izquierdo, M., & Garcia-Hermoso, A. (2022). Association Between Physical Activity, Sedentary Behavior and Physical Fitness and Glycated Hemoglobin in Youth with Type 1 Diabetes: A Systematic Review and Meta-analysis. *Sports medicine (Auckland, N.Z.)*.
- Child and youth population
57. Husoy, A., Dalene, K. E., Steene-Johannessen, J., Anderssen, S. A., Ekelund, U., & Tarp, J. (2021). Effect modification by cardiorespiratory fitness on the association between physical activity and cardiometabolic health in youth: A systematic review. *Journal of sports sciences*, 39(8), 845-853.
- No meta-analysis
58. Kyröläinen, H., Santtila, M., Nindl, B. C., & Vasankari, T. (2010). Physical fitness profiles of young men associations between physical fitness, obesity and health. *Sports Medicine*, 40(11), 907-920.
- No meta-analysis
59. Langeskov-Christensen, M., Heine, M., Kwakkel, G., & Dalgas, U. (2015). Aerobic capacity in persons with multiple sclerosis: a systematic review and meta-analysis. *Sports medicine (Auckland, N.Z.)*, 45(6), 905-923.
- Wrong meta-analysis type – cross-sectional data
60. Lardon, A., Leboeuf-Yde, C., & Le Scanff, C. (2015). Is back pain during childhood or adolescence associated with muscle strength, muscle endurance or aerobic capacity: three systematic literature reviews with one meta-analysis. *Chiropractic & manual therapies*, 23, 21.
- No meta-analysis
61. Lee, C. H. A., Kong, J. C., Ismail, H., Riedel, B., & Heriot, A. (2018). Systematic Review and Meta-analysis of Objective Assessment of Physical Fitness in Patients Undergoing Colorectal Cancer Surgery. *Diseases of the colon and rectum*, 61(3), 400-409.
- Surgical, disease at birth, or pregnant population
62. Lee, J. (2020). Influences of Cardiovascular Fitness and Body Fatness on the Risk of Metabolic Syndrome: A Systematic Review and Meta-Analysis. *American journal of health promotion : AJHP*, 34(7), 796-805.
- Wrong meta-analysis type – cross-sectional data
63. Lona, G., Hauser, C., Kochli, S., Infanger, D., Endes, K., Schmidt-Trucksass, A., & Hanssen, H. (2022). Association of blood pressure, obesity and physical activity with

- arterial stiffness in children: a systematic review and meta-analysis. *Pediatric research*, 91(3), 502-512.
- Child and youth population
64. Maleki, S., Hendrikse, J., Chye, Y., Caeyenberghs, K., Coxon, J. P., Oldham, S., Suo, C., & Yucel, M. (2022). Associations of cardiorespiratory fitness and exercise with brain white matter in healthy adults: A systematic review and meta-analysis. *Brain imaging and behavior*, 16(5), 2402-2425.
- Wrong meta-analysis type – cross-sectional data
65. Marques, A., Gouveira, E. R., Peralta, M., Martins, J., Venturini, J., Henriques-Neto, D., & Sarmiento, H. (2020). Cardiorespiratory fitness and telomere length: a systematic review. *Journal of sports sciences*, 38(14), 1690-1697.
- No meta-analysis
66. Marques, A., Santos, D. A., Hillman, C. H., & Sardinha, L. B. (2018). How does academic achievement relate to cardiorespiratory fitness, self-reported physical activity and objectively reported physical activity: a systematic review in children and adolescents aged 6-18 years. *British Journal of Sports Medicine*, 52(16), 1039.
- No meta-analysis
67. Martins, R., Wamosy, R. M. G., Cardoso, J., Schivinski, C. I. S., & Beltrame, T. S. (2021). Evaluation of cardiopulmonary system outcomes in children with developmental coordination disorder: A systematic review. *Human movement science*, 80, 102888.
- No meta-analysis
68. McAlister, K. L., Zhang, D., Moore, K. N., Chapman, T. M., Zink, J., & Belcher, B. R. (2022). A Systematic Review of the Associations of Adiposity and Cardiorespiratory Fitness with Arterial Structure and Function in Nonclinical Children and Adolescents. *Pediatric exercise science*, 1-12.
- No meta-analysis
69. Medrano-Ureña, M. R., Ortega-Ruiz, R., & Benítez-Sillero, J. D. (2020). Physical fitness, exercise self-efficacy, and quality of life in adulthood: A systematic review. *International Journal of Environmental Research and Public Health*, 17(17), 1-19.
- No meta-analysis
70. Mehanna, E., Hamik, A., & Josephson, R. A. (2016). Cardiorespiratory Fitness and Atherosclerosis: Recent Data and Future Directions. *Current atherosclerosis reports*, 18(5).
- No meta-analysis
71. Mendelson, M., Marillier, M., Bailly, S., Flore, P., Borel, J. C., Vivodtzev, I., Doutreleau, S., Tamisier, R., Pépin, J. L., & Verges, S. (2018). Maximal exercise capacity in patients with obstructive sleep apnoea syndrome: A systematic review and meta-analysis. *European Respiratory Journal*, 51(6).

- Wrong meta-analysis type – cross-sectional data
72. Millard-Stafford, M., Becasen, J. S., Beets, M. W., Nihiser, A. J., Lee, S. M., & Fulton, J. E. (2013). Is Physical Fitness Associated with Health in Overweight and Obese Youth? A Systematic Review. *Kinesiology review (Champaign, Ill.)*, 2(4), 233-247.
- No meta-analysis
73. Mintjens, S., Menting, M. D., Daams, J. G., van Poppel, M. N. M., Roseboom, T. J., & Gemke, R. J. B. J. (2018). Cardiorespiratory Fitness in Childhood and Adolescence Affects Future Cardiovascular Risk Factors: A Systematic Review of Longitudinal Studies. *Sports medicine (Auckland, N.Z.)*, 48(11), 2577-2605.
- No meta-analysis
74. Montero, D. (2015). The association of cardiorespiratory fitness with endothelial or smooth muscle vasodilator function. *European Journal of Preventive Cardiology*, 22(9), 1200-1211.
- No meta-analysis
75. Moore, D., Jung, M., Hillman, C. H., Kang, M., & Loprinzi, P. D. (2022). Interrelationships between exercise, functional connectivity, and cognition among healthy adults: A systematic review. *Psychophysiology*, 59(6), e14014.
- No meta-analysis
76. Morishita, S., Tsubaki, A., & Shirai, N. (2017). Physical function was related to mortality in patients with chronic kidney disease and dialysis. *Hemodialysis International*, 21(4), 483-489.
- No meta-analysis
77. Morrison, J. D., & Mayer, L. (2017). Physical activity and cognitive function in adults with multiple sclerosis: an integrative review. *Disability & Rehabilitation*, 39(19), 1909-1920.
- No meta-analysis
78. Morton-Holtham, L., Swann, N., Brewer, J., & Moir, H. J. (2021). A systematic review of physical activity and physical fitness in sarcoidosis. *Translational Sports Medicine*, 4(6), 741-755.
- No meta-analysis
79. Mucke, M., Ludyga, S., Colledge, F., & Gerber, M. (2018). Influence of Regular Physical Activity and Fitness on Stress Reactivity as Measured with the Trier Social Stress Test Protocol: A Systematic Review. *Sports medicine (Auckland, N.Z.)*, 48(11), 2607-2622.
- No meta-analysis
80. Munsterman, T., Takken, T., & Wittink, H. (2012). Are persons with rheumatoid arthritis deconditioned? A review of physical activity and aerobic capacity. *BMC Musculoskeletal Disorders*, 13, 202.

- No meta-analysis
81. Navarrete-Villanueva, D., Gomez-Cabello, A., Marin-Puyalto, J., Moreno, L. A., Vicente-Rodriguez, G., & Casajus, J. A. (2021). Frailty and Physical Fitness in Elderly People: A Systematic Review and Meta-analysis. *Sports medicine (Auckland, N.Z.)*, *51*(1), 143-160.
 - Wrong meta-analysis type – cross-sectional data
 82. Neil-Sztramko, S. E., Kirkham, A. A., Hung, S. H., Niksirat, N., Nishikawa, K., & Campbell, K. L. (2014). Aerobic capacity and upper limb strength are reduced in women diagnosed with breast cancer: a systematic review. *Journal of Physiotherapy*, *60*(4), 189-200.
 - No meta-analysis
 83. O'Brien, M. W., Petterson, J. L., Wu, Y., Bray, N. W., & Kimmerly, D. S. (2022). What is the impact of aerobic fitness and movement interventions on low-flow-mediated vasoconstriction? A systematic review of observational and intervention studies. *Vascular Medicine (United Kingdom)*, *27*(2), 193-202.
 - No meta-analysis
 84. Oh, S., You, J., & Kim, Y. W. (2022). Physical Fitness for Depression in Adolescents and Adults: A Meta-Analysis. *Iranian journal of public health*, *51*(11), 2425-2434.
 - Wrong meta-analysis type – cross-sectional data
 85. Oliveira, A., Jacome, C., & Marques, A. (2014). Physical fitness and exercise training on individuals with spina bifida: a systematic review. *Research in Developmental Disabilities*, *35*(5), 1119-1136.
 - No meta-analysis
 86. Ortega, F. B., Cadenas-Sanchez, C., Migueles, J. H., Labayen, I., Ruiz, J. R., Sui, X., Blair, S. N., Martínez-Vizcaino, V., Lavie, C. J., & Martínez-Vizcaino, V. (2018). Role of Physical Activity and Fitness in the Characterization and Prognosis of the Metabolically Healthy Obesity Phenotype: A Systematic Review and Meta-analysis. *Progress in cardiovascular diseases*, *61*(2), 190-205.
 - Wrong meta-analysis type – cross-sectional data
 87. Pappasavvas, T., Alhashemi, M., & Micklewright, D. (2017). Association Between Depressive Symptoms and Exercise Capacity in Patients With Heart Disease: A META-ANALYSIS. *Journal of Cardiopulmonary Rehabilitation and Prevention*, *37*(4), 239-249.
 - Wrong meta-analysis type – cross-sectional data
 88. Pappasavvas, T., Bonow, R., Alhashemi, M., & Micklewright, D. (2016). Depression Symptom Severity and Cardiorespiratory Fitness in Healthy and Depressed Adults: A Systematic Review and Meta-Analysis. *Sports Medicine*, *46*(2), 219-230.
 - Wrong meta-analysis type – cross-sectional data

89. Parry, S. M., Nalamalapu, S. R., Nunna, K., Rabiee, A., Friedman, L. A., Colantuoni, E., Needham, D. M., & Dinglas, V. D. (2021). Six-Minute Walk Distance After Critical Illness: A Systematic Review and Meta-Analysis. *Journal of intensive care medicine*, 36(3), 343-351.
- meta-regression or meta-analysis of screening study
90. Pavasini, R., Guralnik, J., Brown, J. C., di Bari, M., Cesari, M., Landi, F., Vaes, B., Legrand, D., Verghese, J., Wang, C., Stenholm, S., Ferrucci, L., Lai, J. C., Bartes, A. A., Espauella, J., Ferrer, M., Lim, J.-Y., Ensrud, K. E., Cawthon, P., Turusheva, A., Frolova, E., Rolland, Y., Lauwers, V., Corsonello, A., Kirk, G. D., Ferrari, R., Volpato, S., & Campo, G. (2016). Short Physical Performance Battery and all-cause mortality: systematic review and meta-analysis. *BMC Medicine*, 14(1), 215.
- No measure of CRF
91. Peel, A. B., Thomas, S. M., Dittus, K., Jones, L. W., & Lakoski, S. G. (2014). Cardiorespiratory fitness in breast cancer patients: A call for normative values. *Journal of the American Heart Association*, 3(1), e000432.
- Not a systematic review
92. Pella, E., Theodorakopoulou, M. P., Boutou, A. K., Alexandrou, M. E., Bakaloudi, D. R., Sarridou, D., Boulmpou, A., Papadopoulos, C., Papagianni, A., & Sarafidis, P. (2022). Cardiopulmonary reserve examined with cardiopulmonary exercise testing in individuals with chronic kidney disease: A systematic review and meta-analysis. *Annals of Physical and Rehabilitation Medicine*, 65(5).
- Wrong meta-analysis type – cross-sectional data
93. Peytremann-Bridevaux, I., Staeger, P., Bridevaux, P. O., Ghali, W. A., & Burnand, B. (2008). Effectiveness of Chronic Obstructive Pulmonary Disease-Management Programs: Systematic Review and Meta-Analysis. *American Journal of Medicine*, 121(5), 433-443.e434.
- Surgical, disease at birth, or pregnant population
94. Poggio, R., Arazi, H. C., Giorgi, M., & Miriuka, S. G. (2010). Prediction of severe cardiovascular events by VE/VCO₂ slope versus peak VO₂ in systolic heart failure: a meta-analysis of the published literature. *American Heart Journal*, 160(6), 1004-1014.
- meta-regression or meta-analysis of screening study
95. Pressler, A. (2017). A run a day keeps lipids at bay? Regular exercise as a treatment of dyslipidaemias. *Deutsche Zeitschrift für Sportmedizin*, 68(11), 253-260.
- No meta-analysis
96. Punekar, Y. S., Riley, J. H., Lloyd, E., Driessen, M., & Singh, S. J. (2017). Systematic review of the association between exercise tests and patient-reported outcomes in patients

with chronic obstructive pulmonary disease. *International journal of chronic obstructive pulmonary disease*, 12, 2487-2506.

