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DISSERTATION

Warum sind manche Menschen fitter als andere? Einflussfaktoren der kardiorespiratorischen Fitness bei Erwachsenen in Deutschland

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Abbildungsverzeichnis

Abkürzungsverzeichnis

BMI	Body-Mass-Index
CASMIN	Comparative Analysis of Social Mobility in Industrial Nations
DEGS1	Studie zur Gesundheit Erwachsener in Deutschland
FFQ	Food Frequency Questionnaire
KI	Konfidenzintervall
KRF	Kardiorespiratorische Fitness
LILACS	Latin American and Caribbean Health Sciences
MeSH	Medical Subject Heading
NCDs	Noncommunicable diseases
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SciELO	Scientific Electronic Library Online
STROBE	Strengthening the Reporting of Observational studies in Epidemiology
$\dot{V}O_2max$	maximale Sauerstoffaufnahme

Zusammenfassung

Die kardiorespiratorische Fitness (KRF) stellt einen wichtigen Indikator für die Gesundheit dar. Die vorliegende kumulative Dissertation hat zum Ziel, den aktuellen Forschungsstand zu den Einflussfaktoren der KRF systematisch zusammenzutragen und potentielle Einflussfaktoren anhand repräsentativer Daten für die deutsche Erwachsenenbevölkerung zu untersuchen. Das Forschungsprojekt gliedert sich in einen Recherche- und einen Auswertungsteil. In einem generischen systematischen Review (Publikation I) wurden, einem semi-quantitativen Ansatz folgend, potentielle individuelle und interpersonelle Einflussfaktoren der KRF aus der Literatur extrahiert, die Ergebnisse zu den einzelnen Faktoren zusammengefasst und in einer Tabellenmatrix dargestellt. In einem zweiten systematischen Review (Publikation II) wurde auf die sozioökonomischen Faktoren fokussiert. Neben einer tabellarischen Darstellung wurden die Ergebnisse mehrerer Studien in Form einer Meta-Analyse zusammengefasst. Daran anschließend wurden, einem quantitativen Forschungsansatz folgend, potentielle Einflussfaktoren anhand bevölkerungsrepräsentativer Daten der *Studie zur Gesundheit Erwachsener in Deutschland* (DEGS1) auf ihre Assoziation mit der KRF überprüft. In DEGS1 (2008-2011) nahmen Männer und Frauen im Alter von 18-64 Jahren an einem standardisierten submaximalen Fahrradergometer-Test teil, auf dessen Basis die maximale Sauerstoffaufnahme ($\dot{V}O_2max$) für 2.826 Personen geschätzt werden konnte. Der Zusammenhang von $\dot{V}O_2max$ mit potentiellen individuellen und interpersonellen Einflussfaktoren wurde anhand linearer Regressionsmodelle überprüft (Publikation III). Anschließend wurde vertiefend untersucht, wie sich freizeitbezogene und arbeitsbezogene körperliche Aktivität hinsichtlich ihrer Beziehung zur einer niedrigen $\dot{V}O_2max$ unterscheiden (Publikation IV).

In Publikation I wurden 78 Studien eingeschlossen. Höheres Alter, weibliches Geschlecht, niedrigere Bildung, höherer Body-Mass-Index, höheres Körpergewicht, größerer Taillenumfang, höherer Körperfettanteil, höhere Ruheherzfrequenz, höheres C-reaktives Protein, niedrigerer Alkoholkonsum, Rauchen sowie ein geringerer Umfang körperlicher Freizeitaktivität zeigten sich konsistent mit einer schlechteren KRF assoziiert. Die vertiefende Meta-Analyse zum Zusammenhang von SES und KRF (Publikation II) ergab für Männer und Frauen mit hohem Bildungsstatus eine höhere KRF im Vergleich zu Personen mit niedrigem Bildungsstatus. Anhand der

DEGS1 Daten zeigte sich eine höhere $\dot{V}O_2max$ mit einem niedrigeren Hüftumfang, niedrigerem Body-Mass-Index und mehr sportlicher Aktivität und darüber hinaus bei Männern mit hohem Obstkonsum sowie einem hohem Gesamtaktivitätslevel und bei Frauen mit höherem Alkoholkonsum sowie hohem Berufsstatus assoziiert (Publikation III). Während bei Frauen diejenigen das höchste Risiko für eine niedrige $\dot{V}O_2max$ hatten, die keine Freizeitaktivität, aber eine hohe Arbeitsaktivität aufwiesen, zeigte sich bei Männern das höchste Risiko für eine niedrige $\dot{V}O_2max$ unter denjenigen mit keiner Freizeitaktivität und niedriger Arbeitsaktivität (Publikation IV). Diese Dissertation liefert wichtige Erkenntnisse für das Verständnis der Einflussfaktoren der KRF, die als Grundlage für die Weiterentwicklung eines ätiologischen Modells der KRF verwendet werden können.

Abstract

Cardiorespiratory fitness (CRF) is an important marker of health. This study aims to systematically synthesize the evidence on influencing factors of CRF and to investigate potential correlates of CRF using representative data of the German adult population. This cumulative thesis is principally divided into a review and an analysis part. A generic systematic literature review on potential individual and interpersonal influencing factors of CRF was conducted (paper I). Results were summarized and tabulated following a semi-quantitative approach. A second systematical review focused on potential socioeconomic factors (paper II). Results were summarized in table format and methodologically similar studies were synthesized using meta-analysis. Potential influencing factors of CRF in the German adult population were investigated using data from the population-based nationwide German Health Interview and Examination Survey (DEGS1). In DEGS1 (2008-2011) men and women aged 18-64 years participated in a standardized sub-maximal cycle ergometer test. Maximal oxygen consumption ($\dot{V}O_2max$) was estimated for 2.826 participants. Linear regression analyses was performed to investigate potential individual and interpersonal correlates of CRF (paper III). The last study aimed to investigate associations between occupational physical activity and leisure time physical activity with low cardiorespiratory fitness (paper IV). In paper I 78 studies were included. Higher age, female sex, lower education, higher body mass index, higher body weight, higher waist circumference, higher body fat percentage, higher resting heart rate, higher C-reactive protein, lower alcohol consumption, smoking and lower leisure-time physical activity were consistently associated with CRF. Meta analyses showed that both men and women with higher education had higher CRF compared to individuals with low education (paper II). Based on DEGS1 data, higher $\dot{V}O_2max$ was associated with lower waist circumference, lower body mass index, and higher levels of physical exercise. In addition, among men higher $\dot{V}O_2max$ was associated with high fruit intake and higher levels of total physical activity and among women with higher alcohol consumption and high occupational status (paper III). While among women those working in physically demanding occupations and not participating in leisure time physical activity had the highest likelihood of having low $\dot{V}O_2max$, among men those who did not engage in leisure time physical activity and were not working in physically demanding occupations had the highest risk of low $\dot{V}O_2max$ (paper IV). This thesis provides important insight into understanding the

influencing factors of CRF which can be used in developing a comprehensive etiological model of CRF.

Vorbemerkung: Die im Rahmen dieses Forschungsprojektes entstandenen Ergebnisse wurden in vier Publikationen in internationalen Zeitschriften mit Peer-Review Verfahren veröffentlicht [1-4].

1. Einleitung

Nicht übertragbare Krankheiten (*noncommunicable diseases*; NCDs), wie Herz-Kreislauf- Erkrankungen, Diabetes, Adipositas oder Depressionen, sind weltweit maßgeblich verantwortlich für vorzeitige Sterblichkeit, Einschränkungen der Lebensqualität und hohe Kosten in den Gesundheitssystemen [5, 6]. Weltweit machen nicht übertragbare Krankheiten 71 % aller Todesfälle aus, in Deutschland sogar über 90 % [7, 8]. Auch wenn NCDs eine sehr heterogene Gruppe von Krankheiten bilden, ist ihnen gemein, dass sie üblicherweise komplexe Ursachen haben und dass gesundheitsrelevante Verhaltensweisen eine wichtige Rolle bei der Entstehung spielen. Diese Faktoren werden ihrerseits stark von den Lebens- und Umweltbedingungen beeinflusst (*causes of the causes*) [5, 9]. Gleichzeitig sind sozial schwächer gestellte Personengruppen häufig deutlich stärker betroffen [10]. Durch den engen Bezug zum Gesundheitsverhalten sind viele NCDs prinzipiell vermeidbar beziehungsweise durch geeignete Maßnahmen beeinflussbar. Neben Fehlernährung, Tabak- und Alkoholkonsum gilt mangelnde körperliche Aktivität als zentraler verhaltensbasierter Faktor zur Prävention chronischer, nicht-übertragbarer Krankheiten [5, 11].

In enger Beziehung zur körperlichen Aktivität steht die körperliche Fitness. Während körperliche Aktivität als jede Form der Bewegung, die durch eine Muskelaktivität hervorgerufen wird und den Energieverbrauch über den Grundumsatz anhebt, definiert ist [12], beschreibt der Begriff körperliche Fitness die Fähigkeit oder Voraussetzung, körperliche Aktivität in einer bestimmten Art und Weise auszuführen, und umfasst Komponenten wie Muskelkraft, Körperzusammensetzung, Beweglichkeit, Ausdauer und Kraftausdauer [12]. Eine nachhaltige Steigerung der körperlichen Aktivität führt daher zwar in der Regel auch zu einer Steigerung der Fitness. Aufgrund unterschiedlicher (genetischer) Voraussetzungen und Rahmenbedingungen kann der Grad dieser physiologischen Anpassung aber stark variieren [13]. Eine spezifische Form der Fitness ist die Ausdauerleistungsfähigkeit. Ausdauer bezeichnet die grundlegende motorische Fähigkeit des Organismus, eine anstrengende Bewegung in bestimmter Intensität über eine bestimmte Dauer aufrechterhalten zu können. Wichtige leistungslimitierende Faktoren sind die Sauerstoffaufnahmefähigkeit und die Sauerstofftransportkapazität des Organismus [14], weswegen die Ausdauerleistungsfähigkeit auch als kardiorespiratorische Fitness (KRF) bezeichnet wird [12]. Entsprechend beschreibt die KRF die Fähigkeit des Atem- und Herzkreislaufsystems, die Skelettmuskulatur während anhaltender körperlicher Aktivität mit Sauerstoff zu versorgen, und ist von mehreren Faktoren abhängig: (1.) dem pulmonalen Gasaustausch, (2.) der Leistung des kardiovaskularen Systems und (3.) dem Metabolismus der Skelettmuskulatur [15].

Die Beziehung zwischen KRF und gesundheitlichen Merkmalen ist seit den 1950er Jahren vielfach untersucht worden [16, 17]. Ab Ende der 1980er Jahre wurde anhand erster großangelegter (Kohorten-) Studien ein starker Zusammenhang zwischen einer niedrigen KRF und allgemeiner Mortalität aufgezeigt [18]. Dieser Zusammenhang wurde seitdem in zahlreichen Studien bestätigt [19]. Personen mit höherer KRF erkranken seltener an Herz-Kreislauf-, Stoffwechsel- sowie Krebserkrankungen und leiden seltener unter Depressionen und anderen psychischen Erkrankungen als Personen mit niedriger KRF [20-29]. In einigen Studien konnte gezeigt werden, dass die KRF der körperlichen Aktivität als Prädiktor für bestimmte Krankheiten und Mortalität überlegen ist [13, 30, 31]. Im Vergleich zur körperlichen Aktivität besteht aus methodischer Sicht ein weiterer Vorteil der KRF hinsichtlich der Validität und Reliabilität der Messergebnisse. Üblicherweise erfolgt die Erhebung der KRF anhand standardisierter Fahrradergometer- oder Laufband-Tests, wohingegen die körperliche Aktivität meist anhand von Selbstangaben erfasst wird. Zwar werden zur Messung der körperlichen Aktivität zunehmend auch Akzelerometer verwendet, die Heterogenität der verwendeten Messverfahren und Auswertungsprotokolle schränkt aber immer noch deren Vergleichbarkeit ein [32]. Ferner ist die KRF eng mit der besonders gesundheitsförderlichen Form der Ausdaueraktivität verbunden, die sich sowohl bei der selbstberichteten Erfassung von Bewegungsverhalten als auch bei der objektiven Messung von Bewegung mit Akzelerometern nur mit großem Aufwand trennscharf von anderen Bewegungsformen abgrenzen lässt [33]. Dieser Aspekt ist in Bezug auf den aktuellen wissenschaftlichen Diskurs relevant, ob freizeitbezogene und arbeitsbezogene körperliche Aktivitäten die gleichen oder unterschiedliche gesundheitliche Effekte haben, da sich deren übliche Bewegungsformen hinsichtlich des Anteils der Ausdaueraktivität unterscheiden [34].

Mit Blick auf die komplexe Pathogenese der NCDs ist es wichtig, aktuelle Evidenz zu den zentralen Determinanten und deren Einflussfaktoren zu generieren. In gleichem Maße wie körperliche Aktivität und KRF unabhängig gesundheitliche Folgen prädiktieren können, besteht die Möglichkeit, dass sich auch die Einflussfaktoren für beide Größen unterscheiden. Dementsprechend ist es wichtig, Faktoren zu identifizieren, die spezifisch mit KRF assoziiert sind bzw. diese beeinflussen [35]. Auf internationaler Ebene liegen zahlreiche Studien vor, die solche Faktoren identifizieren, beispielweise zur genetischen Veranlagung [36], Adipositas [37], Alkohol- [38] und Tabakkonsum [39] oder zur bebauten Wohnumgebung [40]. Auch wenn bereits erste Versuche unternommen wurden, die Determinanten der KRF konzeptionell zu fassen [35, 41], existiert bislang kein umfassendes Modell – wie es beispielsweise schon für Adipositas [42, 43] oder das körperliche Aktivitätsverhalten [44, 45] entwickelt wurde –, das sowohl proximale als auch distale Faktoren sowie deren Interrelation berücksichtigt. Im Gegensatz zu zahlreichen Übersichtsarbeiten zu den Einflussfaktoren der körperlichen Aktivität (z.B. [45]) liegen trotz der eindeutigen Befunde zur gesundheitlichen Bedeutung der KRF bisher keine systematischen Übersichtsarbeiten über Korrelate und Determinanten der KRF vor. Zudem sind potentielle Einflussfaktoren für Deutschland noch nicht anhand repräsentativer Daten auf Bevölkerungsebene untersucht worden.

Vor diesem Hintergrund sollen mit der vorliegenden Arbeit, folgende Forschungsfragen beantwortet werden:

1. Wie stellt sich der aktuelle Forschungsstand hinsichtlich individueller Einflussfaktoren der KRF (a) im Allgemeinen und (b) hinsichtlich sozioökonomischer Einflussfaktoren der KRF im Speziellen dar?

2. Was sind die Einflussfaktoren der KRF bei Frauen und Männern in Deutschland?

3. Wie unterscheiden sich freizeitbezogene und arbeitsbezogene körperliche Aktivität hinsichtlich ihrer Beziehung zur KRF?

Für die Beantwortung dieser Fragen wurde ein zweistufiger Forschungsansatz gewählt, der sich in eine Recherche- und eine Auswertungsphase gliedert. Zunächst wurde in Form von systematischen Reviews und Metaanalysen der internationale Forschungsstand zusammengetragen und ausgewertet (Publikation I&II). Daran anschließend wurden, einem quantitativen Forschungsansatz folgend, die formulierten Fragestellungen anhand bevölkerungsrepräsentativer Daten für Deutschland überprüft (Publikation III&IV).

Im Folgenden werden zunächst die verwendeten Methoden und Daten vorgestellt, bevor die zentralen Ergebnisse der Einzelpublikationen, die in internationalen Zeitschriften mit Peer-Review-Verfahren erschienen sind, zusammengefasst werden. Nachdem die Ergebnisse des Dissertationsprojekts gegliedert nach Einflussbereichen der KRF eingeordnet und Limitationen diskutiert werden, schließt die Arbeit mit einem kurzen Fazit zur Public-Health-Relevanz.

2. Material und Methodik

2.1 Systematische Reviews und Metaanalyse

Die systematische Literaturrecherche und Auswertung wurde in zwei Publikationen gegliedert: In einem generischen systematischen Review [1] erfolgt die Übersicht über Studien zu individuellen Einflussfaktoren der KRF unabhängig vom thematischen Bereich der Korrelate und Determinanten. Eine zweite Publikation fokussiert auf den Zusammenhang von sozioökonomischem Status und KRF.

2.1.1 Publikation I: Systematisches Review zu Determinanten und Korrelaten der KRF

Das systematische Review wurde vorab als Protokoll registriert [46]; das methodische Vorgehen orientiert sich an den *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) [47]. Es erfolgte eine Recherche in den Datenbanken PubMed, EMBASE und Cochrane Library sowie eine Recherche nach grauer Literatur auf Google Scholar. Die letzte Suche wurde am 01.02.2017 durchgeführt. Für den Zeitraum 01.02.2017 bis 06.06.2019 wurde im Rahmen der Aktualisierung der Publikation ein eingeschränktes Update der Suche durchgeführt. Einschlusskriterium für die abhängige Variable KRF war die objektive Messung anhand eines maximalen oder submaximalen Belastungstests. Dementsprechend wurde sowohl eine direkte Messung der KRF, beispielsweise mittels Spiroergometrie, als auch die indirekte Messung anhand metabolischer Gleichungen eingeschlossen. Darüber hinaus wurden nur Studien berücksichtigt, in denen die KRF anhand von Laufband oder Fahrradergometern gemessen wurde. Ausgeschlossen wurden Studien, die an stark selektiven Studienpopulationen durchgeführt wurden (z.B. Soldatinnen und Soldaten), Studien mit Kindern, Jugendlichen oder Hochaltrigen sowie Studien, die ausschließlich univariate Ergebnisse ohne Adjustierung für potentielle *Confounder* berichten. Mögliche individuelle Determinanten und Korrelate der KRF wurden anhand eines *a priori* entwickelten Wirkmodells (Abbildung 1) kategorisiert. Folgende Bereiche wurden berücksichtigt: soziodemografische Faktoren (z.B. Alter), anthropometrische Faktoren (z.B. Body-Mass-Index [BMI]), Vitalparameter (z.B. Blutdruck), Erkrankungen und Medikamente, Biomarker (z.B. C-reaktives Protein), Maße körperlicher Aktivität (z.B. Freizeitaktivität) und weiteres Gesundheitsverhalten (z.B. Rauchstatus). Genetische Faktoren sowie interpersonelle (z.B. soziale Unterstützung) und Umweltfaktoren (z.B. Walkability) wurden ausgeschlossen. In einem mehrstufigen Verfahren wurden zunächst Titel und Abstract und später die Volltexte durch zwei Reviewer bewertet. Ergebnisse und Charakteristika der eingeschlossenen Studien wurden in eine Tabellenmatrix übernommen und die Qualität der Studien anhand eines adaptierten *Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies* [48] bewertet. Um die Ergebnisse in aggregierter Form darzustellen, wurde ein semi-quantitativer Ansatz gewählt, da eine Metaanalyse aufgrund der Heterogenität der potentiellen Korrelate und Determinanten nicht angemessen war. Dieser Ansatz wurde schon in anderen breit angelegten systematischen Übersichtsarbeiten angewendet [49, 50]. In einer Tabellenmatrix wurden für jeden potentiellen Einflussfaktor der KRF Studienanzahl und Richtung des Zusammenhangs (positiv, negativ, kein Zusammenhang) gelistet.

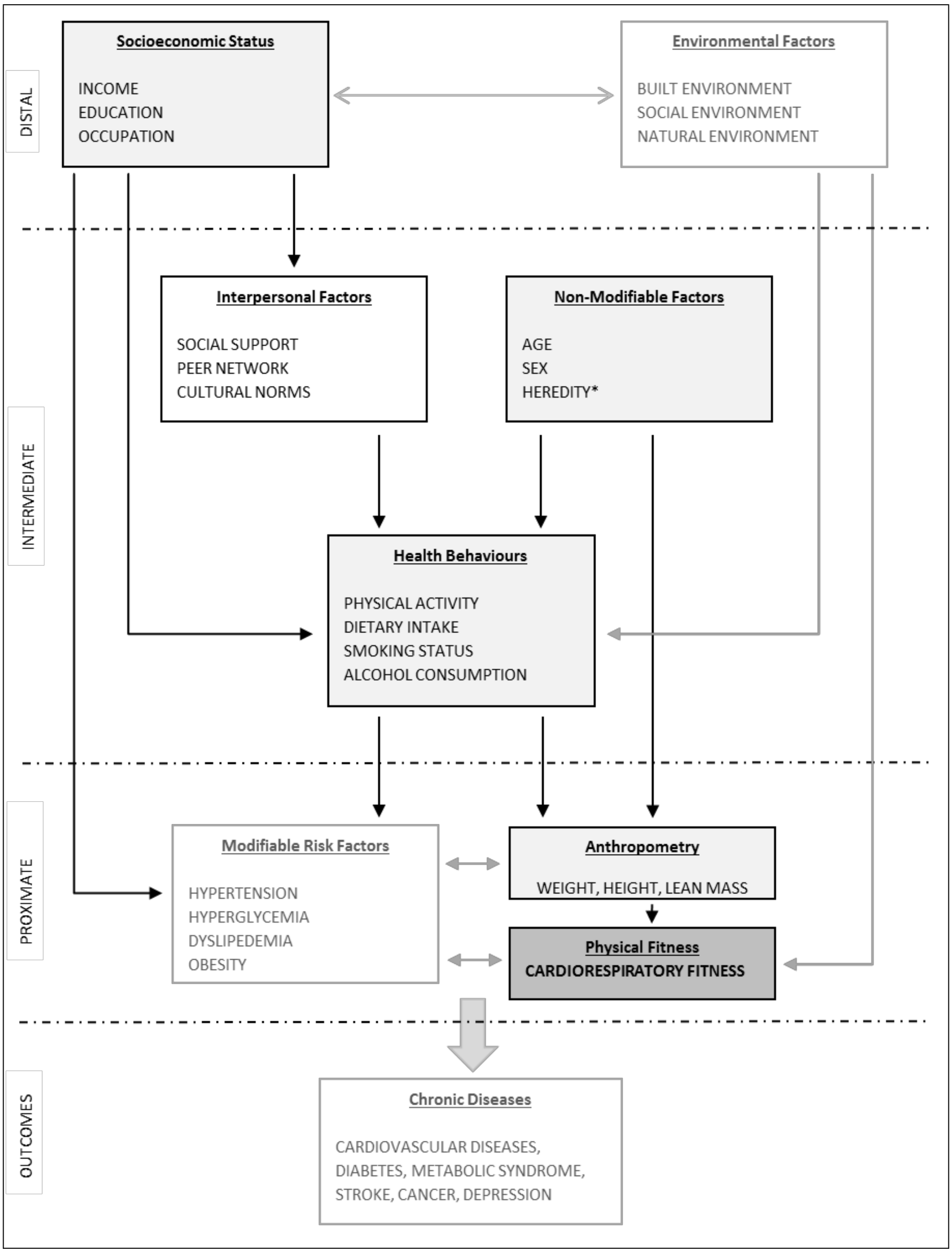

Abbildung 1: Wirkungsmodell potentieller Einflussfaktoren der Kardiorespiratorischen Fitness (übernommen aus [1])

2.1.2 Publikation II: Systematisches Review zu sozioökonomischen Korrelaten der KRF

In den Datenbanken MEDLINE, EMBASE. *Latin American and Caribbean Health Sciences* (LILACS), *Scientific Electronic Library Online* (SciELO) und *Cochrane Library* erfolgte eine Recherche nach potentiellen sozioökonomischen Korrelaten der KRF [2]. Als Indikatoren des sozioökonomischen Status, definiert als Maße von

Ressourcen oder Prestige, die die Stellung eines Menschen innerhalb der Gesellschaft beschreiben [51], wurden alle Begriffe, die unter dem *Medical subject heading* (MeSH) *term „Socioeconomic Factors*“ definiert sind, eingeschlossen. Definition der KRF, Ein- und Ausschlusskriterien sowie das Vorgehen bei der Datenextraktion und Qualitätsbewertung erfolgten weitgehend analog zu Publikation I. Für drei der eingeschlossenen Studien lagen vergleichbare Daten zum Zusammenhang von Bildung und KRF vor, die die Durchführung einer Metaanalyse ermöglichten. Die Bildungsvariable wurde anhand der *Comparative Analysis of Social Mobility in Industrial Nations (CASMIN) Classification* in hoch, mittel und niedrig kategorisiert. Die KRF wurde als maximale Sauerstoffaufnahme ($\dot{V}O_2max$) direkt mittels Spiroergometrie erfasst oder geschätzt auf Basis submaximaler Belastungstests. Die für die potentiellen *confounder* Alter, körperliche Aktivität, Hüftumfang, BMI und Alkoholkonsum adjustierten Effektstärken wurden anhand Hedges' g standardisiert. Die standardisierten Effektstärken wurden anhand einer geschlechtsstratifizierten Random-Effects-Metaanalyse ausgewertet, in der die KRF von Frauen und Männern mit hoher Bildung (Referenzkategorie) in separaten Analysen mit der KRF von Frauen und Männern mit (1.) mittlerer und (2.) niedriger Bildung verglichen wurde. I^2 wurde als Maß für die Studienheterogenität verwendet. Eine Meta-Regressionsanalyse wurde für die potentielle Moderatorvariable körperliche Aktivität (hohe vs. niedrige Aktivität) berechnet.