- No meta-analysis

97. Ramirez-Velez, R., Saavedra, J. M., Lobelo, F., Celis-Morales, C. A., Pozo-Cruz, B. D., & Garcia-Hermoso, A. (2018). Ideal Cardiovascular Health and Incident Cardiovascular Disease Among Adults: A Systematic Review and Meta-analysis. *Mayo Clinic Proceedings*, 93(11), 1589-1599.

- No measure of CRF

98. Rauner, A., Mess, F., & Woll, A. (2013). The relationship between physical activity, physical fitness and overweight in adolescents: A systematic review of studies published in or after 2000. *BMC Pediatrics*, 13(1).

- No meta-analysis

99. Rigdon, B., & Loprinzi, P. D. (2019). The Association of Cardiorespiratory Fitness on Memory Function: Systematic Review. *Medicina (Kaunas, Lithuania)*, 55(5).

- No meta-analysis

100. Rivilis, I., Hay, J., Cairney, J., Klentrou, P., Liu, J., & Fought, B. E. (2011). Physical activity and fitness in children with developmental coordination disorder: A systematic review. *Research in Developmental Disabilities*, 32(3), 894-910.

- No meta-analysis

101. Rodrigues, T., Raposo, S. C., Brito, D., & Lopes, L. R. (2021). Prognostic relevance of exercise testing in hypertrophic cardiomyopathy. A systematic review. *International Journal of Cardiology*, 339, 83-92.

- No meta-analysis

102. Rodriguez, C. C., de Camargo, E. M., Rodriguez-Añez, C. R., & Reis, R. S. (2020). Physical activity, physical fitness and academic achievement in adolescents: A systematic review. *Revista Brasileira de Medicina do Esporte*, 26(5), 441-448.

- No meta-analysis

103. Ruiz, J. R., Castro-Pinero, J., Artero, E. G., Ortega, F. B., Sjostrom, M., Suni, J., & Castillo, M. J. (2009). Predictive validity of health-related fitness in youth: a systematic review. *British Journal of Sports Medicine*, 43(12), 909-923.

- No meta-analysis

104. Ruiz, J. R., Caverio-Redondo, I., Ortega, F. B., Welk, G. J., Andersen, L. B., & Martinez-Vizcaino, V. (2016). Cardiorespiratory fitness cut points to avoid cardiovascular disease risk in children and adolescents; what level of fitness should raise a red flag? A systematic review and meta-analysis. *British Journal of Sports Medicine*, 50(23), 1451-1458.

- meta-regression or meta-analysis of screening study

105. Ruiz-Ariza, A., Grao-Cruces, A., de Loureiro, N. E. M., & Martínez-López, E. J. (2017). Influence of physical fitness on cognitive and academic performance in adolescents: A systematic review from 2005–2015. *International Review of Sport & Exercise Psychology*, *10*(1), 108-133.
- No meta-analysis
106. Santana, C. C. A., Azevedo, L. B., Cattuzzo, M. T., Hill, J. O., Andrade, L. P., & Prado, W. L. (2017). Physical fitness and academic performance in youth: A systematic review. *Scandinavian journal of medicine & science in sports*, *27*(6), 579-603.
- No meta-analysis
107. Savarese, G., Paolillo, S., Costanzo, P., D'Amore, C., Cecere, M., Losco, T., Musella, F., Gargiulo, P., Marciano, C., & Perrone-Filardi, P. (2012). Do changes of 6-minute walk distance predict clinical events in patients with pulmonary arterial hypertension?: A meta-analysis of 22 randomized trials. *Journal of the American College of Cardiology*, *60*(13), 1192-1201.
- meta-regression or meta-analysis of screening study
108. Sawada, S., Miyachi, M., Murakami, H., Kawakami, R., Tanaka, S., Ishikawa-Takata, K., Tabata, I., Oida, Y., Oguma, Y., Miyatake, N., Okamoto, T., Tsukamoto, K., Tanaka, H., Lee, I., & Blair, S. (2012). Dose-response relationship between cardiorespiratory fitness and morbidity/mortality: a systematic review and meta-analysis. *Journal of Science & Medicine in Sport*, *15*, S25-S25.
- Conference abstract
109. Schaan, C. W., de Macedo, A. C. P., Sbruzzi, G., Umpierre, D., Schaan, B. D., & Pellanda, L. C. (2017). Functional capacity in congenital heart disease: A systematic review and Meta-Analysis. *Arquivos brasileiros de cardiologia*, *109*(4), 357-367.
- Child and youth population
110. Schmid, D., & Leitzmann, M. F. (2015). Cardiorespiratory fitness as predictor of cancer mortality: a systematic review and meta-analysis. *Annals of oncology : official journal of the European Society for Medical Oncology*, *26*(2), 272-278.
- Not a systematic review
111. Sivakumar, J., Sivakumar, H., Read, M., Sinclair, R. C. F., Snowden, C. P., & Hii, M. W. (2020). The Role of Cardiopulmonary Exercise Testing as a Risk Assessment Tool in Patients Undergoing Oesophagectomy: A Systematic Review and Meta-analysis. *Annals of surgical oncology*, *27*(10), 3783-3796.
- Surgical, disease at birth, or pregnant population
112. Sun, Y., Li, W., Yin, L., Wei, L., & Wang, Y. (2017). Diagnostic accuracy of treadmill exercise tests among Chinese women with coronary artery diseases: A systematic review and meta-analysis. *International Journal of Cardiology*, *227*, 894-900.
- meta-regression or meta-analysis of screening study

113. Tacchi, M. J., Heggelund, J., & Scott, J. (2019). Predictive validity of objective measures of physical fitness for the new onset of mental disorders in adolescents and young adults. *Early intervention in psychiatry*, 13(6), 1310-1318.
- Wrong meta-analysis type – cross-sectional data
114. Thru, C., Hvid, L. G., Gamborg, M., Dawes, H., Dalgas, U., & Langeskov-Christensen, M. (2022). Aerobic capacity in persons with Parkinson's disease: a systematic review. *Disability and Rehabilitation*, 1-13.
- No meta-analysis
115. Udholm, S., Aldweib, N., Hjortdal, V. E., & Veldtman, G. R. (2018). Prognostic power of cardiopulmonary exercise testing in Fontan patients: a systematic review. *Open heart*, 5(1), e000812.
- No meta-analysis
116. Van Waelvelde, H., Vanden Wyngaert, K., Mariën, T., Baeyens, D., & Calders, P. (2020). The relation between children's aerobic fitness and executive functions: A systematic review. *Infant and Child Development*, 29(3).
- No meta-analysis
117. Vancampfort, D., Mugisha, J., Rosenbaum, S., Firth, J., De Hert, M., Probst, M., & Stubbs, B. (2016). Cardiorespiratory fitness levels and moderators in people with HIV: A systematic review and meta-analysis. *Preventive medicine*, 93, 106-114.
- Wrong meta-analysis type – cross-sectional data
118. Vancampfort, D., Rosenbaum, S., Probst, M., Soundy, A., Mitchell, A. J., De Hert, M., & Stubbs, B. (2015). Promotion of cardiorespiratory fitness in schizophrenia: a clinical overview and meta-analysis. *Acta psychiatrica Scandinavica*, 132(2), 131-143.
- Wrong meta-analysis type – cross-sectional data
119. Vancampfort, D., Rosenbaum, S., Schuch, F., Ward, P., Richards, J., Mugisha, J., Probst, M., & Stubbs, B. (2017). Cardiorespiratory Fitness in Severe Mental Illness: A Systematic Review and Meta-analysis. *Sports Medicine*, 47(2), 343-352.
- Wrong meta-analysis type – cross-sectional data
120. Vancampfort, D., Stubbs, B., Richards, J., Ward, P. B., Firth, J., Schuch, F. B., & Rosenbaum, S. (2017). Physical fitness in people with posttraumatic stress disorder: a systematic review. *Disability and Rehabilitation*, 39(24), 2461-2467.
- No meta-analysis
121. Vancampfort, D., Ward, P. B., & Stubbs, B. (2019). Physical fitness levels and moderators in people with epilepsy: A systematic review and meta-analysis. *Epilepsy & behavior : E&B*, 99, 106448.
- Wrong meta-analysis type – cross-sectional data

122. Vandecasteele, E., De Pauw, M., De Keyser, F., Decuman, S., Deschepper, E., Piette, Y., Brusselle, G., & Smith, V. (2016). Six-minute walk test in systemic sclerosis: A systematic review and meta-analysis. *International Journal of Cardiology*, 212, 265-273.
- Wrong meta-analysis type – cross-sectional data
123. Vendrusculo, F. M., Heinzmann-Filho, J. P., Severo da Silva, J., Ruiz, M. P., & Fagundes Donadio, M. V. (2019). Peak Oxygen Uptake and Mortality in Cystic Fibrosis: Systematic Review and Meta-Analysis. *Respiratory care*, 64(1), 91-98.
- Child and youth population
124. Verweij, N. M., Schiphorst, A. H. W., Pronk, A., van den Bos, F., & Hamaker, M. E. (2016). Physical performance measures for predicting outcome in cancer patients: a systematic review. *Acta Oncologica*, 55(12), 1386-1391.
- No meta-analysis
125. Villaseca-Rojas, Y., Varela-Melo, J., Torres-Castro, R., Vasconcello-Castillo, L., Mazzucco, G., Vilaro, J., & Blanco, I. (2022). Exercise Capacity in Children and Adolescents With Congenital Heart Disease: A Systematic Review and Meta-Analysis. *Frontiers in cardiovascular medicine*, 9, 874700.
- Child and youth population
126. Wadey, C. A., Weston, M. E., Dorobantu, D. M., Pieleas, G. E., Stuart, G., Barker, A. R., Taylor, R. S., & Williams, C. A. (2022). The role of cardiopulmonary exercise testing in predicting mortality and morbidity in people with congenital heart disease: a systematic review and meta-analysis. *European Journal of Preventive Cardiology*, 29(3), 513-533.
- Surgical, disease at birth, or pregnant population
127. Wong, T. E., Majumdar, S., Adams, E., Bergman, S., Damiano, M. L., Deutsche, J., Recht, M., Healthy Weight Working, G., & McAlister S, B. V. C. L. D. K. D. M. K. S. L. S. M. J. W. J. R. K. W. T. (2011). Overweight and obesity in hemophilia: a systematic review of the literature. *American Journal of Preventive Medicine*, 41(6 Suppl 4), S369-375.
- No meta-analysis
128. Yerrakalva, D., Mullis, R., & Mant, J. (2015). The associations of "fatness," "fitness," and physical activity with all-cause mortality in older adults: A systematic review. *Obesity (Silver Spring, Md.)*, 23(10), 1944-1956.
- No meta-analysis
129. Yildiz Kabak, V., Calders, P., Duger, T., Mohammed, J., & van Breda, E. (2019). Short and long-term impairments of cardiopulmonary fitness level in previous childhood cancer cases: a systematic review. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*, 27(1), 69-86.
- No meta-analysis

130. Zambolin, F., Duro-Ocana, P., Faisal, A., Bagley, L., Gregory, W. J., Jones, A. W., & McPhee, J. S. (2022). Fibromyalgia and Chronic Fatigue Syndromes: A systematic review and meta-analysis of cardiorespiratory fitness and neuromuscular function compared with healthy individuals. *PLoS ONE*, *17*(10), e0276009.
- Wrong meta-analysis type – cross-sectional data
131. Zielinska, D., Bellwon, J., Rynkiewicz, A., & Elkady, M. A. (2013). Prognostic value of the six-minute walk test in heart failure patients undergoing cardiac surgery: a literature review. *Rehabilitation research and practice*, *2013*, 965494.
- No meta-analysis