2.2 Analyse der DEGS1-Daten

2.2.1 Publikation III: Korrelate der KRF bei Erwachsenen in Deutschland

Die Analysen basieren auf Querschnittsdaten der *Studie zur Gesundheit Erwachsener in Deutschland* (DEGS1). Die Auswertungen orientierten sich an etablierten epidemiologischen Leitlinien für Beobachtungsstudien (*Strengthening the Reporting of Observational studies in Epidemiology* – STROBE [52]). DEGS1 ist ein bundesweiter Untersuchungssurvey, der im Rahmen des nationalen Gesundheitsmonitorings durch das Robert Koch-Institut zwischen November 2008 und Dezember 2011 durchgeführt wurde [53]. Das Studiendesign von DEGS1 basiert auf einer zweistufigen cluster-randomisierten Stichprobenziehung [54, 55]. In der ersten Stufe wurden zufällig 180 Untersuchungsorte stratifiziert nach regionaler Verteilung gezogen. In der zweiten Stufe erfolgte innerhalb dieser Untersuchungspunkte anhand von Einwohnermeldeamtsstichproben die zufällige

Auswahl von Erwachsenen im Alter von 18 bis 79 Jahren, stratifiziert nach 10-Jahres-Altersgruppen. Das Studienprotokoll wurde von der Ethikkommission der Charité – Universitätsmedizin Berlin (Nr. EA2/047/08) sowie vom Bundesbeauftragten für Datenschutz und Informationsfreiheit geprüft und als unbedenklich eingestuft. Die KRF wurde bei Teilnehmenden im Alter von 18-64 anhand eines standardisierten submaximalen Fahrradergometer-Tests gemessen (Ergosana Sana Bike 350/450, Ergosana, Bitz, Deutschland). Methode, Protokoll sowie Ein- und Ausschlusskriterien wurden im Detail durch Finger et al. [56] beschrieben. Um die Testtauglichkeit zu bestimmen, wurde eine modifizierte Version des *Physical Activity Readiness-Questionnaire* (PAR-Q) eingesetzt. Wurden bei einem der Teilnehmenden Kontraindikationen im Sinne des PAR-Q festgestellt, wurde durch das ärztliche Studienpersonal entschieden, ob eine Teilnahme am Ergometertest möglich war. Testtaugliche Personen absolvierten einen stufenförmigen Belastungstest nach dem von der WHO empfohlenen Schema: Beginnend mit 25 Watt wurde die Belastung alle zwei Minuten um 25 Watt erhöht. Der Test wurde durch das Studienpersonal beendet, wenn 85% der altersspezifischen maximalen Herzfrequenz (208 - 0.7 × Alter) oder die maximale Belastungsstufe von 350 Watt erreicht wurden oder allgemeine Abbruchkriterien bei Belastungstests auftraten. Die Berechnung der geschätzten $\dot{V}O_2max$ erfolgte durch die mittels linearer Regression bestimmte herzfrequenzbezogene Leistung an der altersbasierten maximalen Herzfrequenz (nach [57]) und Umrechnung der Leistung in $\dot{V}O_2max$ anhand der Formel des *American College of Sports Medicine*: 3,5 ml / min / kg + 12,24 × (maximale Leistung) × (Körpergewicht) [58]. Ein Wirkungsmodell bildete die Grundlage für die Auswahl potentieller Einflussfaktoren der KRF. Mögliche interpersonelle Faktoren wurden aus der Literatur zu den Einflussfaktoren körperlicher Aktivität abgeleitet, da diese nicht Bestandteil der systematischen Reviews (Publikation I) waren. Folgende potenzielle Einflussfaktoren wurden untersucht: (1.) Alter [Selbstangaben], (2.) Faktoren des Gesundheitsverhaltens (Rauchen [Selbstangaben], Alkoholkonsum [basierend auf *Food Frequency Questionnaires* (FFQ)], Obstkonsum [FFQ], Gemüsekonsum [FFQ], *Junkfood*-Konsum [FFQ], Konsum zuckerreicher Getränke [FFQ], Konsum zuckerreicher Lebensmittel [FFQ], (3.) Sozioökonomische Faktoren (Bildung [Selbstangaben], Berufsstatus [Selbstangaben] und Einkommen [Selbstangaben], (4.) Interpersonelle Faktoren (Soziale Unterstützung [Selbstangaben]) und

Familienstand [Selbstangaben]), (5.) Anthropometrische Faktoren (BMI [Messwerte] und Hüftumfang [Messwerte]) sowie (6.) Faktoren der sportlichen Aktivität (Sport [Selbstangaben] und allgemeinen körperlichen Aktivität [Selbstangaben]).

Alle Analysen wurden mit *Stata* V.15.1 (Stata Corp.) durchgeführt. Mittels Kreuztabellenanalyse wurde der bivariate Zusammenhang zwischen $\dot{V}O_2max$ und den potentiellen Einflussfaktoren untersucht. Für die Variablen Alter, BMI und Hüftumfang wurde der Zusammenhang zusätzlich anhand Scatterplots und *Fractional-polynomial prediction plots* dargestellt. Im darauffolgenden Analyseschritt wurden in einem mehrstufigen Vorgehen vier geschlechts-stratifizierte multivariable lineare Regressionsmodelle berechnet. Im ersten Modell (Modell 1) wurden zunächst Alter und die Faktoren des Gesundheitsverhaltens aufgenommen. In den darauffolgenden Modellen dann iterativ zusätzlich soziodemografische und interpersonelle Faktoren (Modell 2), anthropometrische Faktoren (Modell 3), und Faktoren der körperlichen Aktivität (Modell 4). Durch die Verwendung von Gewichtungsfaktoren wurde die Stichprobe hinsichtlich der Parameter Alter, Geschlecht, Region und Bildung an die Verteilung in der Grundgesamtheit angepasst, um die Effekte systematischer Nichtteilnahme zu reduzieren [54]. Durch Verwendung der Stata Survey Prozeduren wurde das Design des zweistufigen Ziehungsverfahrens berücksichtigt. Für die multivariable Analyse wurden fehlende Werte mittels multipler Imputation ersetzt [59].

2.2.2 Publikation IV: Bereichsspezifische Muster der körperlichen Aktivität und KRF

Da die Auswertungen in Publikation IV ebenfalls auf den DEGS1-Daten basieren, wird an dieser Stelle nur auf die Erfassung der bereichsspezifischen körperlichen Aktivität und die verwendeten statistischen Analyseverfahren eingegangen. Aufbau und Analyseschritte der Auswertung orientierten sich ebenfalls an der STROBE Leitlinie [52].

Körperliche Aktivität in der Freizeit wurde anhand von Selbstangaben in einem schriftlichen Fragebogen erfasst. Eine Frage lautete: „Wie oft treiben Sie Sport?“ Für die Auswertung wurden die Kategorien der auf eine Woche bezogenen fünfstufigen Antwortskala in die drei Gruppen „keine sportliche Betätigung“, „weniger als 2

Stunden“ und „2 Stunden oder mehr“ zusammengefasst. Üblicherweise wird unter körperlicher Aktivität in der Freizeit jede körperliche Aktivität, die in der frei verfügbaren Zeit durchgeführt wird, verstanden. Da sportliche Aktivität jedoch das Hauptelement der körperlichen Aktivität in der Freizeit darstellt [60], wurde hier diese Variable als Proxy für körperliche Aktivität in der Freizeit für verwendet.

Die arbeitsbezogene körperliche Aktivität wurde anhand einer indirekten Methode über die Berufszugehörigkeit der Teilnehmenden durch die Konstruktion sogenannter Job-Exposure Matrizen erfasst [4]. Diese werden anhand verfügbarer Sekundärdaten gebildet und anschließend über die Berufsklassifikation an den Primärdatensatz angespielt. Im Fall der vorliegenden Studie wurden Daten der BAuA-Berufstätigenbefragung der Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (BAuA) genutzt. Verwendet wurde ein Subindex des von Kroll entwickelten allgemeinen Index für die Arbeitsbelastung in beruflichen Tätigkeiten [61], der schon in früheren Auswertungen zum Einsatz kam [62-64]. Verwendet wurden Daten zum Heben und Tragen schwerer Lasten, die den Berufen, definiert nach *International Classification of Occupations of 1988* (ISCO-88), anhand von für Alter, Geschlecht, Arbeitszeit und Dauer der Tätigkeit adjustierten Mehr-Ebenen- Regressionsmodellen zugeordnet wurden. Die zunächst in Dezile klassifizierten Matrizen wurden für die Auswertungen dichotomisiert (niedrige vs. hohe arbeitsbezogene körperliche Aktivität).

Die analog zu Publikation III ermittelte $\dot{V}O_2max$ wurde anhand geschlechtsspezifischer Quintile in niedrige $\dot{V}O_2max$ (1.-2. Quintil) und mittlere bis hohe $\dot{V}O_2max$ (3.-5. Quintil) kategorisiert.

Um die Assoziation der bereichsspezifischen Aktivitätsvariablen zu untersuchen, wurden zunächst arbeits- und freizeitbezogene körperliche Aktivität kreuztabelliert. Anschließend wurden Prävalenzen und 95% -Konfidenzintervalle für eine niedrige $\dot{V}O_2max$ für bereichsspezifische Aktivitätsvariablen und Kovariate (Alter, BMI, Hüftumfang, Rauchen, Alkoholkonsum und sozioökonomischer Status) berechnet. In einem mehrschrittigen Verfahren wurden dann multivariable logistische geschlechts-spezifische Regressionsmodelle berechnet, um den Zusammenhang zwischen bereichsspezifischen Aktivitätsvariablen (unabhängige Variable) und niedriger $\dot{V}O_2max$ (abhängige Variable) zu schätzen. Dabei wurden im ersten Schritt die

Haupteffekte der bereichsspezifischen Aktivitätsvariablen und im zweiten Schritt die Interaktion beider Variablen untersucht. In beiden Schritten wurde ein altersadjustiertes Modell und ein für alle weiteren Kovariaten adjustiertes Modell berechnet. Auch in Publikation IV wurden alle Analysen mit *Stata* V.15.1 (Stata Corp.) durchgeführt.

3. Ergebnisse

3.1 Hauptergebnisse der Publikation I

Die initiale Suche ergabt 3.016 Treffer. Nach Titel und Abstract Screening verblieben 338 Treffer zur Volltextdurchsicht. Insgesamt wurden 78 Artikel in das systematische Review eingeschlossen. Der überwiegende Anteil der Studien (74) stammte aus Ländern mit hohem Einkommen nach Definition der Weltbank, überwiegend aus Nord- Amerika (31) und Europa (29). Die Fallzahlen reichten von 79 bis 218.820. Als Ergebnis der Qualitätsbewertung der eingeschlossenen Studien wurde für 38% ein niedriges, für 52% ein mittleres und für 9% ein hohes Bias-Risiko festgestellt. Alter, BMI, Hüftumfang, körperliche- Aktivität- Indizes, Rauchen und Bildungsstand waren die am häufigsten untersuchten mit KRF assoziierten Faktoren. Konsistent und unabhängig mit einer schlechteren KRF assoziiert zeigten sich höheres Alter, weibliches Geschlecht, , niedrigere Bildung, höherer BMI, höheres Körpergewicht, größerer Taillenumfang, höherer Körperfettanteil, höhere Ruheherzfrequenz , höheres C-reaktives Protein, niedrigerer Alkoholkonsum, Rauchen sowie ein geringerer Umfang körperlicher Freizeitaktivität [1].

3.2 Hauptergebnisse der Publikation II

Die initiale Suche ergab 3.233 Treffer. Nach Titel und Abstract Screening verblieben 346 Artikel zur Volltextdurchsicht. Insgesamt wurden 15 Artikel in das systematische Review eingeschlossen. Die eingeschlossenen Studien stammten aus acht verschiedenen Ländern mit Fallzahlen von 528 bis 4.968. Verschiedene sozioökonomische Maße wie sozioökonomische Indizes und sozioökonomische Kategorisierungen des Wohnumfeldes zeigten einen positiven Zusammenhang mit KRF. Studien, die den Bildungsstand als Indikator des sozioökonomischen Status verwendeten, zeigten entweder ebenfalls einen positiven Zusammenhang oder einen U-förmigen Zusammenhang mit KRF. Drei Studien (davon eine mit zwei unabhängigen Kohorten) mit insgesamt 4.815 Fällen konnten in die Metaanalyse eingeschlossen werden. Im Vergleich zu Personen mit niedrigem Bildungsstatus zeigten Männer und Frauen mit hohem Bildungsstatus eine höhere KRF (Männer Hedges *g* effect size (*g*) 0,12; 95%-Konfidenzintervall [0,04, 0,20], Frauen *g* 0,19; 95%-KI [0,02, 0,36]). Für Personen mit mittlerem Bildungsstatus zeigten sich keine Unterschiede in der KRF im Vergleich zu Personen mit niedrigem Bildungsstatus (Männer *g* 0,03; 95%- KI [–0,04, 0,11], Frauen *g* 0,09; 95%- KI [-0,03, 0,21]). Eine Adjustierung der Modelle für körperliche Aktivität zeigte keinen signifikanten Einfluss auf die Ergebnisse [2].