Excluded after the updated search (1 Nov 2022 to 9 March 2024):

132. Arbee-Kalidas, N., Moutlana, H. J., Moodley, Y., Kebalepile, M. M., & Motshabi Chakane, P. (2023). The association between cardiopulmonary exercise testing and postoperative outcomes in patients with lung cancer undergoing lung resection surgery: A systematic review and meta-analysis. *PloS one*, *18*(12), e0295430.
- Surgical, disease at birth, or pregnant population
133. Eckstein, M. L., Aberer, F., Dobler, F. J. R., Aziz, F., Heise, T., Sourij, H., & Moser, O. (2022). Association of HbA1c with VO2max in Individuals with Type 1 Diabetes: A Systematic Review and Meta-Analysis. *Metabolites*, *12*(11), 1017.
- Wrong meta-analysis type – cross-sectional data
134. Huerta-Uribe, N., Ramírez-Vélez, R., Izquierdo, M., & García-Hermoso, A. (2023). Association Between Physical Activity, Sedentary Behavior and Physical Fitness and Glycated Hemoglobin in Youth with Type 1 Diabetes: A Systematic Review and Meta-analysis. *Sports medicine (Auckland, N.Z.)*, *53*(1), 111–123.
- Included in previous search
135. Madigan, S., Proudman, S., Schembri, D., Davies, H., & Adams, R. (2024). Use of exercise tests in screening for pulmonary arterial hypertension in systemic sclerosis: A systematic literature review. *Journal of scleroderma and related disorders*, *9*(1), 50–58.
- No meta-analysis
136. Badrooj, N., Jayedi, A., & Shab-Bidar, S. (2023). Ideal cardiovascular health metrics and risk of type 2 diabetes: A systematic review and dose-response meta-analysis of prospective cohort studies. *Nutrition, metabolism, and cardiovascular diseases : NMCD*, *33*(11), 2067–2075.
- No measure of CRF
137. Te Hoonte, F., Spronk, M., Sun, Q., Wu, K., Fan, S., Wang, Z., Bots, M. L., Van der Schouw, Y. T., Uijl, A., & Vernooij, R. W. M. (2023). Ideal cardiovascular health

- and cardiovascular related events: a systematic review and meta-analysis. *European journal of preventive cardiology*, zwad405. Advance online publication.
- No measure of CRF
138. Macedo, A. C. P., Schaan, C. W., Bock, P. M., Pinto, M. B., Botton, C. E., Umpierre, D., & Schaan, B. D. (2023). Cardiorespiratory fitness in individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. *Archives of endocrinology and metabolism*, 67(5), e230040.
- Wrong meta-analysis type – cross-sectional data
139. Cirone, D., Berbrier, D. E., Gibbs, J. C., & Usselman, C. W. (2024). Health-related physical fitness in women with polycystic ovary syndrome versus controls: a systematic review and meta-analysis. *Archives of gynecology and obstetrics*, 309(1), 17–36.
- Wrong meta-analysis type – cross-sectional data
140. Zambolin, F., Duro-Ocana, P., Faisal, A., Bagley, L., Gregory, W. J., Jones, A. W., & McPhee, J. S. (2022). Fibromyalgia and Chronic Fatigue Syndromes: A systematic review and meta-analysis of cardiorespiratory fitness and neuromuscular function compared with healthy individuals. *PloS one*, 17(10), e0276009.
- Wrong meta-analysis type – cross-sectional data
141. Villaseca-Rojas, Y., Varela-Melo, J., Torres-Castro, R., Vasconcello-Castillo, L., Mazzucco, G., Vilaró, J., & Blanco, I. (2022). Exercise Capacity in Children and Adolescents With Congenital Heart Disease: A Systematic Review and Meta-Analysis. *Frontiers in cardiovascular medicine*, 9, 874700.
- Included in previous search
142. Yang, L., He, Y., & Li, X. (2023). Physical function and all-cause mortality in patients with chronic kidney disease and end-stage renal disease: a systematic review and meta-analysis. *International urology and nephrology*, 55(5), 1219–1228.
- Included in previous search
143. Demers, K., Bak, M. T. J., Bongers, B. C., de Vries, A. C., Jonkers, D. M. A. E., Pierik, M. J., & Stassen, L. P. S. (2023). Scoping review on health-related physical fitness in patients with inflammatory bowel disease: Assessment, interventions, and future directions. *World journal of gastroenterology*, 29(38), 5406–5427.
- No meta-analysis
144. Campos, N. E., Vendrusculo, F. M., DA Costa, G. A., DE Almeida, I. S., Becker, N. A., & Donadio, M. V. F. (2022). The Association of Field Test Outcomes with Peak Oxygen Uptake in Patients with Cystic Fibrosis: A Systematic Review. *International journal of exercise science*, 15(3), 1381–1394.
- No meta-analysis
145. Oh, S., You, J., & Kim, Y. W. (2022). Physical Fitness for Depression in

- Adolescents and Adults: A Meta-Analysis. *Iranian journal of public health*, 51(11), 2425–2434.
- Wrong meta-analysis type – cross-sectional data
146. Soydara, C., Jurgens, C. Y., & Lewis, G. D. (2023). Postexercise Oxygen Uptake Recovery Delay Among Patients with Heart Failure: A systematic review. *Heart and Mind*, 7(1), 40–44.
- No meta-analysis
147. Lee J. (2021). Cardiorespiratory Fitness, Physical Activity, Walking Speed, Lack of Participation in Leisure Activities, and Lung Cancer Mortality: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. *Cancer nursing*, 44(6), 453–464.
- Included in previous search
148. Liu, C., He, Y., Venn, A. J., Jose, M. D., & Tian, J. (2023). Childhood modifiable risk factors and later life chronic kidney disease: a systematic review. *BMC nephrology*, 24(1), 184.
- No meta-analysis
149. Núñez-Cortés, R., Padilla-Acevedo, P., Vergara-Peña, F., Mollà-Casanova, S., Espinoza-Bravo, C., Torres-Castro, R., & Cruz-Montecinos, C. (2022). Clinical assessment of balance and functional impairments in people with stable chronic obstructive pulmonary disease: a systematic review and meta-analysis. *ERJ open research*, 8(4), 00164-2022.
- Wrong meta-analysis type – cross-sectional data
150. Thru, C., Hvid, L. G., Gamborg, M., Dawes, H., Dalgas, U., & Langeskov-Christensen, M. (2023). Aerobic capacity in persons with Parkinson's disease: a systematic review. *Disability and rehabilitation*, 45(15), 2409–2421.
- No meta-analysis
151. Carballada, C., Mihalik, M., Newman-Caro, A., & Walter, A. (2023). Effectiveness of the 6-Minute Walk Test as a Predictive Measure on Hospital Readmission and Mortality in Individuals With Heart Failure: A Systematic Review of the Literature. *Journal of Acute Care Physical Therapy*, 14(1), 33–44.
- No meta-analysis
152. Cruz-Montecinos, C., Núñez-Cortés, R., Vasconcello-Castillo, L., Solís-Navarro, L., Carrasco-Alonso, B., Calatayud, J., Pérez-Alenda, S., & Torres-Castro, R. (2022). Exercise capacity in people with haemophilia: A systematic review. *Haemophilia: the official journal of the World Federation of Hemophilia*, 28(6), 891–901.
- No meta-analysis
153. McAlister, K. L., Zhang, D., Moore, K. N., Chapman, T. M., Zink, J., & Belcher, B. R. (2022). A Systematic Review of the Associations of Adiposity and Cardiorespiratory Fitness With Arterial Structure and Function in Nonclinical Children

- and Adolescents. *Pediatric exercise science*, 35(3), 174–185.
- No meta-analysis
154. Cheng, C., Zhang, D., Chen, S., & Duan, G. (2022). The association of cardiorespiratory fitness and the risk of hypertension: a systematic review and dose-response meta-analysis. *Journal of human hypertension*, 36(8), 744–752.
- Included in previous search
155. Capic, I., Stankovic, M., Spirtovic, O., Corovic, M., Mujanovic, D., Mojsilovic, Z., Jelaska, I., & Zilic-Fiser, S. (2023). Cardiovascular Fitness in Normal Weight and Obese Children and Adolescents – A Systematic Review of Studies Published After 2000s. *International Journal of Morphology*, 41(6), 1852–1862.
- No meta-analysis
156. Dewar, A., Kass, L., Stephens, R. C. M., Tetlow, N., & Desai, T. (2023). Heart Rate Recovery Assessed by Cardiopulmonary Exercise Testing in Patients with Cardiovascular Disease: Relationship with Prognosis. *International journal of environmental research and public health*, 20(6), 4678.
- No meta-analysis
157. Al-Huda, F., Shapiro, G. D., Davenport, M. H., Bertagnolli, M., & Dayan, N. (2022). Association between Cardiorespiratory Fitness and Hypertensive Disorders of Pregnancy: A Systematic Review and Meta-Analysis. *Journal of clinical medicine*, 11(15), 4364.
- Surgical, disease at birth, or pregnant population
158. Barry Walsh, C., Cahalan, R., Hinman, R. S., & O' Sullivan, K. (2022). Psychometric properties of performance-based measures of physical function administered via telehealth among people with chronic conditions: A systematic review. *PloS one*, 17(9), e0274349.
- No meta-analysis
159. Rocha, V., Paixão, C., & Marques, A. (2022). Physical activity, exercise capacity and mortality risk in people with interstitial lung disease: A systematic review and meta-analysis. *Journal of science and medicine in sport*, 25(11), 903–910.
- Included in previous search
160. Carrasco-Vega, E., Ruiz-Muñoz, M., Cuesta-Vargas, A., Romero-Galisteo, R. P., & González-Sánchez, M. (2022). Individuals with fibromyalgia have a different gait pattern and a reduced walk functional capacity: a systematic review with meta-analysis. *PeerJ*, 10, e12908.
- Wrong meta-analysis type – cross-sectional data
161. Steiman De Visser, H., Fast, I., Brunton, N., Arevalo, E., Askin, N., Rabbani, R., Abou-Setta, A. M., & McGavock, J. (2024). Cardiorespiratory Fitness and Physical Activity in Pediatric Diabetes: A Systemic Review and Meta-Analysis. *JAMA network*

open, 7(2), e240235.

- Child and youth population

162. Dun, Y., Wu, S., Cui, N., Thomas, R. J., Olson, T. P., Zhou, N., Li, Q., & Liu, S. (2021). Screening for Asymptomatic Coronary Artery Disease via Exercise Stress Testing in Patients With Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Frontiers in cardiovascular medicine*, 8, 770648.

- Meta-regression or meta-analysis of screening studies

163. Huerta-Uribe, N., Hormazábal-Aguayo, I. A., Izquierdo, M., & García-Hermoso, A. (2023). Youth with type 1 diabetes mellitus are more inactive and sedentary than apparently healthy peers: A systematic review and meta-analysis. *Diabetes research and clinical practice*, 200, 110697.

- Child and youth population

164. Pella, E., Sgouropoulou, V., Theodorakopoulou, M., Iatridi, F., Boutou, A., Karpetas, A., Papagianni, A., Sarafidis, P., & Dimitroulas, T. (2023). Cardiorespiratory fitness assessed with cardiopulmonary exercise testing in patients with juvenile idiopathic arthritis: a systematic review and meta-analysis. *Rheumatology (Oxford, England)*, 62(11), 3526–3533.

- Child and youth population

165. Schmidt-Andersen, P., Stage, A., Pouplier, A., Bastholm, L. H., Müller, K. G., Larsen, A., Ness, K. K., Larsen, H. B., Christensen, J., & Fridh, M. K. (2024). Physical capacity in children and adolescents with newly diagnosed cancer: A systematic review and meta-analysis. *Pediatric blood & cancer*, 71(1), e30746.