3.3 Hauptergebnisse der Publikation III

Insgesamt konnte für 2.925 Frauen und Männer die $\dot{V}O_2max$ auf Basis eines submaximalen Fahrradergometer-Tests geschätzt werden. Die mittlere $\dot{V}O_2max$ (in ml/kg/min) lag für Männer (36,5; 95%-KI [36,0, 37,0]) höher als für Frauen (30,3; 95%-KI [29,8, 30,7]). Die multivariable Analyse zeigte für Frauen in höheren Altersgruppen eine deutlich niedrigere geschätzte $\dot{V}O_2max$ im Vergleich zur Altersgruppe der 18- bis 24-Jährigen, für Frauen mit hohem Alkoholkonsum einen höhere $\dot{V}O_2max$ (β = 2.20; 95%-KI [0,98, 3,42]) im Vergleich zu Frauen mit niedrigem Alkoholkonsum und für Frauen mit hohem Berufsstatus eine höhere $\dot{V}O_2max$ (β = 1.83; 95%-KI [0,21, 3,44]) im Vergleich zu Frauen mit niedrigem Berufsstatus. Für Männer zeigte sich ein hoher Obstkonsum (β = 1,52; 95%-KI [0,63, 2,40]) im Vergleich zu einem mittlerem bis niedrigen Obstkonsum und die Durchführung von mindesten 2,5 Stunden körperlicher Aktivität pro Woche (β = 2,19; 95%-KI [1,11, 3,28]) im Vergleich zu weniger als 2,5 Stunden körperlicher Aktivität pro Woche mit einer höheren $\dot{V}O_2max$ assoziiert. Sowohl bei Frauen als auch bei Männern zeigte sich Übergewicht (Frauen: β = -2,36; 95%-KI [-3.26, -1.46]; Männer: β = -3,00; 95%-KI [-4,00, -1,99]) und Adipositas (Frauen: β = -4,88; 95%-KI [-6,19, -3,57]; Männer: β = -5,79; 95%-KI [-7,39, -4,20]), erhöhter (Frauen: β = -1,56; 95%-KI [-2,45, -0,68]; Männer: β = -1,58; 95%-KI [-2,71, -0,45]) und stark erhöhter Taillenumfang (Frauen: β = -1,61; 95%-KI [-2,85, -0,38]; Männer: β = -2,92; 95%-KI [4,23, -1,60]) sowie eine höhere wöchentliche Sportdauer von bis zu 2 Stunden (Frauen: β = 1,68; 95%-KI [0,84, 2,52]; Männer: β = 1,99; 95%-KI [1,00, 2,98]) und ≥ 2 Stunden (Frauen: β = 4,20; 95%-KI [3,10, 5,30]; Männer: β = 3,74; 95%-KI [2,59, 4,88]) deutlich mit einer höheren $\dot{V}O_2max$ assoziiert [3].

3.4 Hauptergebnisse der Publikation IV

Gültige Angaben zu $\dot{V}O_2max$, körperlicher Freizeit- und Arbeitsaktivität lagen für 2.495 Studienteilnehmende vor. Nach Adjustierung für potentielle *Confounder* zeigte ein niedrigeres Level von körperlicher Freizeitaktivität einen deutlichen Zusammenhang mit einer niedrigen $\dot{V}O_2max$, wohingegen zwischen körperlicher Arbeitsaktivität und niedriger $\dot{V}O_2max$ keine bedeutsame Assoziation festgestellt werden konnte. Werden Freizeit- und Arbeitsaktivität kombiniert betrachtet, zeigt sich ein unterschiedliches Bild zwischen Männern und Frauen: während bei Frauen diejenigen das höchste Risiko für eine niedrige $\dot{V}O_2max$ hatten, die keine Freizeitaktivität, aber eine hohe Arbeitsaktivität aufwiesen, zeigte sich bei Männern das höchste Risiko für eine niedrige $\dot{V}O_2max$ unter denjenigen mit keiner Freizeitaktivität und niedriger Arbeitsaktivität (Abbildung 2) [4].

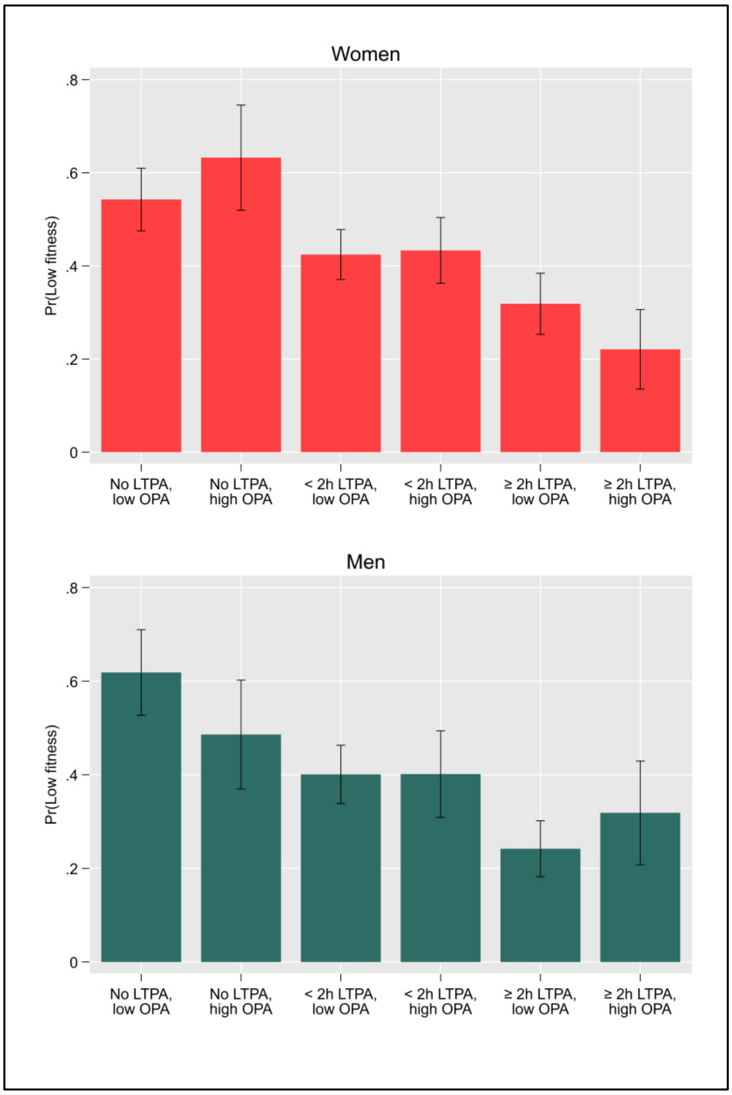

Abbildung 2: vorhergesagte Wahrscheinlichkeiten (mit 95% -Konfidenzintervallen) der niedrigen kardiorespiratorischen Fitness ($\dot{V}O_2max$) nach bereichsspezifischer körperlicher Aktivität bei Frauen und Männern (adjustiert für Alter, Body-Mass-Index, Hüftumfang, Rauchen, Alkoholkonsum und sozioökonomischer Status) (übernommen aus [4]). LTPA: *Leasure time physical activity*, freizeitbezogene körperliche Aktivität; OPA; *Occupational physical activity*, arbeitsbezogene körperliche Aktivität

4. Diskussion

Im Rahmen des Forschungsprojektes konnte erstmalig ein breiter und systematischer Überblick über den internationalen Forschungsstand zu potentiellen Einflussfaktoren der KRF gegeben werden, die in Bezug auf den Zusammenhang mit dem sozioökonomischen Status noch durch einen detaillierteren Blick und Auswertungen ergänzt wurden. Anhand einer großen repräsentativen Stichprobe der Erwachsenenbevölkerung Deutschlands konnten zudem mögliche Einflussfaktoren auf ihren Zusammenhang mit der KRF überprüft werden. Im Folgenden werden diese Einflussfaktoren entsprechend dem in Abbildung 1 skizzierten Wirkmodell von proximal nach distal diskutiert.

4.1 Anthropometrische Faktoren

Anthropometrische Maße wie Körpergewicht, BMI, Hüftumfang oder Körperfettanteil wurden in vielen Studien untersucht und zeigten sich meist konsistent invers mit KRF assoziiert [1]. In Übereinstimmung mit den Ergebnissen aus dem systematischen Review zeigte sich auch anhand der DEGS1-Daten ein deutlicher negativer unabhängiger Zusammenhang sowohl zwischen Übergewicht und Adipositas gemessen mit BMI als auch zwischen Hüftumfang und KRF [3]. Berücksichtigt werden muss, dass diese Effekte stark von der verwendeten Standardisierung des KRF-Maßes beeinflusst werden können [65, 66]. Sowohl in den Auswertungen von DEGS1 als auch in den meisten im systematischen Review eingeschlossenen Studien wurden für das Körpergewicht adjustierte Maße der KRF verwendet (z.B. $\dot{V}O_2max$ in ml / min / kg). Sensitivitätsanalysen zeigten jedoch für die Assoziation zwischen BMI und KRF keinen signifikanten Unterschied zwischen Studien mit und ohne Körpergewichtsstandardisierung der KRF [1].

4.2 Faktoren der körperlichen Aktivität

Als Reaktion auf körperliche Aktivität im Allgemeinen und insbesondere sportliche Aktivität reagiert der menschliche Organismus üblicherweise mit kurz- und langfristigen physiologischen Adaptionsprozessen, die auch zu einer Steigerung der KRF führen. Da größere Aktivitätsumfänge auch zu höherer Steigerung der KRF führen, ist es naheliegend, dass sowohl im überwiegenden Teil der in Publikation I eingeschlossenen Studien als auch in den Auswertungen der DEGS1 Studie in Publikation III ein positiver Zusammenhang zwischen Umfang der körperlichen Aktivität und Ausmaß der KRF beobachtet werden konnte [1, 3]. Wie in Publikation I gezeigt, wurde in den meisten Fällen sportliche Aktivität oder körperliche Aktivität in der Freizeit erfasst [1]. Studien konnten jedoch zeigen, dass die bereichsspezifische körperliche Aktivität durchaus unterschiedliche Gesundheitseffekte haben kann. Insbesondere zur arbeitsbezogenen körperlichen Aktivität liegen in Bezug auf unterschiedliche *Outcomes* Studien vor, die auf keinen oder sogar einen negativen Effekt von arbeitsbezogener körperlicher Aktivität hindeuten [67, 68]. Als ein möglicher Erklärungsansatz für diesen geringeren Gesundheitsnutzen wird diskutiert, dass arbeitsbezogene körperliche Aktivität häufig nicht eine ausreichende Intensität und Dauer hat, um die KRF nachhaltig zu verbessern [34, 69]. Die Auswertungen der DEGS1 Studie können diesen Befund zumindest teilweise bestätigen. So zeigt sich für Frauen, aber nicht für Männer, dass insbesondere die Kombination von wenig freizeitbezogener, aber hoher arbeitsbezogener körperlicher Aktivität mit einer niedrigen KRF einhergeht. Eine mögliche Erklärung für diesen Unterschied könnte in der unterschiedlichen Berufsstruktur von Männern und Frauen zu finden sein: Wie auch Auswertungen der DEGS1-Daten zeigen, arbeiten Männer in körperlich anspruchsvollen Berufen überwiegend in handwerklichen und technischen Berufen, während Frauen in körperlich anspruchsvollen Berufen überwiegend in der Pflege und im Servicebereich tätig sind [4]. Gerade diese Berufe sind im überwiegenden Maße durch geringere Entscheidungsautonomie und hohe Arbeitsbelastungen betroffen, wie beispielsweise für Deutschland Studien aus dem Pflegebereich zeigen [70, 71].

4.3 Weitere Verhaltensfaktoren

In den Auswertungen der DEGS1 Studie zeigt sich ein inverser Zusammenhang zwischen ehemaligem Rauchen und KRF, der jedoch nach Kontrolle für anthropometrische Maße und körperliches Aktivitätslevel nicht mehr nachweisbar war [3]. Auch in der Literaturübersicht konnten nicht alle Studien einen Zusammenhang nachweisen, insbesondere Längsschnittuntersuchungen zeigten jedoch einen Zusammenhang zwischen Tabakkonsum und KRF. Als mögliche Erklärungsansätze können die tabak-assoziierte Schädigung der Lungenfunktion und die damit verbundene Einschränkung der KRF [72], aber auch eine mögliche Konfundierung mit dem Bildungsstatus in Betracht gezogen werden.

Im Gegensatz zum Rauchen zeigen die Auswertungen der DEGS1 Studie für Frauen einen positiven Zusammenhang zwischen Alkoholkonsum und KRF [3]. Dieser Befund wurde auch in anderen Studien beobachtet, wobei insgesamt nur wenige Studien vorliegen [1]. Auch hier kann eine Konfundierung durch den sozioökonomischen Status in Betracht gezogen werden, da sowohl Alkoholkonsum als auch körperliche Aktivität und KRF insbesondere bei Frauen mit einem höheren Sozialstatus assoziiert sind.

Das Ernährungsverhalten ist in Bezug auf einen Zusammenhang mit KRF noch sehr wenig untersucht worden [1]. In den Auswertungen der DEGS1-Daten zeigte sich ausschließlich für den Obstkonsum eine deutliche Assoziation mit der KRF bei Männern [3]. Dabei muss berücksichtigt werden, dass hierbei nicht für den Energieverbrauch adjustiert werden konnte. Dementsprechend könnte der Zusammenhang auch durch einen grundsätzlich höheren Energiebedarf und eine dementsprechend höhere Nährstoffzufuhr bei Personen mit hoher KRF erklärt werden. Die Adjustierung für BMI, Körpergewicht und körperliche Aktivität kann diesen Effekt jedoch möglicherweise teilweise wieder ausgleichen.

4.4 Soziodemografische Faktoren: Alter und Geschlecht

Die in der Literatur konsistent beschriebene niedrigere KRF bei Frauen im Vergleich zu Männern [1] zeigte sich in den Auswertungen der DEGS1 Studie auch für die Erwachsenenbevölkerung Deutschlands [3]. Als Begründung wird in erster Linie die durchschnittlich niedrigere Körper- und Organgröße, das niedrigere Herzzeitvolumen und der höhere Körperfettanteil bei Frauen im Vergleich zu Männern angeführt [17]. Hierfür spricht auch, dass, wenn die KRF relativ zur Muskelmasse dargestellt wird, häufig kein Geschlechterunterschied mehr feststellbar ist [73]. Gleichzeitig könnten auch soziale und verhaltensbasierte Unterschiede als mögliche Ursache für Unterschiede in der KRF zwischen Frauen und Männern in Betracht gezogen werden [74].