- Child and youth population

Eligible systematic reviews excluded with reason:

1. Aune, D., Norat, T., Leitzmann, M., Tonstad, S., & Vatten, L. J. (2015). Physical activity and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis. *European journal of epidemiology*, 30(7), 529–542.
 - A lower quality study
2. Fan, Y., Gu, X., & Zhang, H. (2019). Prognostic value of six-minute walk distance in patients with heart failure: A meta-analysis. *European journal of preventive cardiology*, 26(6), 664–667.
 - Older study
3. Jiménez-Pavón, D., Lavie, C. J., & Blair, S. N. (2019). The role of cardiorespiratory fitness on the risk of sudden cardiac death at the population level: A systematic review and meta-analysis of the available evidence. *Progress in cardiovascular diseases*, 62(3), 279–287.
 - Older study

4. Qiu, S., Cai, X., Liu, J., Yang, B., Sun, Z., Zügel, M., Steinacker, J. M., & Schumann, U. (2019). Association Between Cardiorespiratory Fitness and Risk of Heart Failure: A Meta-Analysis. *Journal of cardiac failure*, *25*(7), 537–544.
 - Older study
5. Qiu, S., Cai, X., Yang, B., Du, Z., Cai, M., Sun, Z., Zügel, M., Michael Steinacker, J., & Schumann, U. (2019). Association Between Cardiorespiratory Fitness and Risk of Type 2 Diabetes: A Meta-Analysis. *Obesity (Silver Spring, Md.)*, *27*(2), 315–324.
 - Lower quality study
6. Schuch, F. B., Vancampfort, D., Sui, X., Rosenbaum, S., Firth, J., Richards, J., Ward, P. B., & Stubbs, B. (2016). Are lower levels of cardiorespiratory fitness associated with incident depression? A systematic review of prospective cohort studies. *Preventive medicine*, *93*, 159–165.
 - Older study
7. Yamamoto S, Yamaga T, Nishie K, Sakai Y, Ishida T, Oka K, Ikegami S, Horiuchi H. Impact of physical performance on prognosis among patients with heart failure: Systematic review and meta-analysis. *J Cardiol*. 2020 Aug;*76*(2):139-146.
 - Lower quality study
8. Zaccardi, F., O'Donovan, G., Webb, D. R., Yates, T., Kurl, S., Khunti, K., Davies, M. J., & Laukkanen, J. A. (2015). Cardiorespiratory fitness and risk of type 2 diabetes mellitus: A 23-year cohort study and a meta-analysis of prospective studies. *Atherosclerosis*, *243*(1), 131–137.
 - Lower quality study

eTable 1. Summary of Decision Rules: GRADE Assessments for Certainty of Evidence

Domain	Judgment	Scoring	Criteria
Risk of Bias* (1)	No serious ROB	0	<ul style="list-style-type: none"> Most (>80%) primary studies assessed as having a low risk of bias (e.g., score of 7-9 on NOS).
	Serious ROB	-1 point	<ul style="list-style-type: none"> All primary studies were assessed to be at low to moderate risk of bias (e.g., score of 5 to 9 on the NOS) with a potential for bias arising from a lack of clarity on eligibility criteria, measurement of exposure or outcome, confounding, and/or loss to follow-up.
	Very serious ROB	-2 points	<ul style="list-style-type: none"> At least one of the primary studies was assessed to be of high risk of bias (e.g., score of 4 or less on the NOS), but the relative contribution of each study to the overall results will be considered for assessing the overall level of bias. Risk of biases include not having appropriate eligibility criteria and the populations are not generalizable, there is a serious flaw in the measurement of the exposure (non-exercise prediction equations vs. exercise-based measures) and/or outcome (i.e., self-report vs. medical records), there is a failure to adequately control for confounding (i.e., age, sex), and/or a loss to follow-up >10%. Biases related to generalizability, measurement of exposure and adequate control for confounding are considered the most important for the study.
Inconsistency (2)	No serious inconsistency	0	<ul style="list-style-type: none"> Point estimates are similar across studies with overlap of confidence intervals. Statistical tests for heterogeneity are not significant and the I^2 is low to moderate (i.e., <50%).
	Serious inconsistency	-1 point	<ul style="list-style-type: none"> Heterogeneity is high but can be explained by important sub-group differences (e.g., test types).
	Very serious inconsistency	-2 points	<ul style="list-style-type: none"> Point estimates vary widely across studies. Confidence intervals show minimal or no overlap. The statistical test for heterogeneity is significant at $p < 0.05$ and cannot be explained by sub-group analyses. The I^2 is large (i.e., $\geq 50\%$).
Indirectness (3)	No serious indirectness	0	<ul style="list-style-type: none"> There was good global representation within the primary studies (e.g., variety of populations, sex distribution). The tests used to assess CRF all used objective measurement (e.g., used maximal or submaximal exercise testing including treadmill, cycle ergometry, field tests). There was little-to-no inclusion of participants <18 years and relatively equal distribution of males and females captured in the studies.
	Serious indirectness	-1 point	The studies were limited by having one of the following:

			<ul style="list-style-type: none"> Limited global representation of primary studies with consideration for their relative contribution to the estimate. Inclusion of self-reported and objective measures used to assess CRF across the studies. Considerable inclusion of participants <18 years or only one sex captured in the studies.
	Very serious indirectness	-2 points	<p>The studies were limited by having two or more of the following:</p> <ul style="list-style-type: none"> Limited global representation of primary studies. Considerable inclusion of participants <18 years or only one sex captured in the studies. Considerable inclusion of self-reported tests used to assess CRF across the studies.
Imprecision (4)	No serious imprecision	0	<ul style="list-style-type: none"> Total number of participants was ≥ 4000. The 95% CIs for the pooled estimates include 1.0, but the sample size is ≥ 4000 and the CIs exclude important benefit or harm (i.e., 10%).
	Serious imprecision	-1 point	<ul style="list-style-type: none"> Total number of participants was <4000. The 95% CIs for the pooled estimate do not include 1.0 but are very wide despite a large sample size. The 95% CIs for the pooled estimates include 1.0 and the sample size is ≥ 4000, but the CIs include important benefit or harm (i.e., 10%). For example, sample >10,000, RR = 1.24, 95% CI: 0.99, 1.56 (small reduction in mortality & substantial increase of 56% remain plausible).
	Very serious imprecision	-2 points	<ul style="list-style-type: none"> There are very few events and the CIs around the estimates of effect include both appreciable benefit and appreciable harm (e.g., RR = 0.96, 95% CI: 0.56, 1.69)
Publication Bias (5)	No serious publication bias	0	<ul style="list-style-type: none"> There is no suspected evidence of publication bias as reported in the systematic review based on Egger's test and/or visual inspection of funnel plots. There were an insufficient number of included studies to assess publication bias (<10 studies). The search strategy appears comprehensive.
	Serious publication bias	-1 point	<p>The studies were limited by having at least one of the following:</p> <ul style="list-style-type: none"> There is evidence of publication bias arising from asymmetrical rather than symmetrical funnel plots, if statistical tests of asymmetry are positive, or if the meta-analysis is based on small observational studies (N<4000). Publication bias was not assessed and there were ≥ 10 studies. The search strategy is not comprehensive.
	Very serious publication bias	-2 points	<p>The studies were limited by having two or more of the following:</p> <ul style="list-style-type: none"> There is evidence of publication bias arising from asymmetrical rather than symmetrical funnel plots, if statistical tests of asymmetry are positive, or if the meta-analysis is based on small observational studies (N<4000). Publication bias was not assessed and there were ≥ 10 studies.

- | | | | |
|--|--|--|---|
| | | | <ul style="list-style-type: none"> • The search strategy is not comprehensive. |
|--|--|--|---|

CI – confidence interval, CRF – cardiorespiratory fitness, NOS – Newcastle-Ottawa Scale, RoB – risk of bias

*Risk of bias will be based on the quality assessment of the primary studies included in the systematic reviews. If a RoB assessment is not provided within the systematic review, a de novo RoB assessment will be conducted using the Newcastle-Ottawa Scale.

- The quality of the evidence was upgraded, if there was no cause to downgrade, and there was evidence of a large magnitude of effect from meta-analyses with sufficiently narrow confidence intervals that do not overlap the chosen thresholds* (+1 large effect, +2 very large), evidence of a dose-response gradient (+1), or when all residual confounding would decrease the magnitude of the effect (+1). *Large effect is defined as HR >2 or <0.5, very large effect is defined as HR >5 or <0.2.
- The quality of the evidence **per each outcome** can be interpreted as follows (6):
 - High:** we are confident that the true magnitude of effect between CRF and the health outcome lies close to the effect estimated in the meta-analysis and further research is unlikely to change our confidence in the magnitude of effect.
 - Moderate:** we are moderately confident that the true magnitude of effect between CRF and the health outcome is likely to be close to the effect estimated in the meta-analysis, but there is a possibility that it is substantially different; further research is likely to have an important impact on the confidence in the direction of association and may change the direction of association.
 - Low:** we have limited confidence; the true magnitude of effect between CRF and the health outcome may be substantially different from the estimate.
 - Very low:** we have very little confidence; the true magnitude of effect between CRF and the health outcome may be substantially different from the estimate.

References:

1. Guyatt GH, Oxman AD, Vist G, Kunz R, Brozek J, Alonso-Coello P, et al. GRADE guidelines: 4. Rating the quality of evidence—study limitations (risk of bias). *Journal of Clinical Epidemiology*. 2011;64(4):407-15.
2. Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, et al. GRADE guidelines: 7. Rating the quality of evidence--inconsistency. *J Clin Epidemiol*. 2011;64(12):1294-302.
3. Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, et al. GRADE guidelines: 8. Rating the quality of evidence--indirectness. *J Clin Epidemiol*. 2011;64(12):1303-10.
4. Guyatt GH, Oxman AD, Kunz R, Brozek J, Alonso-Coello P, Rind D, et al. GRADE guidelines 6. Rating the quality of evidence--imprecision. *J Clin Epidemiol*. 2011;64(12):1283-93.
5. Guyatt GH, Oxman AD, Montori V, Vist G, Kunz R, Brozek J, et al. GRADE guidelines: 5. Rating the quality of evidence--publication bias. *J Clin Epidemiol*. 2011;64(12):1277-82.
6. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol*. 2011;64(4):383-94.

eTable 2: AMSTAR2 assessment

First author, year	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14	Item 15	Item 16	Rating
<i>General population without known disease at baseline and mortality outcomes</i>																	
Aune, 2020	Yes	No	Yes	Partial yes	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes	Yes	Yes	Critically low
Barry, 2014	Yes	No	Yes	Partial yes	No	No	Partial yes	Partial yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Low
Barry, 2018	No	No	Yes	Partial yes	Yes	No	Partial yes	Partial yes	Yes	No	No	Yes	Yes	No	Yes	Yes	Low
Han, 2022	Yes	No	No	Partial yes	Yes	Yes	Partial yes	Partial yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Kodama, 2009	Yes	No	Yes	Partial yes	Yes	Yes	Partial yes	Partial yes	No	No	Yes	No	No	Yes	Yes	Yes	Critically low
Laukkanen, 2022	Yes	Partial yes	Yes	Yes	Yes	Yes	Partial yes	Yes	Partial yes	No	Yes	Yes	Yes	Yes	Yes	Yes	High
Lee, 2020	No	No	Yes	Partial yes	No	No	Partial yes	Partial yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low
Qui, 2021	Yes	Partial yes	Yes	Yes	No	No	Partial yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
<i>General population without known disease at baseline and incident outcomes</i>																	
Aune, 2021	No	No	Yes	Partial yes	No	No	Partial yes	Partial yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Cheng, 2022	Yes	Yes	No	Partial yes	Yes	Yes	Partial yes	Partial yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Kandola, 2019	No	Yes	Yes	Partial yes	Yes	Yes	Partial yes	No	Yes	No	Yes	No	No	Yes	Yes	Yes	Critically low
Kunutsor, 2023	Yes	Yes	Yes	Partial yes	Yes	Yes	Partial yes	Yes	Partial yes	No	Yes	Yes	Yes	No	Yes	Yes	Moderate
Lee, 2021	Yes	No	Yes	Partial yes	Yes	No	Partial yes	Yes	No	No	Yes	No	No	Yes	Yes	Yes	Critically low
Pozuelo-Carrascosa, 2019	No	Yes	Yes	Partial yes	Yes	Yes	Partial yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Tarp, 2019	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	High
Wang, 2020	No	Partial yes	No	Partial yes	No	Yes	Partial yes	Partial yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Xue, 2020	No	No	No	Partial yes	Yes	Yes	Partial yes	Partial yes	Yes	No	Yes	No	No	No	Yes	Yes	Critically low
<i>Clinical population with diagnosed chronic disease at baseline and mortality outcomes</i>																	
Barbagelata, 2022	Yes	Partial yes	Yes	Partial yes	Yes	No	Partial yes	Partial yes	Yes	No	No	No	No	Yes	Yes	Yes	Critically low
Cantone, 2023	Yes	Yes	Yes	Partial yes	Yes	No	Partial yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Moderate
Ezzatvar, 2021a	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	No	Yes	No	No	No	Yes	Yes	Critically low

Ezzatvar, 2021b	Yes	Yes	Yes	Partial yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Low
Fuentes-Abolafo, 2020	Yes	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Lachman, 2018	Yes	Yes	Yes	Partial yes	Yes	Yes	Partial yes	Partial yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Critically low
Morris, 2014	Yes	No	No	Partial yes	No	Yes	Partial yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Critically low
Rocha, 2022	No	Yes	Yes	Partial yes	Yes	No	Partial yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	Critically low
Yang, 2022	No	No	No	Partial yes	Yes	Yes	Partial yes	Partial yes	Yes	No	No	No	No	No	Yes	No	Critically low

Ezzatvar, 2021a: Ezzatvar Y, Izquierdo M, Núñez J, Calatayud J, Ramírez-Vélez R, García-Hermoso A. Cardiorespiratory fitness measured with cardiopulmonary exercise testing and mortality in patients with cardiovascular disease: A systematic review and meta-analysis. *J Sport Health Sci.* 2021;10(6):609-619.