Der Rückgang der KRF mit dem Alter, der in der Literatur weitgehend konsistent beschrieben ist [1], kann durch körperliche Effekte wie der Muskelatrophie im Zuge des biologischen Alterungsprozesses, Lebensstilveränderungen wie ein eingeschränktes Aktivitätsverhalten sowie eine höhere Krankheitslast im Alter erklärt werden [75]. Eine negative Assoziation zwischen Alter und KRF zeigt sich auch anhand der DEGS1-Daten, jedoch nach Adjustierung für körperliche Aktivität nur noch bei Frauen [3]. Der Effekt von körperlicher Aktivität auf die KRF im Altersgang ist in verschiedenen Studien untersucht worden: während auf Basis von Querschnittsdaten kein Einfluss der körperlichen Aktivität festgestellt werden konnte [76, 77], zeigen Längsschnittstudien einen geringeren Abfall der KRF bei Personen mit höherem Aktivitätslevel [78].

4.5 Sozioökonomische und interpersonelle Faktoren

Sozioökonomische Maße wie sozioökonomische Indizes und sozioökonomische Kategorisierungen des Wohnumfeldes zeigten sich in der Literatur überwiegend positiv mit KRF assoziiert [2]. Wurde der Bildungsstand als Indikator des sozioökonomischen Status verwendet, zeigte sich entweder ebenfalls ein positiver Zusammenhang oder ein U-förmiger Zusammenhang mit KRF. In der in Publikation II durchgeführten Metaanalyse zeigten Männer und Frauen mit hohem Bildungsstatus eine höhere KRF im Vergleich zu Personen mit niedrigem Bildungsstatus [2]. Diese Ergebnisse sind in Übereinstimmung mit den Ergebnissen von Studien, die den Zusammenhang von körperlicher Aktivität in der Freizeit und Sozialstatus untersuchen [79]. Da körperliche Aktivität in der Freizeit wiederum stark mit einer höheren KRF assoziiert ist, könnte dieser Effekt eine mögliche Erklärung für den Zusammenhang von Sozialstatus und KRF sein. Darüber hinaus ist ein niedriger Sozialstatus noch mit weiteren Faktoren wie Rauchen [80] und Adipositas [81] assoziiert, die ebenfalls mit einer niedrigeren KRF einhergehen, was den Effekt des Sozialstatus auf die KRF noch verstärken könnte. Im Unterschied zu diesen Befunden zeigen die Auswertungen der DEGS1-Daten keine Assoziation der KRF mit Bildung und Einkommen. Nur bei Frauen ist ein höherer Berufsstatus mit einer höheren KRF assoziiert [3], was durch wenige Studien, die den Zusammenhang von Berufsstatus und KRF untersuchen, gestützt wird [1, 2]. Der Zusammenhang von Berufsstatus und KRF könnte damit erklärt werden, dass ein niedriger Berufsstatus mit einem höheren Maß an arbeitsbezogener körperlicher Aktivität einhergeht, was, wie oben erläutert, insbesondere bei Frauen mit einer niedrigen Fitness assoziiert ist [4].

Die Auswertungen der DEGS1-Daten lieferten darüber hinaus keinen deutlichen Hinweis darauf, dass interpersonelle Faktoren wie soziale Unterstützung oder der Familienstatus mit KRF assoziiert sind [3].

4.6 Stärken und Limitationen

4.6.1 Publikation I & II

Bei beiden Publikationen handelt es sich um die ersten systematischen Reviews zu potentiellen Korrelaten und Determinanten der KRF. Die Vergleichbarkeit der eingeschlossenen Studien ist dadurch erschwert, dass sich in vielen Fällen die verwendeten Messverfahren der KRF teilweise erheblich unterscheiden. Ebenfalls unterscheiden sich die verwendeten statistischen Verfahren und Kontrollvariablen zwischen den eingeschlossenen Studien, so dass im Fall von Publikation I keine, im Fall von Publikation II nur eine Metaanalyse auf Basis von vier Studien durchgeführt werden konnte, die zudem für Frauen eine hohe Heterogenität aufwies. Darüber hinaus wurde in der Ergebniszusammenfassung nicht zwischen Quer- oder Längsschnittstudien unterschieden, so dass keine Unterscheidung der untersuchten potentiellen Einflussfaktoren in Determinanten und Korrelate bzw. Moderatoren und Mediatoren möglich war. Die Generalisierbarkeit der Ergebnisse ist zudem dadurch eingeschränkt, dass ein sehr großer Teil der eingeschlossenen Studien aus Hocheinkommensländern stammt.

4.6.2 Publikation III & IV

Bei den verwendeten Daten der DEGS1-Studie handelt es sich um Querschnittsdaten, die keine Rückschlüsse über die Kausalbeziehung von KRF und potentiellen Einflussfaktoren ermöglichen. Zudem ist die Generalisierbarkeit der Ergebnisse möglicherweise dadurch eingeschränkt, dass durch die vor Durchführung des Ergometer-Tests erfolgte Feststellung der Testtauglichkeit beispielsweise Personen mit Einnahme von Antihypertonika vom Test ausgeschlossen wurden und es sich dementsprechend um eine relativ gesunde Studienpopulation handelt. Es ist zu erwarten, dass testuntaugliche Personen eine niedrigere KRF haben als in die Untersuchung eingeschlossenen Teilnehmenden. Wie in großen epidemiologischen Studien üblich, wurde die $\dot{V}O_2max$ nicht durch den „Goldstandard" maximaler Belastungstests mit Gasanalyse erfasst, sondern auf Basis eines submaximalen Ergometertests geschätzt, der im Vergleich zu maximalen Belastungstests mit einer niedrigeren Validität einhergeht [82], aber als üblicher Standard in vergleichbaren bevölkerungsbezogenen Studien gilt. In Publikation III und IV wurden umfangreich Variablen in die Analyse mit einbezogen, die zum großen Teil anhand von Selbstangaben der Teilnehmenden erfasst wurden. Dementsprechend kann ein Reporting-Bias, beispielsweise durch sozial erwünschtes Antwortverhalten oder Erinnerungsfehler, nicht ausgeschlossen werden.

5. Fazit

Für die Prävention nicht übertragbarer Krankheiten stellt die KRF eine wichtige Gesundheitsressource dar. Weltweit wurde in langfristigen Trenduntersuchungen eine sinkende Tendenz der KRF seit den 1980er Jahren festgestellt [83, 84]. Demensprechend sollte die Verbesserung der KRF in der Bevölkerung und insbesondere in besonders gefährdeten Gruppen ein zentrales Ziel einer (nationalen) Strategie zur Prävention nicht übertragbarer Krankheiten sein. Für die Planung und Durchführung von Maßnahmen zur Prävention nichtübertragbarer Krankheiten ist es von entscheidender Bedeutung, an den „Ursachen der Ursachen“ dieser Erkrankungen anzusetzen [85, 86]. Diese Dissertation liefert dabei wichtige Erkenntnisse für das Verständnis warum manche Menschen fitter als andere sind. Erstmalig wurden in systematischen Reviews potentielle individuelle Einflussfaktoren der KRF identifiziert. Von diesen Ergebnissen ausgehend wurde die Assoziation dieser Faktoren mit Messdaten der KRF eines repräsentativen Samples der Erwachsenenbevölkerung Deutschlands überprüft.

Diese Ergebnisse können als Grundlage für die Weiterentwicklung eines ätiologischen Modells der KRF verwendet werden, das die Wechselwirkungen der einzelnen Faktoren berücksichtigt. Für ein tiefgreifenderes Verständnis dieser Beziehungen ist weitere bevölkerungsbasierte als auch klinische Forschung mit sowohl longitudinalen Beobachtungs- als auch Interventionsstudien notwendig, da für einige der Faktoren noch unklar ist, ob tatsächlich eine Kausalbeziehung vorliegt. Zudem ist es wichtig in zukünftigen Forschungsansätzen, Umwelt- und politische Rahmenbedingungen (z.B. bebaute Wohnumgebung, Radverkehrsnetz) zu berücksichtigen und die Beziehung zwischen diesen Faktoren und KRF weiter zu untersuchen.

6. Literaturverzeichnis

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Eidesstattliche Versicherung

„Ich, Johannes Zeiher, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: „*Warum sind manche Menschen fitter als andere? Einflussfaktoren der kardiorespiratorischen Fitness bei Erwachsenen in Deutschland (Why are some people fitter than others? Influencing factors of cardiorespiratory fitness among adults in Germany)*“ selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.

Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren/innen beruhen, sind als solche in korrekter Zitierung kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) werden von mir verantwortet.

Ich versichere ferner, dass ich die in Zusammenarbeit mit anderen Personen generierten Daten, Datenauswertungen und Schlussfolgerungen korrekt gekennzeichnet und meinen eigenen Beitrag sowie die Beiträge anderer Personen korrekt kenntlich gemacht habe (siehe Anteilserklärung). Texte oder Textteile, die gemeinsam mit anderen erstellt oder verwendet wurden, habe ich korrekt kenntlich gemacht.

Meine Anteile an etwaigen Publikationen zu dieser Dissertation entsprechen denen, die in der untenstehenden gemeinsamen Erklärung mit dem/der Erstbetreuer/in, angegeben sind. Für sämtliche im Rahmen der Dissertation entstandenen Publikationen wurden die Richtlinien des ICMJE (International Committee of Medical Journal Editors; www.icmje.og) zur Autorenschaft eingehalten. Ich erkläre ferner, dass ich mich zur Einhaltung der Satzung der Charité – Universitätsmedizin Berlin zur Sicherung Guter Wissenschaftlicher Praxis verpflichte.

Weiterhin versichere ich, dass ich diese Dissertation weder in gleicher noch in ähnlicher Form bereits an einer anderen Fakultät eingereicht habe.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§§156, 161 des Strafgesetzbuches) sind mir bekannt und bewusst.“

Berlin, den 28.08.2020

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Johannes Zeiher

Anteilserklärung

Publikation	Impact Factor	Anteilserklärung

1. Zeiher J, Ombrellaro KJ, Perumal N, Keil T, Mensink GBM, Finger JD (2019) Correlates and determinants of cardiorespiratory fitness in adults: a systematic review. Sports Medicine - Open 5(39) 10.1186/s40798-019-0211-2	-	- Federführende Erstellung der Recherchestrategie und Auswertungsstrategie
		- Eigenständiges Durchführen der Literaturrecherche zu den Einflussfaktoren der KRF in Absprache mit Betreuern
		    - Screening der gefundenen Treffer (Abb. 2)
		    - Extraktion der Daten aus den eingeschlossenen Studien (Tab. 1&2, Abb. 3&4).
		    - Qualitätsbewertung der eingeschlossenen Studien (Appendix 1).
		- Erstellung aller Tabellen und Abbildungen
		- Durchführung der Evidenzsynthese (Tab. 2)
		- Federführende Verfassung des Manuskripts

2. Ombrellaro KJ, Perumal N, Zeiher J, Hoebel J, Ittermann T, Ewert R, Dorr M, Keil T, Mensink GBM, Finger JD (2018) Socioeconomic Correlates and Determinants of Cardiorespiratory Fitness in the General Adult Population: a Systematic Review and Meta-Analysis. Sports Medicine - Open 4(1):25. 10.1186/s40798-018-0137-0	-	- Mitarbeit bei der Durchführung der Literaturrecherche zu den sozioökonomischen Einflussfaktoren der KRF :
		    - Extraktion der Daten aus den eingeschlossenen Studien (Tab. 2).
		    - Qualitätsbewertung der eingeschlossenen Studien (Tab. 1).
		- Mitarbeit beim Verfassen des Manuskripts
		- Zweiter Blick bei der Durchführung der statistischen Analyse (Meta-Analyse; Abbildung 2)

3. Zeiher J, Manz K, Kuntz B, Perumal N, Keil T, Mensink GBM, Finger JD (2020) Individual and Interpersonal Correlates of Cardiorespiratory Fitness in Adults – Findings from the German health interview and examination survey Scientific Reports 10(445). 10.1038/s41598-019-56698-z	3.998	- Federführende Erstellung der Auswertungsstrategie in Absprache mit Betreuern - Eigenständige Aufbereitung der Surveydaten (DEGS1) - Planung und Berechnung aller statistischen Auswertungen zu den Einflussfaktoren der KRF (Tab.1-3, Abb.2) - Eigenständiges Durchführen der Literaturrecherche - Federführende Verfassung des Manuskripts - Korrespondenz im Publikationsprozess
4. Zeiher J, Duch M, Kroll LE, Mensink GBM, Finger JD, Keil T (2020) Domain-specific physical activity patterns and cardiorespiratory fitness among the working population: Findings from the cross-sectional German Health Interview and Examination Survey. BMJ Open 10(4). 10.1136/bmjopen-2019-034610	2.496	- Federführende Erstellung der Auswertungsstrategie in Absprache mit Betreuern - Eigenständige Aufbereitung der Surveydaten (DEGS1, Tab. 1) - Planung und Berechnung der statistischen Modelle zum Zusammenhang der bereichsspezifischen körperlichen Aktivität und KRF (Tab. 2-4; Abb. 2) - Eigenständiges Durchführen der Literaturrecherche - Federführende Verfassung des Manuskripts - Korrespondenz im Publikationsprozess

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Unterschrift, Datum und Stempel des/der erstbetreuenden Hochschullehrers/in

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Unterschrift des Doktoranden/der Doktorandin

Originalarbeiten als Promotionsleistung

Publikation I

Zeiher J, Ombrellaro KJ, Perumal N, Keil T, Mensink GBM, Finger JD (2019) Correlates and determinants of cardiorespiratory fitness in adults: a systematic review. Sports Medicine - Open 5(39) 10.1186/s40798-019-0211-2

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Sports Medicine - Open

SYSTEMATIC REVIEW

Open Access

Correlates and Determinants of Cardiorespiratory Fitness in Adults: a Systematic Review

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Abstract

Background: Enhanced cardiorespiratory fitness (CRF) is now a well-established predictor of numerous adverse health outcomes. Knowledge about the pathways leading to enhanced CRF is essential for developing appropriate interventions. Hence, the aim of this review was to provide a detailed overview of the current state of research regarding individual factors associated with or influencing CRF among the general adult population.

Methods: We searched the PubMed, EMBASE, and Cochrane Library databases and also conducted a search for grey literature (Google Scholar). Eligible indicators of CRF were objectively assessed measures of CRF by submaximal or maximal exercise testing measured using treadmill or cycle ergometer tests. We included quantitative observational studies of the general adult population. Using a semi-quantitative approach, we compiled summary tables aggregating the study results for each potential correlate or determinant of CRF.

Results: We identified 3005 studies, 78 of which met the inclusion criteria. Almost all of these studies were conducted in high-income countries. Study quality scores assessing the risk of bias in the individual studies ranged from 40 to 100%. Male sex, age (inverse), education, socioeconomic status, ethnicity, body mass index (inverse), body weight (inverse), waist circumference, body fat (inverse), resting heart rate (inverse), C-reactive protein (inverse), smoking (inverse), alcohol consumption, and multiple measures of leisure-time physical activity were independently and consistently associated with CRF.

Conclusions: In synthesizing the current research on the correlates and determinants of CRF among adults, this systematic review identified gaps in the current understanding of factors influencing CRF. Beyond the scope of this review, environmental and interpersonal determinants should be further investigated.

Systematic Review Registration: PROSPERO, CRD42017055456.

Keywords: Cardiorespiratory fitness, Aerobic fitness, Risk factors, Individual factors, VO_{2max}, Health behavior, Systematic review

Key Points

- This study is a systematic review of evidence concerning the correlates and determinants of CRF among adults in 78 included studies, which were conducted in 20 countries.
- Whereas factors such as age and waist circumference were consistently associated with cardiorespiratory fitness, there was conflicting evidence for many other factors, revealing research gaps for future studies to address.
- This comprehensive summary of a large body of evidence may be used to develop evidence-based interventions to improve fitness levels in the general adult population.

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Background

A key aspect of the global strategy to tackle non-communicable diseases (NCDs) is the promotion of physical activity (PA) and the reduction of sedentary behavior [79, 80]. PA has been linked to positive health outcomes, such as lower risks of ischemic heart disease, stroke, diabetes, and depression, and to a reduction in all-cause mortality [81]. Cardiorespiratory fitness (CRF) is another dimension of physical health linked to beneficial health outcomes. Whereas PA is behavioral and can be described as any bodily movement that is produced by skeletal muscles and requires energy exposure, CRF is a trait and is defined as the ability of the circulatory, respiratory, and muscular systems to supply oxygen during prolonged moderate-to-vigorous dynamic exercise [82, 83]. Therefore, PA and CRF are related, but not identical. CRF is usually measured using treadmill or ergometer exercise tests and is often expressed as maximal oxygen consumption (VO_{2max}), whereas PA is often assessed through self-report.

Over the past 30 years, research has shown that the positive effects of enhanced physical fitness, and especially CRF, are comparable to or even greater than those of PA [85–89]. In addition to predicting all-cause mortality, low CRF is an established predictor of cancer mortality [90], depression [91, 92], and metabolic syndrome [93, 94]. Among the risk factors for cardiovascular disease (CVD), poor CRF has been found to be the most powerful predictor of morbidity [95].

Because of the importance of CRF in NCD prevention, it is crucial to better understand the correlates and determinants of CRF in the general population. CRF is known to be partly genetically determined [96, 97]. In addition to hereditary determinants and PA, many other individual and environmental factors are presumed to influence CRF [84, 88, 98]. A growing body of work links CRF to factors such as age [99], sex [100], smoking [8], alcohol consumption [101], body mass index (BMI) [23], educational status [102], and the residential built environment [103]. Although initial attempts have been made to develop a model of CRF and its determinants [84, 98], so far, there is no comprehensive model or framework that incorporates a wide range of influencing factors and the interrelations among them, as has been done in models of obesity [104, 105] and PA [106, 107]. Moreover, although researchers have systematically reviewed the factors associated with PA [106], to our knowledge, there has been no systematic review of the factors associated with CRF. Knowledge about the various pathways leading to the development of fitness is essential for creating appropriate interventions.

Hence, the aim of this systematic review was to provide a detailed overview of the current state of research regarding factors associated with ("correlates") or influencing ("determinants") CRF among the general adult population. Furthermore, we aimed to analyze the consistency of the reported associations. To narrow the study focus, we concentrated on individual factors associated with CRF, omitting interpersonal and environmental correlates and determinants.

Methods

Protocol and Registration

The review methodology, including the search strategy, data collection, and quality assessment of the included studies, was pre-specified and has been published in a review protocol [108]. The review was registered in the International Prospective Register of Systematic Reviews (PROSPERO, CRD42017055456). We followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines whenever applicable.

Search Strategy and Eligibility Criteria

Relevant studies were located from different sources: We searched the PubMed, EMBASE, and Cochrane Library databases from inception to Present. The last search was run on 1 February 2017. In addition, we conducted a search for grey literature (Google Scholar). A limited update literature search was performed from 01 February 2017 to 6 June 2019 on PubMed. We used a broad range of search terms for CRF measures (outcome; e.g., "cardiorespiratory fitness") and general correlates and determinants (exposures; e.g., "health behavior") to ensure that all potentially relevant articles investigating the factors associated with CRF were included [108]. We also cross-checked the references of the articles selected for full-text screening to locate additional studies. No language, text availability, publication status, or date restrictions were imposed. Eligible indicators of CRF were objectively assessed measures of CRF by submaximal or maximal exercise testing. Therefore, both direct indicators measured via spiroergometry and indirect indicators calculated via metabolic equations of oxygen consumption were included. We only included studies that assessed CRF by treadmill or cycle ergometer. The preferred laboratory measure of CRF (the "gold standard") is maximal oxygen consumption (VO_{2max}), which is measured in milliliters per kilogram per minute (ml/kg/min) during exercise and reflects a person's maximal ability in terms of oxygen uptake, use, and transport [109]. VO_{2max} is defined as the point when oxygen consumption reaches a plateau and cannot be increased with an increase in effort [83, 110]. However, in exercise testing, such a clear plateau often cannot be achieved, and, instead, the highest obtained VO_2 value, regardless the subject's effort, (VO_{2peak}) is used [110]. Because the distinction between these two measures was not always clear in the included studies [111], this review uses the term VO_{2max} for both VO_{2max} and VO_{2peak}.

To structure our search strategy, we used a conceptual framework that locates CRF on the pathway to NCDs and defines and categorizes potential factors associated with CRF. Based on the method recommended by Victoria et al. [112], we proposed this framework by adopting elements of different ecological models [108] (Fig. 1).

As mentioned above, to limit the scope of this systematic review, we focused on individual correlates and determinants of CRF and excluded environmental (e.g., public green spaces) and interpersonal (e.g., social support) factors. The following categories of factors were considered: (1) sociodemographic factors (e.g., age, sex, and education); (2) anthropometric measures (e.g., BMI, weight, and waist circumference [WC]; (3) vital parameters (e.g., resting heart rate [HR] and blood pressure [BP]); (4) comorbidities and medications; (5) biomarkers (e.g., C-reactive protein [CRP]); (6) PA parameters (e.g., leisure-time PA [LTPA]); and (7) other health-related behaviors (e.g., smoking and nutrition). Genetic factors, such as specific genetic variants associated with CRF trainability [113], were not included in this review.

In this review, we included quantitative observational studies (cohort studies, case–control studies, and cross-sectional studies) reporting individual correlates of CRF

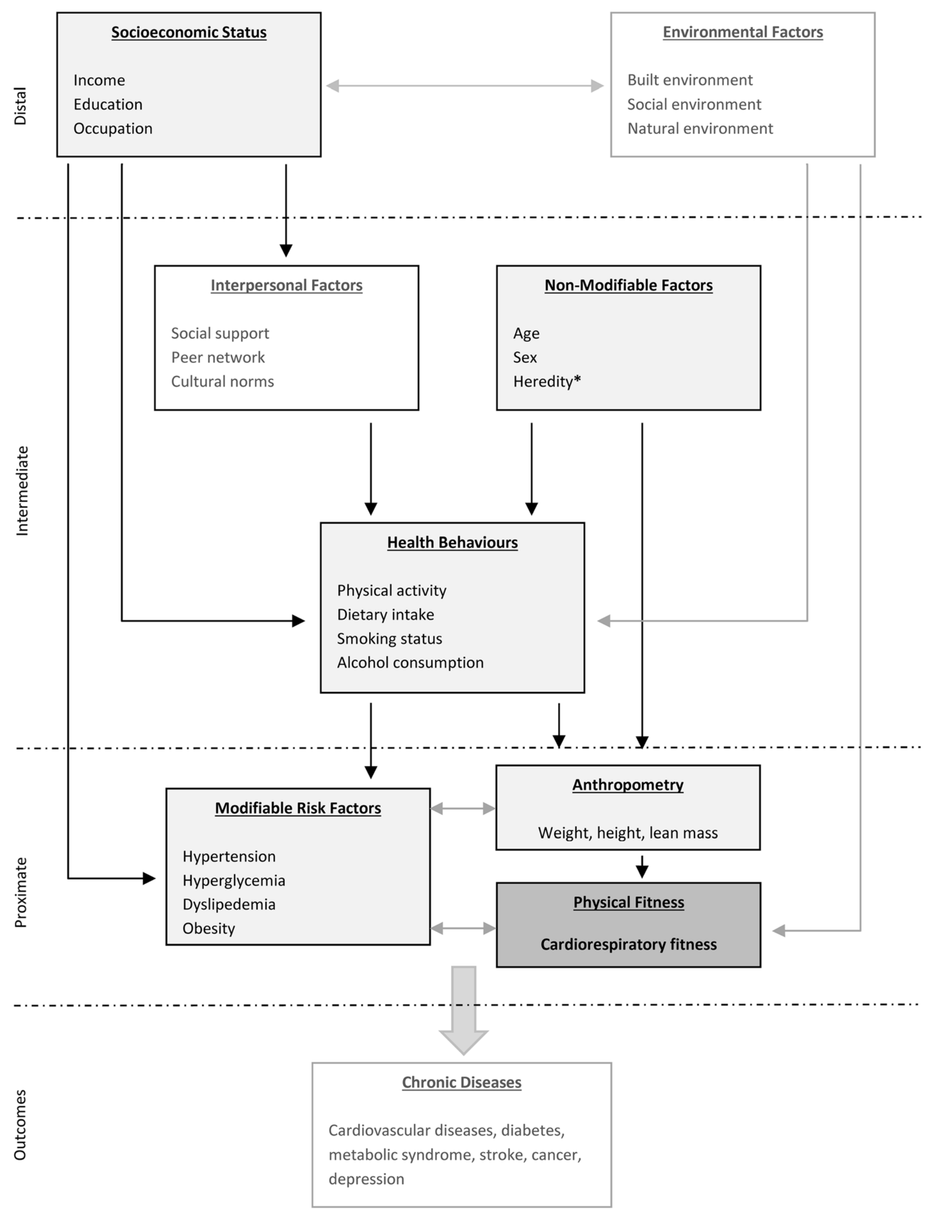

Fig. 1 Conceptual framework of the correlates and determinants of cardiorespiratory fitness. Light grey boxes: potential individual correlates and determinants of cardiorespiratory fitness. *Genetic factors were not in the scope of this review

in the general adult population. The following exclusion criteria were applied: (1) studies on interventions or trials promoting CRF or PA; (2) studies focusing on children (aged 0–11 years), adolescents (aged 12–17 years), or older adults (aged 80+ years), although studies investigating a broad age range were not excluded and may include participants aged younger than 18 years or older than 80 years; (3) studies with highly select groups of participants not representative of CRF/PA in the general population (e.g., specific occupations such as firefighters or special forces, athletes, sports students, or institutionalized populations such as patients in hospitals or nursing homes); (4) studies presenting only univariate results that were unadjusted for confounding; (5) studies that assessed CRF by means other than bicycle ergometer or treadmill; and (6) reviews, letters to the editor, commentaries, and editorials.

Data Extraction and Quality Assessment

We imported all search results into Endnote X7 (Thomas Reuters, USA) reference management software and removed duplicates. At the first stage of screening, we reviewed the titles and abstracts. At the second stage, we assessed full-text articles for eligibility. The assessment was performed by two independent reviewers (NP and KJO at the first stage, JZ and KJO at the second stage). If the reviewers disagreed, a third reviewer was included in the discussion (JDF). Final decisions were made by consensus. From the final included studies, the following information was extracted and transferred to a detailed extraction worksheet, which was developed and pilot tested in advance: study characteristics (title, year, study name, country, and study period), study methods (e.g., study type, sample size, and inclusion/exclusion criteria), study population characteristics (e.g., age range and sex ratio), details of CRF assessment (e.g., test machine and exercise test protocol), analytical methods (e.g., statistical method and type of reported outcome), results, and reported limitations (Additional file 4: Data extraction table). When different multivariable models were reported for a sample, we extracted the fully adjusted models. The data extraction was conducted independently by two authors (JZ and KJO). Disagreements were solved by discussion; if agreement could not be reached, a third author (JDF) was involved, and decisions were made by a simple majority. The limited search update was performed by two authors (JZ and JDF [10% random sample at title and abstract screening, full sample at full text screening]). Information from eligible studies retrieved in the update was extracted to a separate table (Additional file 3: Table OR1).