Ezzatvar, 2021b: Ezzatvar Y, Ramírez-Vélez R, Sáez de Asteasu ML, Martínez-Velilla N, Zambom-Ferraresi F, Lobelo F, Izquierdo M, García-Hermoso A. Cardiorespiratory fitness and all-cause mortality in adults diagnosed with cancer systematic review and meta-analysis. *Scand J Med Sci Sports.* 2021;31(9):1745-1752.

Item 1. Did the research questions and inclusion criteria for the review include the components of PICO? For Yes: Population Intervention Comparator group Outcome Optional (recommended) Timeframe for follow-up

Item 2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol? For Partial Yes: The authors state that they had a written protocol or guide that included ALL the following: review question(s) a search strategy inclusion/exclusion criteria a risk of bias assessment For Yes: As for partial yes, plus the protocol should be registered and should also have specified: a meta-analysis/synthesis plan, if appropriate, and a plan for investigating causes of heterogeneity justification for any deviations from the protocol

Item 3. Did the review authors explain their selection of the study designs for inclusion in the review? For Yes, the review should satisfy ONE of the following: Explanation for including only RCTs OR Explanation for including only observational designs OR Explanation for including both

Item 4. Did the review authors use a comprehensive literature search strategy? For Partial Yes (all the following): searched at least 2 databases (relevant to research question) provided key word and/or search strategy justified publication restrictions (e.g. language) For Yes, should also have (all the following): searched the reference lists / bibliographies of included studies searched trial/study registries included/consulted content experts in the field where relevant, searched for grey literature conducted search within 24 months of completion of the review

Item 5. Did the review authors perform study selection in duplicate? For Yes, either ONE of the following: at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder selected by one reviewer.

Item 6. Did the review authors perform data extraction in duplicate? For Yes, either ONE of the following: at least two reviewers achieved consensus on which data to extract from included studies OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder extracted by one reviewer.

Item 7. Did the review authors provide a list of excluded studies and justify the exclusions? For Partial Yes: provided list of exclusions with number of studies in the PRISMA or in-text. For Yes, must also have: Justified the exclusion from the review of each potentially relevant study

Item 8. Did the review authors describe the included studies in adequate detail? For Partial Yes (ALL the following): described populations described interventions described comparators described outcomes described research designs For Yes, should also have ALL the following: described population in detail described intervention in detail (including doses where relevant) described comparator in detail (including doses where relevant) described study's setting timeframe for follow-up

Item 9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? For Partial Yes, must have assessed RoB: from confounding, and from selection bias For Yes, must also have assessed RoB: methods used to ascertain exposures and outcomes, and selection of the reported result from among multiple measurements or analyses of a specified outcome

Item 10. Did the review authors report on the sources of funding for the studies included in the review? For Yes Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies

Item 11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results? For Yes: The authors justified combining the data in a meta-analysis AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present AND they statistically combined effect estimates from observational studies that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available AND they reported separate summary estimates for different study designs separately when two or more were included in the review

Item 12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis? For Yes: included only low risk of bias RCTs OR, if the pooled estimate was based on RCTs and/or observational studies at variable RoB, the authors performed analyses to investigate possible impact of RoB on summary estimates of effect.

Item 13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review? For Yes: included only low risk of bias RCTs OR, if RCTs with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results





Item 14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? For Yes: There was no significant heterogeneity in the results OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review





Item 15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review? For Yes: performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias.




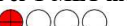
Item 16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review? For Yes: The authors reported no competing interests OR The authors described their funding sources and how they managed potential conflicts of interest





Final Risk of Bias. *Note: Multiple non-critical weaknesses may diminish confidence in the review and it may be appropriate to move the overall appraisal down from moderate to low confidence. Non-critical weakness = Q1, Q3, Q5, Q6, Q8, Q10, Q14, Q16 Critical weakness = Q2, Q4, Q7, Q11, Q15 Critical flaw = Q9, Q12, Q13

eTable 3: Summary of findings table




Study design	Effect estimates or summary of effect	# of participants (# of studies)	Certainty (quality) of evidence	Interpretation of findings
Mortality outcomes in general populations				
All-cause mortality	Comparing high vs low CRF: HR = 0.55, 95% CI: 0.50 – 0.61 (Laukkanen, 2022) HR = 0.47, 95% CI: 0.39 – 0.56 (Han, 2022) HR = 0.59, 95% CI: 0.52 – 0.66 (Kodama, 2009)	2,255,441 (37) 2,187,550 (19) 31,010 (15)	High vs. low CRF  Very low certainty (only reported for Laukkanen, 2022 as the largest and most recent study) RoB: -1 point, studies at moderate RoB for confounding Inconsistency: -1 point, I ² = 90% but the heterogeneity could be partially explained by sub-group analysis. Indirectness: -1 point, most of the included participants were male. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: -1 point, asymmetry was identified using funnel plots and Egger's test	There is very low certainty of a protective effect of high compared to low CRF on risk of all-cause mortality.
	Per 1-MET increase based on objective measures: HR = 0.89, 95% CI: 0.86 – 0.92 (Laukkanen, 2022) HR = 0.88, 95% CI: 0.83 – 0.93 (Han, 2022) HR = 0.87, 95% CI: 0.84 – 0.90 (Kodama, 2009)	360,131 (10) 625,400 (14) 85,315 (18)	Per 1-MET increase based on direct measures  Low certainty (only reported for Han 2022 as the largest and most recent study. Laukkanen 2022 did not assess RoB or publication bias, both needed to assess GRADE for the outcome) RoB: 0 points, all studies rated at good quality Inconsistency: -2 points, I ² = 99.4%, heterogeneity could not be explained by sub-group analysis. Indirectness: 0 points, all objective tests and mixed male and female samples. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, no evidence of publication bias.	There is low certainty of a dose-response effect of CRF on risk of all-cause mortality.
	Per 1-MET increase based on self-report measures: HR = 0.83, 95% CI: 0.78 – 0.88 (Qiu, 2021)	154,015 (7)	Per 1-MET increase based on self-report  Low certainty RoB: 0 points, all studies rated as low RoB. Inconsistency: -2 points, I ² = 93.6% and could not be explained by sub-group analysis. Indirectness: 0 points, good distribution of sexes, all >18 years, used estimated eCRF, but did not subtract points for this as the estimate is reported separately. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, no evidence of publication bias.	There is low certainty of a dose-response effect of estimated CRF on risk of all-cause mortality.
	CRF from normal weight unfit, overweight unfit, and obese unfit compared to normal weight fit (Barry, 2014):		Normal, overweight and obese unfit vs. normal weight fit  Very low certainty RoB: -2 points, all studies of high RoB	There is very low certainty of a protected effect of high compared to low CRF on risk of





	HR (normal) = 0.41, 95% CI: 0.33 – 0.51 HR (overweight) = 0.47, 95% CI: 0.39 – 0.56 HR (obese) = 0.41, 95% CI: 0.32 – 0.52		Inconsistency: -2 points, I ² ranged from 46.7 to 72.1% but the heterogeneity could be partially explained by sub-group analysis. Indirectness: -2 points, most of the included participants were male, unclear of CRF measures. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 point, no evidence of publication bias	all-cause mortality regardless of body mass.
CVD mortality	Comparing high vs low CRF: HR = 0.49, 95% CI: 0.0.42 – 0.56	1,952,352 (13)	High vs. low CRF  Moderate certainty RoB: 0 points, all studies were of low RoB. Inconsistency: 0 points, I ² = 40.5% with similar estimates across studies and confidence intervals that overlap. Indirectness: -1 point, seven of the included studies only included populations of male participants. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, no evidence of publication bias by funnel plot and Egger's test.	There is moderate certainty of a protective effect of high compared to low CRF on risk of CVD mortality.
	Per 1-MET increase based on objective measures: HR = 0.87, 95% CI: 0.83 – 0.91	392 240 (10)	Per 1-MET increase based on direct measures  Very low certainty RoB: 0 points, all studies of low RoB Inconsistency: -2 point, I ² = 80.3%, heterogeneity could not be explained by sub-group differences. Indirectness: 0 points, all objective tests and included mixed samples of males and females Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: -1 point, evidence of publication bias	There is very low certainty of a dose-response effect of CRF on risk of cardiovascular disease mortality.
	Per 1 MET increase based on self-reported CRF: HR = 0.83, 95% CI: 0.80 – 0.86	174,075 (6)	Per 1-MET increase based on self-report  Low certainty RoB: 0 points, all studies rated as low RoB. Inconsistency: -2 points, I ² = 65.0% and could not be explained by sub-group analysis. Indirectness: 0 points, good distribution of sexes, all >18 years, used estimated eCRF, but did not discount for this as the estimate is reported separately. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, no evidence of publication bias by tests	There is low certainty of a dose-response effect of estimated CRF on risk of cardiovascular disease mortality.
	Comparing CRF for normal weight unfit, overweight unfit, and obese unfit compared to normal weight fit (Barry, 2018): HR (normal) = 0.46, 95% CI: 0.40 – 0.53	134,331 (8)	Normal, overweight and obese unfit vs. normal weight fit  Very low certainty RoB: -1 point, all studies of moderate to high quality	There is very low certainty of a protected effect of high compared to low CRF on risk of cardiovascular mortality regardless of body mass.



	HR (overweight) = 0.42, 95% CI: 0.32 – 0.55 HR (obese) = 0.32, 95% CI: 0.25 – 0.42		Inconsistency: -2 points, I ² ranged from 8.7 to 74.0% and could not be explained. Indirectness: -2 points, almost all included participants were male, unclear of CRF measures. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 point, no evidence of publication bias	
Sudden cardiac death	Comparing high vs. low CRF: HR = 0.58, 95% CI: 0.41 – 0.81	57,813 (2)	High vs. low CRF  Moderate certainty RoB: 0 points, both studies at low RoB, both had potential for selection bias due to representativeness of sample Inconsistency: 0 points, only two studies, CIs overlap considerably Indirectness: -1 point, largely male dominated samples Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, insufficient # of studies to assess, search strategy is comprehensive.	There is moderate certainty of a protective effect of high compared to low CRF on risk of sudden cardiac death.
	Per 1-MET unit increase: HR = 0.49, 95% CI: 0.33 – 0.73	57,813 (2)	Per 1-MET increase in CRF  Moderate certainty RoB: 0 points, both studies at low RoB, both had potential for selection bias due to representativeness of sample Inconsistency: 0 points, only two studies, CIs overlap considerably Indirectness: -1 point, largely male dominated samples Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, insufficient # of studies to assess, search strategy is comprehensive.	There is moderate certainty of a dose-response effect of CRF on risk of sudden cardiac death.
All cancer mortality	Comparing high vs low CRF: HR = 0.49, 95% CI: 0.42 – 0.71	409,422 (11)	High vs. low CRF  Low certainty RoB: 0 points, all studies were of low risk of bias. Inconsistency: -1 point, I ² = 75% but the heterogeneity could be partially explained by sub-group analysis. Indirectness: -1 point, several of the included studies only included samples of males. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, no evidence of publication bias by funnel plot or Egger's test.	There is low certainty of a protective effect of high compared to low CRF on risk of all cancer mortality.
	Per 1-MET unit increase: HR = 0.93, 95% CI: 0.91 – 0.96	409,594 (10)	Per 1-MET increase in CRF  Very low certainty RoB: 0 points, all studies at low RoB. Inconsistency: -2 points, I ² = 76.6%, heterogeneity could not be explained by sub-group differences.	There is very low certainty of a dose-response effect of CRF on risk of all cancer mortality.