Additional information was obtained through a request to the author for one study, where further results were mentioned but not presented in detail [49]. The author responded, but this additional information was not used because the results violated the inclusion criteria. We contacted authors of two studies to clarify the direction of a reported association [18] and for further details about the study period [65]. Both of these authors responded, and the additional information was included in this study.

Risk of bias in each study was also assessed independently by two authors (JZ and KJO) using a customized version of the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, published by the National Heart, Lung, and Blood Institute at the National Institutes of Health, USA [114]. We categorized risk of bias as "high" when a study reached < 50% of the fulfillment score, "moderate" when a study reached 50–75%, and "low" when > 75% of the criteria were fulfilled. Further details about this risk assessment procedure have been published elsewhere [108].

Coding and Summarizing

We compiled summary tables aggregating the existing research on each potential correlate or determinant of CRF. For this purpose, we modified the "semi-quantitative approach" originally proposed by Sallis et al. [115] (adapted by [116, 117]). This approach allowed summary measures to be calculated for each analyzed exposure, even when the heterogeneity among studies was high and no meta-analysis was possible. Following this approach, in the present article, we distinguish between the terms "study" and "sample." Each article included in this review is referred to as a study. Studies where the results were presented separately for men and women were counted as two samples. Studies that presented results only for the total population (men and women) and those that focused on only men or women were counted as one sample. Hereafter, we use the term "study" to refer to each article included in this review and the term "sample" to refer to each (sex-specific) sample or subsample.

For each sample, a significant direct or inverse association between CRF and the exposure is presented as "+" or "−" in the column "related to CRF"; non-significant associations are shown in the column "unrelated to CRF" ("0"). The findings are summarized by presenting the total number of samples and the numbers of samples with direct, indirect, and non-significant associations. Finally, following an approach applied in other semi-quantitative reviews [115–117], a summary measure for each association was calculated as follows: Agreement in direction in at least 60% of all samples was graded as a positive ("+"), negative ("−"), or non-significant association ("0"). If none of the categories had a majority of at least 60%, the correlate was assessed as unclear ("?"). Outcomes that were heavily investigated (i.e., in at least ten independent samples) for which there was result agreement in at least 80% of the samples are denoted by "++," "− −," or "00." Summary measures were calculated only if an exposure was investigated in three or more individual samples; otherwise, the correlate was marked as not applicable ("n/a"). Each unique association is reported separately. Separate studies drawing on the same study population and reporting redundant exposures are presented in parentheses and were counted as one unit of analysis. For example, the two studies using the National Health and Nutrition Examination Survey data from the same study period that presented data on the association of age with CRF are both listed in the summary table but were counted as only one sample. In rare cases when separate studies using the same sample had contradictory results, we present the relevant details in a footnote.

Outcome Variable: CRF

For each sample included in this review, we extracted only one CRF measure, even if multiple measures were reported. Where it was assessed, we used the results for VO_{2max} because this is the gold standard for measuring CRF. If VO_{2max} was not reported, we summarize the results for the reported measures if they showed the same direction. When the results varied regarding the reported association with a specific exposure, we report the divergent results in a note at the end of the summary table. Additional information is also provided as a footnote to this table for cases where the association between CRF and a given exposure was non-linear (e.g., U-shaped) or the association was reported only for subgroups divided by variables other than sex (e.g., by ethnicity).

Exposure Variables: Individual Correlates and Determinants of CRF

We extracted each individual correlate or determinant of CRF and grouped them into the following categories: sociodemographic factors, anthropometric measures, vital parameters, comorbidities and medications, biomarkers, activity parameters, and other health behaviors. Correlates or determinants considered as individual factors that were not assignable to one of these categories (e.g., preterm birth) were grouped under "other." Where possible, we clustered similar factors to enable the calculation of summary measures.

We performed sensitivity analyses for all exposures that were reported in at least ten samples. We cross-tabulated the numbers of samples with positive associations, negative associations, and null findings by sex (men/women/mixed sample), test machine (cycle ergometer/treadmill), and CRF measure (VO_{2max}, direct/VO_{2max}, indirect/other) and checked for significant differences using Fisher's exact test. Using the same approach, we checked whether the results for BMI varied across CRF measures adjusting for body weight vs. measures that did not adjust for body weight.

Results

Study Characteristics

We identified a total of 78 articles for inclusion in this review. The complete selection process is shown in the PRISMA Flow Diagram (Fig. 2).

The initial search in PubMed, EMBASE, and the Cochrane Library yielded 3016 records. Following the removal of duplicates, 216 articles were added from Google Scholar and the reference cross-check. After title and abstract screening, 338 records remained for full-text screening. A total of 260 of these records did not fulfil the eligibility criteria. All included studies were published in English. The dates of publication ranged from 1966 to 2017; the vast majority of articles were published after 2000 (see Fig. 3).

General characteristics of the studies reviewed can be found in Table 1.

Most studies were from North America (31) or Europe (29), and there were 14 from Asia and four from Oceania (including Australia). Thus, almost all studies were from high-income countries (74), according to the World Bank classification; only four were from lower-middle or upper-middle-income countries, and none were from low-income countries. Except for one case–control study, all of the studies were cross-sectional (59) or cohort (18) studies. Almost two-thirds of the studies investigated both men and women (48), whereas eight studies reported results only for women and 17 reported results only for men. Five studies did not report the sex ratio of the study participants. The age range across the studies was 13 to 96 years. Sample sizes ranged from 79 to 218,820. A variety of statistical techniques were used to investigate the associations between CRF and potential correlates and determinants, including general linear models such as analysis of variance; analysis of covariance; (multiple) linear, logistic, and quadratic regression; partial correlation; and general estimating equations.

The quality scores assessing the risk of bias in the individual studies ranged from 40 to 100% (Additional file 1: Table OR1.1). Thirty studies were classified as having low risk of bias, 41 were classified as having medium risk of bias, and seven were classified as having high risk of bias.

CRF

Half of the studies (39) used directly assessed VO_{2max} via gas analysis as the outcome variable, 19 reported estimated VO_{2max}, and 19 used only measures other than VO_{2max} as the outcome variables. Directly assessed VO_{2max} via gas analysis was more common in studies with smaller sample sizes. No studies with more than

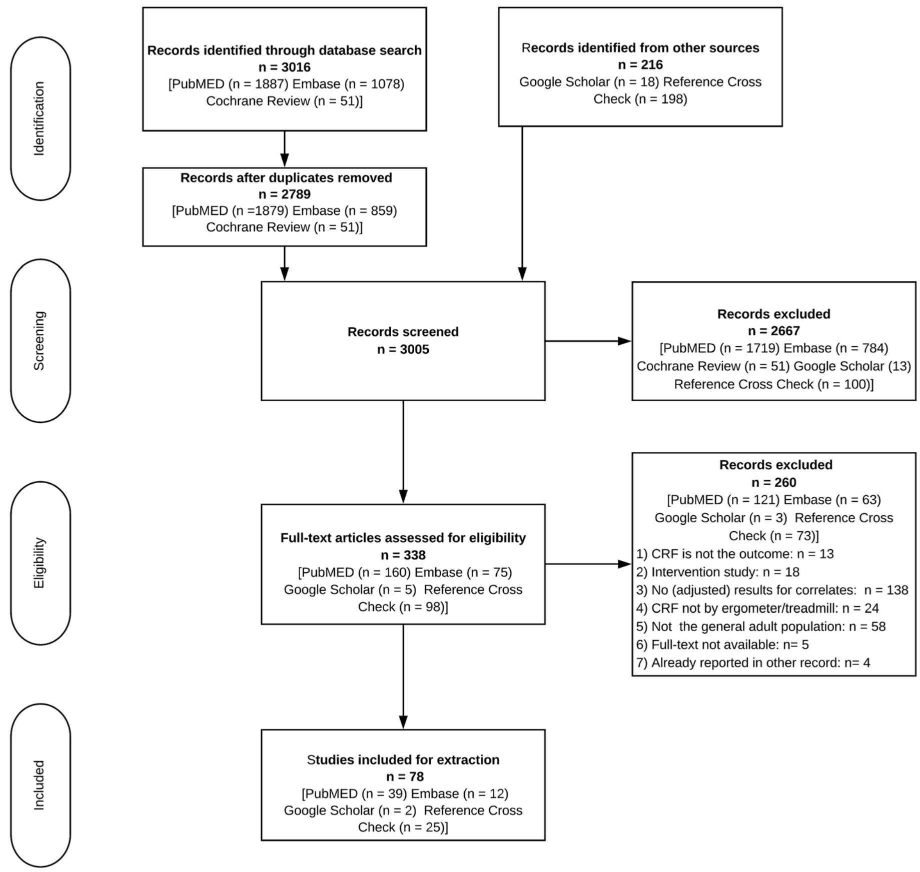

Fig. 2 PRISMA flow diagram. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

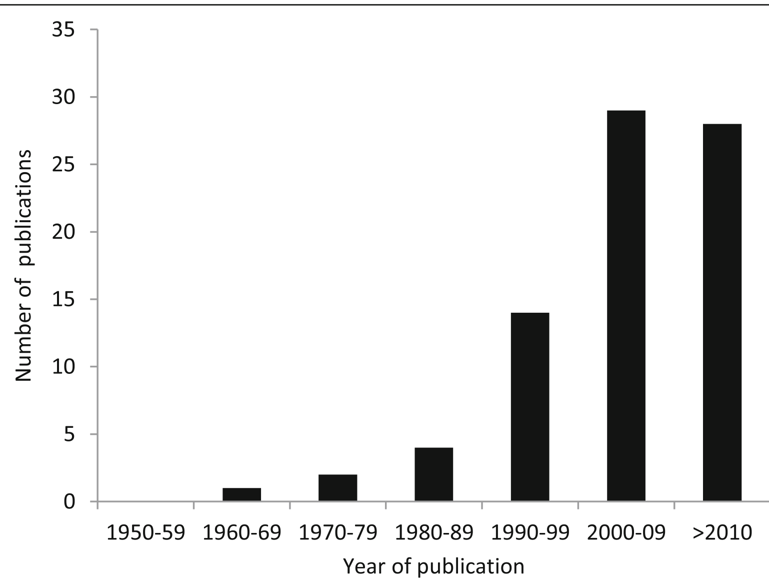

Fig. 3 Distribution of publications by year of publication (*n* = 78)

Table 1 Included studies categorized by study characteristics

	Number of studies	%	Reference numbers
Risk of bias			
Low	30	38%	[1, 2, 4, 12, 14–16, 18, 20, 23–26, 31, 34, 36, 40, 42–44, 49, 50, 57, 59, 60, 62, 67, 75–77]
Medium	41	53%	[5–9, 13, 17, 21, 22, 28–30, 32, 33, 35, 37–39, 45–48, 51, 55, 56, 58, 61, 63–66, 68–74, 78]
High	7	9%	[3, 19, 27, 41, 52–54]
Sample size			
< 100	5	6%	[5, 17, 41, 53, 71]
100–299	19	24%	[4, 6, 7, 9, 10, 13, 21, 27, 29, 32, 48, 51, 52, 66, 68, 70, 73, 75, 76]
300–499	9	12%	[3, 8, 16, 33, 38, 39, 49, 72, 78]
500–1999	25	32%	[15, 18, 19, 22–26, 30, 31, 35, 40, 43, 44, 46, 47, 50, 54, 55, 60, 61, 63, 65, 69, 74]
2000–4999	14	18%	[1, 12, 14, 20, 34, 36, 42, 45, 56, 57, 59, 62, 67, 77]
> 5000	6	8%	[2, 11, 28, 37, 58, 64]
Region			
North America	31	40%	[1, 2, 4, 5, 10–12, 14, 17, 19, 21, 22, 28, 33, 34, 37, 42–44, 50–53, 57, 59, 60, 63, 65, 67, 69, 77]
Europe	29	37%	[6, 7, 18, 20, 23–27, 29, 30, 36, 38, 40, 45, 47–49, 55, 56, 62, 64, 66, 70, 71, 75, 76]
Asia	14	18%	[13, 16, 32, 35, 39, 41, 54, 58, 61, 68, 72–74, 78]
Oceania (including Australia)	4	5%	[3, 15, 31, 46]
World Bank income classification			
High-income countries	74	95%	[1–29, 33–60, 62–71, 74–78]
Upper-middle-income countries	2	3%	[72, 73]
Lower-middle-income countries	2	3%	[32, 61]
Low-income countries	0	0%	–
Country			
Canada	1	1%	[51]
United States	30	38%	[1, 2, 4, 5, 10–12, 14, 17, 19, 21, 22, 28, 33, 34, 37, 42–44, 50, 52, 53, 57, 59, 60, 63, 65, 67, 69, 77]
Finland	5	6%	[23, 30, 45, 47, 66]
Sweden	3	4%	[6, 7, 64]
Norway	3	4%	[18, 55, 62]
Netherlands	4	5%	[8, 38, 70, 71]
Germany	6	8%	[20, 25, 26, 29, 36, 40]
United Kingdom	2	3%	[24, 49]
Belgium	2	3%	[48, 76]
Lithuania	1	1%	[27]
Italy	1	1%	[56]
Spain	1	1%	[75]
Israel	3	4%	[16, 35, 58]
Jordan	1	1%	[32]
India	1	1%	[61]
China	2	3%	[72, 73]
Korea	2	3%	[39, 78]
Japan	5	6%	[13, 41, 54, 68, 74]
Australia	2	3%	[15]
New Zealand	2	3%	[31, 46]