			Indirectness: -1 point, all objective tests (mostly treadmill), several studies only included males. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, no evidence of publication bias by funnel plot or Egger's test.	
Lung cancer mortality	Comparing high vs. low CRF: HR = 0.53, 95% CI: 0.44 – 0.64	12,758 (5)	High vs. low CRF  Very low certainty RoB: 0 points, all studies at low RoB. Inconsistency: -1 point, I ² = 68%, CIs overlap. Indirectness: -2 points, one used perceived fitness, one symptom-limited and one maximal test, relatively similar ages, one cohort included veterans. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: -1 point, insufficient # of studies to assess, unclear if search strategy is comprehensive, no model search strategy provided, and one author searched literature.	There is very low certainty of a protective effect of high compared to low CRF on risk of lung cancer mortality.
Incident outcomes				
Hypertension	Comparing high vs. low CRF: HR = 0.63, 95% CI: 0.56 - 0.70	1,618,067 (9)	High vs. low CRF  Low certainty RoB: 0 points, only one of nine studies was of moderate risk of bias. Inconsistency: -1 point, I ² = 80.7% and could partially be explained by sub-group analyses. Indirectness: -1 point, the majority of studies only included populations of male participants. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, no evidence of publication bias by test.	There is low certainty of a protective effect of high compared to low CRF on risk of hypertension
	Per 1-MET unit increase: HR = 0.92, 95% CI: 0.90 - 0.94	1,618,067 (9)	Per 1-MET increase in CRF  Low certainty RoB: 0 points, only one of nine studies was of moderate risk of bias. Inconsistency: -1 point, I ² = 89.4% and could partially be explained by sub-group analyses. Indirectness: -1 point, the majority of studies only included populations of male participants. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, no evidence of publication bias by test.	There is low certainty of a dose-response effect of CRF on risk of hypertension.
Heart failure	Comparing high vs low CRF: HR = 0.31, 95% CI: 0.19 – 0.49	1,505,114 (6)	High vs. low CRF  Very low certainty RoB: 0 points, all studies were low risk of bias.	There is very low certainty of a protective effect of high compared to low CRF on risk of heart failure.




			<p>Inconsistency: -2 points, $I^2 = 96.1\%$ and heterogeneity could not be adequately explained by sub-group analyses.</p> <p>Indirectness: -2 points, two of six studies only included samples of male participants, one contributed 88% of the total sample.</p> <p>Imprecision: 0 points, sample size >4000, the CIs do not include 1.0.</p> <p>Publication bias: 0 points, no evidence of publication bias by Egger's and Begg's test.</p>	
	<p>Per 1-MET unit increase:</p> <p>HR = 0.82, 95% CI: 0.79 – 0.84</p>	173,678 (5)	<p>Per 1-MET increase in CRF</p> <p>●○○○○</p> <p>Very low certainty</p> <p>RoB: 0 point, all studies were low risk of bias.</p> <p>Inconsistency: -2 points, $I^2 = 70.0\%$, sub-group analyses not explored.</p> <p>Indirectness: -2 points, two studies only included samples of male participants, no description of CRF tests.</p> <p>Imprecision: 0 points, sample size >4000, the CIs do not include 1.0.</p> <p>Publication bias: 0 points, insufficient # of studies to assess, search strategy is comprehensive.</p>	There is very low certainty of a dose-response effect of CRF on risk of heart failure.
Stroke	<p>Comparing high vs. low CRF:</p> <p>HR = 0.58, 95% CI: 0.51 – 0.66</p>	1,409,340 (14)	<p>High vs. low CRF</p> <p>●○○○○</p> <p>Very low certainty</p> <p>RoB: -1 point, most studies at low to moderate RoB, two studies with high RoB contributed lower weights to meta-analysis.</p> <p>Inconsistency: -1 point, $I^2 = 65\%$, estimates differed, but most CIs overlap.</p> <p>Indirectness: -1 point, objective tests, but largely male studies.</p> <p>Imprecision: 0 points, sample size >4000, the CIs do not include 1.0.</p> <p>Publication bias: 0 points, no evidence of publication bias by funnel plot or Egger's test.</p>	There is very low certainty of a protective effect of high compared to low CRF on risk of stroke.
	<p>Per 1-MET unit increase:</p> <p>HR = 0.97, 95% CI: 0.96 – 0.98</p>	NR (9)	<p>Per 1-MET increase in CRF</p> <p>●○○○○</p> <p>Very low certainty</p> <p>RoB: -1 point, cannot assess individual study RoB, based on reporting from high vs. low CRF assessment.</p> <p>Inconsistency: -2 points, $I^2 = 68\%$, no assessment of sub-group differences and individual study estimates not provided.</p> <p>Indirectness: -1 point, objective tests, but appears to largely be male studies.</p> <p>Imprecision: 0 points, sample size >4000 (based on case #s), the CIs do not include 1.0.</p> <p>Publication bias: 0 points, insufficient # of studies to assess, search strategy appears comprehensive.</p>	There is very low certainty of a small dose-response effect of CRF on risk of stroke.
Atrial fibrillation	<p>Comparing high vs. low CRF:</p> <p>HR = 0.60, 95% CI: 0.51 – 0.72</p>	2,168,739 (7)	<p>High vs. low CRF</p> <p>●○○○○</p> <p>Very low certainty</p>	There is very low certainty of a protective effect of high


			<p>RoB: 0 points, all studies at low RoB. Inconsistency: -2 points, $I^2 = 97%$, estimates and CIs do not overlap, subgroups not explored Indirectness: -1 point, one study used a non-exercise algorithm, different population sources of samples (i.e., general population, veterans, hospital patients), most cohorts included males and females. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, insufficient # of studies to assess, search strategy is comprehensive.</p>	compared to low CRF on risk of atrial fibrillation.
	<p>Per 1-MET unit increase: HR = 0.91, 95% CI: 0.86 – 0.95</p>	222,124 (7)	<p>Per 1-MET increase in CRF  Very low certainty RoB: 0 points, all studies at low RoB. Inconsistency: -2 points, $I^2 = 94%$, estimates and CIs do not overlap, subgroups not explored Indirectness: -1 point, one study used a non-exercise algorithm, different population sources of samples (i.e., general population, veterans, hospital patients), most cohorts included males and females. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, although <10 studies, publication bias assessed and not observed. Search strategy is comprehensive.</p>	There is very low certainty in a dose-response effect of CRF on incidence of atrial fibrillation.
Type 2 diabetes	<p>Per 1-MET unit increase: HR = 0.92, 95% CI: 0.90 – 0.94</p>	1,601,490 (10)	<p>Per 1-MET increase in CRF  Very low certainty RoB: -1 point, studies at low to moderate RoB for confounding. Inconsistency: -1 point, $I^2 = 83%$ and could partially be explained by subgroup analyses. Indirectness: -2 points, includes a mix of treadmill and cycle ergometer tests with several studies only including male populations. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: -1 point, small study bias detected using funnel-plot.</p>	There is very low certainty in a dose-response effect of CRF on risk of type 2 diabetes.
Dementia	<p>Comparing high vs. low CRF: HR = 0.36, 95% CI: 0.27 – 0.49</p>	11,694 (3)	<p>High vs. low CRF  Very low certainty RoB: -1 point, all studies at low to moderate RoB. Inconsistency: -1 point, $I^2 = 70%$, CIs overlap. Indirectness: -2 points, one used perceived fitness, one symptom-limited and one maximal test, relatively similar ages, one cohort included veterans, two cohorts only included males. Imprecision: 0 points, sample size >4000, the CIs do not include 1. Publication bias: -1 point, insufficient # of studies to assess, unclear if search strategy is comprehensive, no model search strategy provided and one author searched literature.</p>	There is very low certainty of protective effect of high compared to low CRF on risk of dementia.

Chronic kidney disease	Comparing high vs. low CRF: HR = 0.58, 95% CI: 0.46 – 0.73	32,447 (5)	High vs. low CRF  Very low certainty RoB: -2 points, all studies were low RoB. Inconsistency: -2 points, I ² = 76%, did not explore a subgroup analysis Indirectness: -1 point, limited global representation and larger sample of males (>75%). Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, insufficient # of studies to assess, search strategy is comprehensive.	There is very low certainty of protective effect of high compared to low CRF on risk of chronic kidney disease.
Depression	Comparing high vs. low CRF: HR = 0.61, 95% CI: 0.48 – 0.78	1,145,655 (3)	High vs. low CRF  Very low certainty RoB: 0 points, all studies were low RoB. Inconsistency: -2 points, I ² = 78%, estimates and CIs did not overlap. Indirectness: -2 points, two used maximal tests, one used estimated equation, age differed at baseline, one cohort (the largest) was only in males and one only included 22% females. Imprecision: 0 points, sample size >4000, the CIs do not include 1.0. Publication bias: 0 points, insufficient # of studies to assess, search strategy is comprehensive.	There is very low certainty of protective effect of high compared to low CRF on risk of depression.
Clinical populations				
Chronic kidney disease & all-cause mortality	Comparing high vs. low CRF based on 6MWT: HR = 0.34, 95% CI: 0.15 – 0.79	415 (2)	High vs. low CRF  Very low certainty RoB: 0 points, both studies at low RoB Inconsistency: 0 points, only two studies, but the CIs overlap considerably Indirectness: 0 points, both used 6MWT in patients with chronic kidney disease (stages 2-5), both older populations, one study only included males but was smaller and the larger study included mostly females. Imprecision: -2 points, total sample size is small, the CIs around the estimate include both benefit and harm and are relatively wide around 1.0. Publication bias: -1 point, insufficient # of studies to assess. The search strategy does not appear fully comprehensive.	There is very low certainty of a protective effect of high compared to low CRF on risk of all-cause mortality among people living with chronic kidney disease.
Heart failure & all-cause mortality	Comparing high vs. low CRF based on 6MWT: HR = 0.44, 95% CI: 0.35 – 0.54	5,170 (5)	High vs. low CRF  Low certainty RoB: -1 point, one study was rated as moderate 6/9 RoB. Inconsistency: 0 points, I ² = 0% with lots of overlap. Indirectness: -1 point, all included older patients with heart failure and CRF was measured using the 6MWT, most samples were majority males. Imprecision: 0 points, sample was >4000 and CI didn't cross 1.0.	There is low certainty of a protective effect of high compared to low CRF on risk of all-cause mortality among people living with heart failure

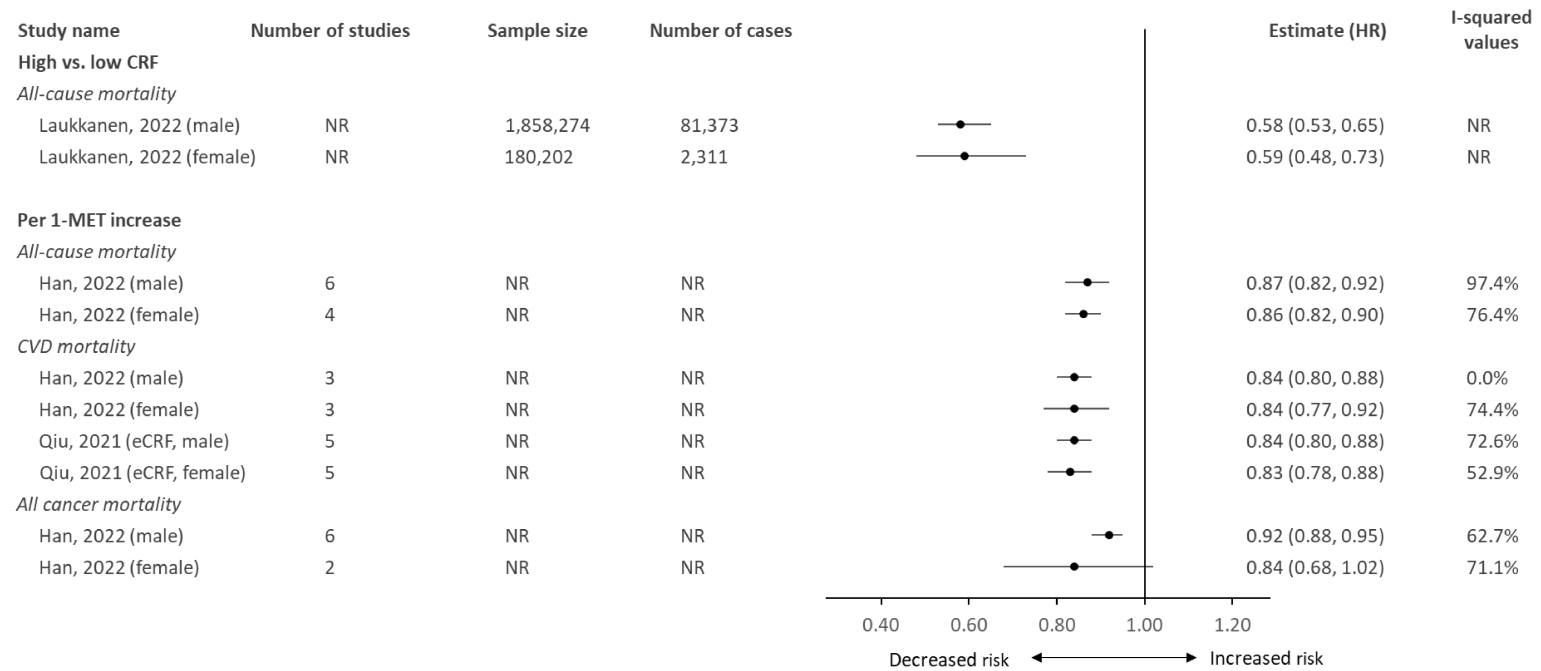
			Publication bias: 0 points, insufficient # of studies to assess, search strategy is comprehensive.	
Heart failure & heart failure mortality	Comparing high vs. low CRF based on 6MWT: HR = 0.42, 95% CI: 0.39 – 0.45	982 (4)	High vs. low CRF  Low certainty RoB: -1 point, one of four studies was rated as moderate RoB due to selection bias and bias involved with detecting the outcome. Inconsistency: 0 point, I ² = 0% with high overlap between studies. One study reported a substantially larger effect than other included studies. Indirectness: 0 points, similar age and sex groups. Imprecision: -1 point, sample size <4000, the CIs, do not include 1.0. Publication bias: 0 points, insufficient # of studies to assess, search strategy is comprehensive.	There is low certainty of a protective effect of high compared to low CRF on risk of heart failure mortality among people living with heart failure.
Peripheral artery disease & all-cause mortality	Compared high vs. low CRF based on 6MWT + treadmill ramp: HR = 0.40, 95% CI: 0.23 – 0.71	2,793 (3)	High vs. low CRF  Very low certainty RoB: -2 points, one study had a high RoB related to confounding and generalizability, 1 had RoB due to inadequate follow-up Inconsistency: 0 points, I ² = 22% indicating low heterogeneity. Point estimates were similar with lots of overlap. Indirectness: -1 point, CRF was assessed by 6MWT in two and ramp treadmill in one. Comparison group thresholds differed between studies; all cohorts were largely comprised of males. Imprecision: -1 point, sample size <4000, the CIs, do not include 1.0 Publication bias: 0 points, insufficient # of studies to assess, search strategy is comprehensive.	There is very low certainty of a protective effect of high compared to low CRF on risk of all-cause mortality among people living with peripheral artery disease.

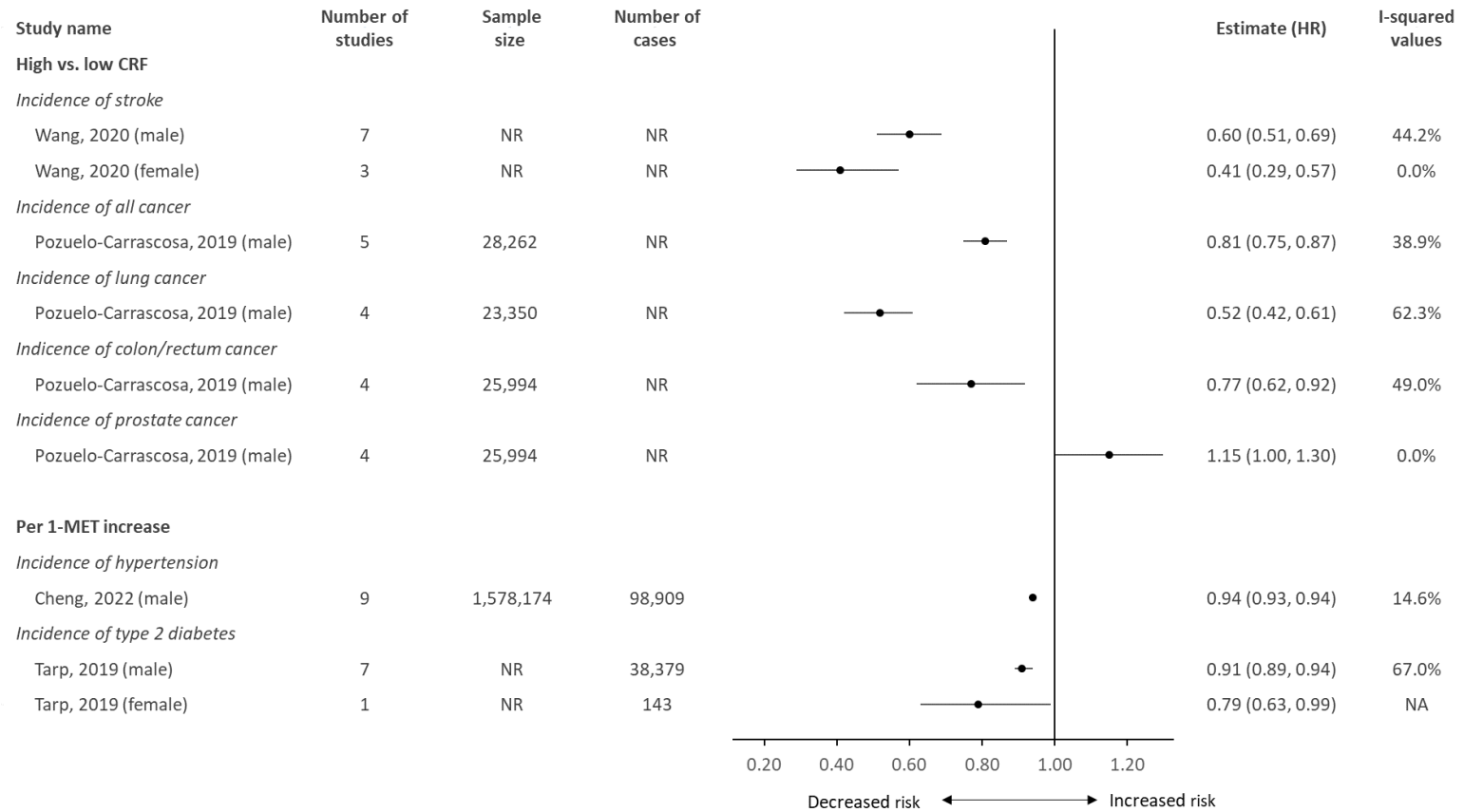
Peripheral artery disease & cardiovascular mortality	Compared high vs. low CRF based on 6MWT + treadmill ramp: HR = 0.48, 95% CI: 0.37 – 0.62	2,793 (3)	High vs. low CRF  Very low certainty RoB: -2 points, one study had a high RoB related to confounding and generalizability, one had RoB due to inadequate follow-up Inconsistency: 0 points, I ² = 58% indicating low heterogeneity. Point estimates were similar between two studies, but the CIs of all three overlapped. Indirectness: -1 point, CRF was assessed by 6MWT in two and ramp treadmill in one. Comparison group thresholds differed between studies, all cohorts were largely comprised of males. Imprecision: -1 point, sample size <4000, the CIs, do not include 1.0 Publication bias: 0 points, insufficient # of studies to assess, search strategy is comprehensive.	There is very low certainty of a protective effect of high compared to low CRF on risk of cardiovascular death, hospitalization for adverse events (I.e., congestive heart failure, and all-cause mortality) among people living with coronary artery disease.
Amyloid cardiomyopathy & all-cause mortality	Per 1-MET increase: HR = 0.67, 95% CI: 0.54 – 0.81	233 (3)	Per 1-MET increase  Low certainty RoB: 0 points, all studies were high quality. Inconsistency: 0 points, I ² = 0% indicating very low heterogeneity. Indirectness: -1 point, limited global representation. Imprecision: -1 point, sample size <4000, the CIs, do not include 1.0 Publication bias: 0 points, insufficient # of studies to assess, search strategy is comprehensive.	There is low certainty of a protective effect of CRF per MET increase on risk of all-cause mortality among people living with amyloid cardiomyopathy.
Coronary artery disease & adverse events	Compared non-delayed heart rate recovery to delayed heart rate recovery based on cycle and treadmill tests: HR = 0.17, 95% CI: 0.10 – 0.31	2,146 (3)	Delayed vs. non-delayed HRR  Very low certainty RoB: -1 point, two studies were moderate and one high quality. All three studies had a RoB related to missing data/attrition. Inconsistency: 0 points, I ² = 32% indicating low heterogeneity. Point estimates were similar between two studies, but the CIs of all three overlapped. Indirectness: -2 points, different outcomes across studies (e.g., composite outcome, cardiac death, all-cause mortality), majority of total sample (73%) is male Imprecision: -1 point, sample size <4000, the CIs, do not include 1.0 Publication bias: 0 points, insufficient # of studies to assess, search strategy is comprehensive.	There is very low certainty of a protective effect of high compared to low CRF on risk cardiovascular death, hospitalization for adverse events (i.e., congestive heart failure, and all-cause mortality) among people living with coronary artery disease.
Cardiovascular disease & all-cause mortality	Compared high vs low CRF: HR = 0.42, 95% CI: 0.28 – 0.61	22,274 (11)	High vs. low CRF  Very low certainty RoB: -1 point, nearly half the studies had fair quality.	There is very low certainty of a protective effect of high compared to low CRF on risk of all-cause mortality among people living with cardiovascular disease.

			<p>Inconsistency: -2 points, $I^2 = 96.6\%$ that could not be explained by subgroup analyses.</p> <p>Indirectness: -1 point, small inconsistencies in the CRF measures used between studies, studies had a high % males.</p> <p>Imprecision: 0 points, sample was >4000 and CI did not include 1.0.</p> <p>Publication bias: -1 points, major asymmetry detected using Luis Furuya-Kanamori index.</p>	
Cardiovascular disease & cardiovascular disease mortality	<p>Compared high vs low CRF:</p> <p>HR = 0.27, 95% CI: 0.16 – 0.48</p>	5,821 (4)	<p>High vs. low CRF</p> <p></p> <p>Very low certainty</p> <p>RoB: -1 point, 3 of 4 studies were rated as fair quality.</p> <p>Inconsistency: 0 points, $I^2 = 0\%$ indicating no heterogeneity. Point estimates were similar with lots of overlap.</p> <p>Indirectness: -1 point, small inconsistencies in the CRF measures used between studies, majority male participants</p> <p>Imprecision: 0 points, sample was >4000 and CIs did not include 1.0.</p> <p>Publication bias: -1 points, major asymmetry detected using Luis Furuya-Kanamori index.</p>	There is very low certainty of a protective effect of high compared to low CRF on risk of cardiovascular disease mortality among people living with cardiovascular disease
Interstitial lung disease & all-cause mortality	<p>Compared high vs. low CRF based on 6MWT:</p> <p>HR = 0.40, 95% CI: 0.27 – 0.60*</p> <p>*Note 2/3 studies included in the meta-analysis were from the same trial</p>	1,908 (3)	<p>High vs. low CRF</p> <p></p> <p>Very low certainty</p> <p>RoB: -2 points: all three studies were at moderate to high RoB with scores ranging from 4-6 on the NOS</p> <p>Inconsistency: 0 points, $I^2 = 0\%$ indicating no heterogeneity. Point estimates were similar with lots of overlap.</p> <p>Indirectness: -2 points, all used 6MWT, two of the included studies were from the same trial, majority of sample was male >70%.</p> <p>Imprecision: -1 point, sample size <4000, the CIs do not include 1.0</p> <p>Publication bias: 0 points, insufficient # of studies to assess, search strategy is comprehensive.</p>	There is very low certainty of a protective effect of high compared to low CRF on risk of all-cause mortality among people living with interstitial lung disease.
Pulmonary hypertension & adverse events	<p>Compared with high vs. low CRF based on peak VO₂ from CPET:</p> <p>HR = 0.81, 95% CI: 0.78 – 0.85</p>	986 (9)	<p>High vs. low CRF</p> <p></p> <p>Very low certainty</p> <p>RoB: -1 point: all studies were deemed to be of moderate-to high quality, but individual NOS scores not provided.</p> <p>Inconsistency: 0 points, $I^2 = 29\%$ indicating low heterogeneity, two point estimates differed, but CIs overlapped.</p> <p>Indirectness: -2 points, different thresholds for defining low peak VO₂ used, all used direct measures of CRF, appears that majority of sample was female</p> <p>Imprecision: 0 points, sample was >4000 and CI did not include 1.0.</p>	There is very low certainty of a protective effect of high compared to low CRF on risk of adverse events (i.e., mortality, heart or lung transplantation) among people living with pulmonary hypertension.

			Publication bias: 0 points, although insufficient # of studies, Egger's test suggests symmetry, sensitivity analyses removing individual studies suggested no publication bias	
Cancer & all-cause mortality	Compared with high vs low CRF based on cardiopulmonary test, stair climber test, Bruce protocol, 6MWT, and modified Balke protocol: HR = 0.52, 95% CI: 0.35 – 0.77	4343 (9)	High vs. low CRF  Very low certainty RoB: -1 point, seven of 11 studies rated as fair quality. Inconsistency: -2 points, $I^2 = 77.6\%$ and could not be explained by subgroup analysis. Indirectness: -1 point, combined data from patients with different cancer types, variety of objective CRF tests, majority of sample was male (68%). Imprecision: 0 points, sample was >4000 and CI did not include 1.0. Publication bias: -1 points, major asymmetry detected using Luis Furuya-Kanamori index.	There is very low certainty of a protective effect of high compared to low CRF on risk of all-cause mortality among people living with cancer.

6MWT – six-minute walk test, CI – confidence interval, CPET – cardiopulmonary exercise testing, CRF – cardiorespiratory fitness, HR – hazard ratio, HRR – heart rate response, NOS – Newcastle-Ottawa Scale, RoB – risk of bias

eFigure 1. Mortality outcomes by sex.

eFigure 2. Incident outcomes by sex.

eMETHODS

Eligibility criteria

Population: Adult populations (≥ 18 years), including participants who were apparently healthy and clinical populations with diagnosed chronic conditions. If evidence for children and youth were not reported separately from adult data, we included studies if $\geq 80\%$ of the evidence was from adults, or if the mean age of participants across all included studies was ≥ 18 years. We excluded studies that focused on populations recovering from surgery and special interest groups (i.e., athletes, pregnancy).

Exposure: The primary exposure was CRF measured using three possible approaches: 1) maximal exercise testing with gas analysis (i.e., directly measured $\dot{V}O_{2\max/\text{peak}}$), 2) maximal or submaximal exercise testing without gas analysis, which used either exercise prediction equations to estimate CRF or the measured exercise performance (i.e., indirect measures), and 3) non-exercise prediction equations for estimating CRF. CRF could be tested using any modality, including treadmill, cycle ergometry, running, walking, or bench stepping, and expressed as $\dot{V}O_{2\max/\text{peak}}$, METs, distance covered, heart rate response, or any other performance-related measure.

Outcome: We did not pre-specify outcomes for this study. As a result, any health-related outcome such as all-cause or cause-specific mortality, incident conditions related to physical risk factors, physical chronic conditions, or mental health issues were included. Among populations with diagnosed chronic conditions, we included evidence on prognostic outcomes such as mortality or disease severity.

Study designs: Only systematic reviews with meta-analyses that searched a minimum of two bibliographic databases and provided a sample search strategy either in-text or in supplemental files were included. We included meta-analyses that pooled data from primary prospective/retrospective cohort or case-control studies. These studies were the focus because of their ability to assess some degree of causality for observational research.

Publication status and language restriction: Only reviews published in English, French, or Spanish were eligible based on the authors' language capacity. Only systematic reviews published in peer-reviewed journals were eligible. Conference abstracts or papers, commentaries, editorials, dissertations, or grey literature were not eligible.

Timeframe: Systematic reviews published during the past 20 years from 1 January 2002 to March 2024.

Information sources

We searched five bibliographic databases. OVID Medline, OVID Embase, Scopus, CINAHL and EBSCOhost SPORTDiscus were searched from A search of OVID Medline, Embase, and Scopus was conducted from 1 January 2002 to 2118 November 2022. The search was later updated from 1 November 2022 to 8 March 2024.

Search Strategy

A research librarian (KM) created the search strategy in collaboration with the authorship team. The search strategy was originally developed in Medline. A January 2002 date limit was applied because the authorship group agreed it was unlikely that a topical systematic review with meta-analysis was published beforehand and to help manage the screening load. An adapted systematic review filter was also applied to the search.^{1,2} Trial searches were run to ensure that pre-identified eligible studies were captured by the search strategy. The search strategy was also peer-reviewed by an independent research librarian using the Peer Review of Electronic Search Strategies (PRESS) guidelines.³ The final Medline search strategy was subsequently translated to the other bibliographic databases. The search strategies for each database are available in Supplement 1. The reference lists of included papers were also searched for additional relevant systematic reviews.

Selection process

All records were imported into RefWorks where duplicates were removed using automated and manual methods. Records were imported into Covidence for screening. Reviewers were not blinded to the study metadata when screening. The title and abstract from each record were screened by two independent reviewers (JJL, SAP, CCS, JPC, BJB, TM, BS, and GRT) against the inclusion criteria. Full-text articles were obtained for each record that met the inclusion criteria or provided insufficient evidence to make a conclusive decision at the title and abstract stage. Conflicts during title and abstract screening automatically advanced to full text screening. Each full-text record was screened by two independent reviewers (JJL, SAP, CCS, JPC, BJB, TM, BS, and GRT) against the inclusion criteria. Conflicts at the full-text stage were resolved

through discussion by two reviewers (JJL and SAP), with a third reviewer invited to resolve disagreements.

Data collection process

Data extraction was completed in Covidence using a form that was piloted by the authorship group for accuracy. Data from included studies were extracted by two independent reviewers (JJL, SAP, CCS, JPC, BJF, TM, FBO, BS, and GRT). Conflicts were resolved by one reviewer (JJL), with the reviewers who extracted the data contacted when necessary to resolve any remaining conflicts.

Data items

The data extraction form included the: title of the paper; lead author; publication year; aim of study; target population; search date range; databases; inclusion and exclusion criteria; origin countries; number of included primary studies; publication date range; study design(s); population description; age range; sample size; mean follow-up period; CRF measures; health outcomes; details on the risk of bias tool used and the findings from the assessment; and, the analytical approach. For each meta-analysis the following were extracted: a description of the outcome measure; the population group; the comparator; the effect size estimate; the 95% confidence interval; a measure of heterogeneity or dispersion; sample size included in the analysis; and, the number of individuals with the health condition. We additionally extracted results on any modification or sensitivity analysis, the publication bias results, and the summary of findings and conclusions.

Study quality

We extracted the original risk of bias assessment for each primary study, as reported by the study authors. Most of the included studies used the Newcastle-Ottawa Scale (NOS) to assess risk of bias for cohort studies.⁴ We also assessed quality of the systematic reviews using the second edition of A Measurement Tool to Assess systematic Reviews 2 (AMSTAR2) checklist.⁵ We implemented one minor modification to question 7 of the AMSTAR2 to allow for a ‘partial yes’ if reasons for exclusions were summarised in a Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram. Studies were assessed as being of ‘critically low’ quality if more than one critical flaw was present including a lack of assessment of the risk of bias of primary studies, not assessing the impact of the risk of bias in the meta-analysis, or not accounting for the risk of bias when discussing the results of the study. Study quality was rated as ‘high’ if zero or one non-critical weakness, but no critical flaws were present; ‘moderate’ if more than one critical weakness, but no critical flaws were present; and ‘low’ if one critical flaw with or without non-critical weaknesses were present. The overall assessment could be downgraded from ‘moderate’ to ‘low’ if multiple non-critical weaknesses were present. Two independent reviewers (JJL, SAP, CCS, JPC, BJF, TM, FBO, BS, and GRT) assessed the study quality. Conflicts were resolved by one reviewer (JJL), with the reviewers who extracted the data contacted to resolve outstanding conflicts.

Effect measures

We present pooled hazard ratios (HR) or relative risks (RR) for an incident event (i.e., mortality or morbidity) across the included systematic reviews. Models that compared high vs low CRF

and those that examined the impact of a 1-MET increase as the comparator group were prioritised. We also prioritised sex stratified models.

Synthesis of data

We followed an outcome-centric approach, as outlined by Kho et al.⁶ Our goal was to identify systematic reviews with non-overlapping primary studies for each outcome to avoid double counting evidence. When more than one eligible systematic review was identified for a single outcome, we calculated the corrected covered area (CCA) to assess the degree of overlap in the primary studies.⁷ The CCA was interpreted as slight (0%–5%), moderate (6%–10%), high (11%–15%), or very high (>15%). If the CCA was slight or moderate, we included multiple systematic reviews per outcome. If the CCA was high or very high, we selected the highest quality systematic review according to the AMSTAR2 assessment. We included only the most recent systematic review when identified reviews of the same outcome were rated as equal in quality.

Synthesis of results

For each health outcome, we reported evidence for apparently healthy and clinical populations separately. We summarized results using a narrative synthesis approach using summary of findings tables. Results are reported as described by the systematic review authors. In some cases, the direction of the association was inverted to align with other included studies (i.e., HR = 2.00 was changed to HR = 0.50) or the dose response analysis was re-calculated to represent a 1-MET increase in CRF. Meta-analysis results, including the effect, confidence limits, number of studies, and number of participants, are presented by outcome using a figure to allow for easy comparison between studies. RR values were taken to approximate the HR, and thus, we present

estimates from both together. When comparing high vs. low CRF we inverted the scale when studies compared low vs high by dividing the values by one. Dose-response values were converted to 1-MET increase when more than 1-MET was used by converting to the natural log, dividing, and exponentiating results. Subgroup analyses for sex were described when available.

Certainty of the evidence assessment

For each outcome, the certainty of the evidence was assessed using a modified Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach.⁸ Briefly, certainty of the evidence was rated across five domains: risk of bias, imprecision, inconsistency, indirectness, and publication bias. Where provided, the risk of bias assessments reported in the systematic reviews were used, for those where a risk of bias assessment was not conducted, the Newcastle-Ottawa Scale was used to determine risk of bias for the review.⁴ Observational evidence began at 'high' certainty because randomized controlled trials were not feasible for our research question.⁹ The certainty of the evidence could be rated down based on the five domains. We assessed certainty of the evidence for high vs. low CRF as the primary estimate, and only assessed evidence per 1-MET increase if the study didn't assess high vs low CRF. See Supplement 1 for a GRADE decision table that was developed to help guide decisions.

Protocol deviations

This overview is a sub-study of a large overview of reviews looking at the prospective associations between CRF and health across the lifespan. Due to the large volume of evidence, for the purpose of this overview, we explicitly examined all systematic review evidence among

adults. Two separate overviews looking at youth (<18 years) and the diagnostic accuracy of CRF to predict outcomes are reported elsewhere.

REFERENCES

1. CADTH Search Filters Database. Ottawa: CADTH; 2022: <https://searchfilters.cadth.ca/link/33>." Accessed 2022-10-28.
2. Salvador-Oliván JA, Marco-Cuenca G, Arquero-Avilés R. Development of an efficient search filter to retrieve systematic reviews from PubMed. *J Med Libr Assoc*. 2021 Oct 1;109(4):561-574. doi: 10.5195/jmla.2021.1223.
3. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. *J Clin Epidemiol*. 2016 Jul;75:40-6. doi: 10.1016/j.jclinepi.2016.01.021.
4. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses, 2013. Available from: https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
5. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ*. 2017 Sep 21;358:j4008. doi: 10.1136/bmj.j4008.
6. Kho ME, Poitras VJ, Janssen I, Chaput JP, Saunders TJ, Giangregorio LM, Tomasone JR, Ross-White A, Ross R. Development and application of an outcome-centric approach for conducting overviews of reviews. *Appl Physiol Nutr Metab*. 2020 Oct;45(10 (Suppl. 2)):S151-S164. doi: 10.1139/apnm-2020-0564.
7. Pieper D, Antoine SL, Mathes T, Neugebauer EA, Eikermann M. Systematic review finds overlapping reviews were not mentioned in every other overview. *J Clin Epidemiol*. 2014 Apr;67(4):368-75. doi: 10.1016/j.jclinepi.2013.11.007.
8. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008 Apr 26;336(7650):924-6.
9. Iorio A, Spencer FA, Falavigna M, Alba C, Lang E, Burnand B, McGinn T, Hayden J, Williams K, Shea B, Wolff R, Kujpers T, Perel P, Vandvik PO, Glasziou P, Schunemann H, Guyatt G. Use of GRADE for assessment of evidence about prognosis: rating confidence in estimates of event rates in broad categories of patients. *BMJ*. 2015 Mar 16;350:h870.