Table 1 Included studies categorized by study characteristics *(Continued)*

	Number of studies	%	Reference numbers
Multiple countries	1	1%	[9]
Study design			
Cross-sectional	59	76%	[1–3, 9–14, 16, 18–21, 23–30, 32–36, 39–45, 47–52, 54, 56–59, 61, 62, 65–69, 72, 74, 75, 77, 78]
Longitudinal	18	23%	[6, 15, 17, 22, 31, 37, 38, 46, 53, 55, 60, 63, 64, 70, 73, 76]
Case–control	1	1%	[71]
Sex			
Women only	8	10%	[13, 19, 28, 39, 52, 53, 63, 73]
Men only	17	22%	[3, 5, 10, 17, 23, 32, 35, 45, 47, 48, 50, 55, 56, 61, 64, 74, 76]
Women and men	48	62%	[2, 4, 6–8, 11, 12, 14–16, 18, 20–22, 24–27, 29, 30, 33, 34, 36–38, 40–44, 49, 51, 54, 57–60, 65–72, 75, 78, 79]
NR	5	6%	[1, 9, 31, 46, 62]
Maximal or submaximal exercise testing			
Maximal	48	62%	[8, 11–13, 16–18, 21–23, 25–30, 33–40, 45, 47, 48, 51–53, 55–57, 59–61, 63–66, 69–71, 73–75, 77]
Submaximal	27	35%	[1, 5–7, 9, 14, 15, 19, 20, 24, 31, 41–44, 46, 49, 50, 54, 58, 62, 67, 68, 72, 76]
NR	3	4%	[10, 32, 78]
Exercise test machine			
Cycle	34	44%	[3, 5–7, 9, 13, 15, 20, 23–27, 30–32, 36, 40, 45–48, 51, 55, 56, 64, 66, 68, 71–76]
Treadmill	44	56%	[1, 2, 4, 8, 10–12, 14, 16–19, 21, 22, 28, 29, 33–35, 37–39, 41–44, 49, 50, 52–54, 57–63, 65, 67, 69, 70, 77, 78]
CRF measure			
VO_{2max}, direct (among others)	39	50%	[4, 5, 8, 10, 13, 17, 18, 21–27, 29, 30, 33, 35, 38–40, 45, 47–49, 51–54, 62, 65, 66, 69–73, 75, 76]
VO_{2max} indirect (among others)	19	24%	[1, 6, 7, 9, 14, 16, 31, 41–44, 46, 50, 67, 68, 74, 77]
Only other measures	19	24%	[11, 12, 15, 19, 20, 28, 32, 34, 36, 37, 55–61, 63, 64]
NR	1	1%	[78]

CRF cardiorespiratory fitness, *NR* not reported, VO_{2max} maximal oxygen consumption

5000 participants performed gas analysis to asses VO_{2max} (see Fig. 4).

In addition to VO_{2max}, the following indicators of CRF were included in the selected studies: maximal physical working capacity (PWC) in Watts, PWC in Watts at variable and fixed HR thresholds (e.g., PWC at 75% of the predicted maximal heart rate or PWC at a heart rate of 170 beats per minute [PWC170]), time in seconds to HR threshold (e.g., exercise test duration to reach an HR of 130 beats per minute), energy expenditure in metabolic equivalents, and total exercise duration (in minutes or seconds). Eleven studies reported results for multiple measures of CRF. Almost two-thirds (48) of the studies applied maximal exercise testing (symptom limited), and one-third (27) applied submaximal testing. The treadmill (44) and the cycle ergometer (34) were commonly used exercise test machines in the included studies. Whereas the majority of European studies utilized cycle ergometers (76%), almost all studies conducted in North America used treadmills for exercise testing (94%; see Fig. 5).

Exposure

Sociodemographic Characteristics

Table 2 summarizes the adjusted associations between CRF and potential correlates or determinants. Unsurprisingly, the most studied individual correlate of CRF was age. More than 80% of the samples found a negative association with CRF, indicating that fitness declined with age. Three samples found no significant relation between age and CRF. A positive association was reported for two samples, but the age ranges were relatively narrow in these studies (21 to 43 years [12] and 18 to 30 years [12, 59]).

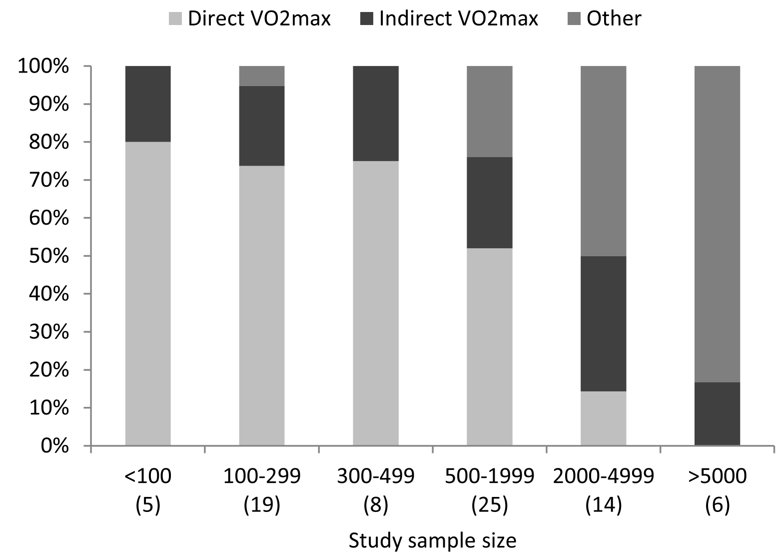

Fig. 4 Cardiorespiratory fitness measurement used by study sample size (the number of studies appears in parentheses. The studies sum to *n* = 77 because one study did not report whether they used direct or indirect VO_{2max}) VO_{2max} maximal oxygen consumption

Sex differences were investigated in six studies, all of which reported significantly higher CRF among men than among women.

The association between CRF and ethnicity was investigated in five samples, all in the USA. In four samples, higher CRF was observed among "whites" than among "blacks," whereas one sample of men observed no association between ethnicity and CRF.

We identified 19 samples investigating the associations between CRF measures and socioeconomic status (SES) variables. The most common SES measure was education (ten samples), and a positive association between education and CRF was reported for a majority of the samples, although in some samples no significant association was observed. Composite SES indexes were investigated in three samples, with summary measures also showing a positive association with CRF.

Anthropometric Measures

Anthropometric measures were frequently investigated in the included studies. BMI, the most frequently analyzed anthropometric factor (24 samples), showed an inverse association with CRF, as did WC and body fat. Weight and total lean mass were positively associated with CRF in at least 60% of the samples.

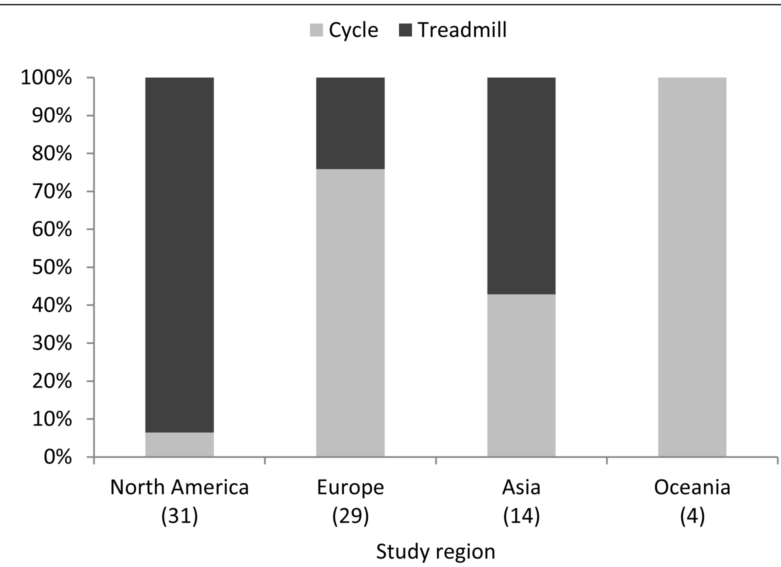

Fig. 5 Exercise test machine used by study region (the number of studies appears in parentheses)

Table 2 Summary of individual correlates and determinants of cardiorespiratory fitness

	Related to CRF		Unrelated to CRF	Summary of associations				
	Reference numbers	Association (+/−)	Reference numbers	#	#+	#−	#0	Association (+/−)
Sociodemographic characteristics								
Age	23, (12m[36], 59m[36])	+	(12f[15],59f[17]), *60f*, 68m	43	2	38	3	− −
	3m, 5m, 13f, (14, 67), 16f, 16m, *17m*, 18, *22*, 24, 27f, 27m, 28f, 29f, 29m, 30m, 32m, 33, 35m, *37f*, *37m*, 39f, 40, 45m, 47m, *53f*, 54f, 54m, 56m[16], *60m*[18], 61m, 65f, 65m, 68f, 69f, 69m, 72f, 72m	−						
Sex (women vs. men)	(14, 67), *22*, 24, 33, 40, 18	−		6		6		−
Ethnicity	19f, 12f, 12m[37], 14f		14m	5				n/a
Marital status (married vs. single)	45m	+		1	1			n/a
Socioeconomic status								
Education	*6f*, (12m[5], 59m[7]), (12f[5], 59f), 23m, 45m, 58[6]	+	*7f*, *7m*, (14m, 67), (14f, 67)	10	6		4	+
Parental education	*15*[38]	−		1		1		n/a
Maternal education	*15*[39]	+		1	1			n/a
Paternal education	*15*[40]	−		1		1		n/a
Composite SES index	20f, 58	+	20m	3	2		1	+
Occupation	58, 45m[14]	+		2	2			n/a
Employment	45m	+		1				n/a
Working mother			6m	1			1	n/a
Income	45m	+		1	1			n/a
Financial strain	58[13]	+		1	1			n/a
Anthropometric measures								
Body mass index	10m, 13f, 16f, 18, 23m, *37m*, *37f*, 59m, 59f, *64m*[1], 65m, 65f, 66m, 66f, 77m, 77f, 78m, 78f	−	*7f*, *7m*, 16m	24	3	18	3	−
	32m, 40, 56m	+						
Overweight	*63f*	−	67	2		1	1	n/a
Obese	*63f*, 67	−		2		2		n/a
Relative weight	11m, 11f	−		2		2		n/a
Body shape			3m	1			1	n/a
Waist circumference	13f, (14m, 77m), 16m, 16f, 23m, 30m, 30f, 78m, 78f	−	(77f, 14f)[8]	10		9	1	− −
Waist-to-hip circumference ratio	47m	−		1		1		n/a
Weight	6m	−		4	3	1		+
	24, 35m, 47m	+						
Body fat (%)	10m, 33m, 33f, 39f, 61m, 68m, 68f[2]	−		7		7		+
Total fat mass	72f, 72m	−		2		2		n/a
Lean mass (%)	9, *22*	+		2	2			n/a
Total lean mass	72m, 72f	+	9	3	2		1	+
Skeletal muscle mass	54m, 54f	+		2	2			n/a
Sum subscapular	12m, 12f	−		2		2		n/a
Appendicular lean mass/height squared			9	1			1	n/a

Table 2 Summary of individual correlates and determinants of cardiorespiratory fitness *(Continued)*

	Related to CRF		Unrelated to CRF	Summary of associations				
	Reference numbers	Association (+/−)	Reference numbers	#	#+	#−	#0	Association (+/−)
Appendicular lean mass (%)	9	+		1	1			n/a
Height	35m	+	10m	2	1		1	n/a
Birth weight	*64m*	+		1	1			n/a
Vital parameters								
Heart rate, resting	10m, 11m, 11f, 47m, 56m, 67	−		6		6		−
Heart rate, maximal exercise	47m	+		1	1			n/a
Heart rate, after CRF test	66m, 66f[4]	−		2		2		n/a
Mean blood pressure	56m, 68	−		2		2		n/a
Systolic blood pressure	12m, 12f, 77m	−	77f	4		3	1	−
Diastolic blood pressure	77m, 77f	−		2		2		n/a
Forced expiratory volume in 1 s	47m, 59m[3], 59f[3]	+		3	3			+
Vital capacity	11m, 11f, 51	+		3	3			+
Aortic augmentation index	10m	−		1		1		n/a
Comorbidities and medications								
Coronary heart disease	47m	−		1		1		n/a
Asthma	47m	−		1		1		n/a
Hypertension			67	1			1	n/a
Diabetes			67	1			1	n/a
Beta-blocker use	30f, 30m	−		2		2		n/a
Shortness of breath upon exertion			32m	1			1	n/a
Biomarkers								
Bicarbonate	1	+		1	1			n/a
Anion gap	1	−		1		1		n/a
Vitamin D	4	+		1	1			n/a
(High-sensitivity) C-reactive protein	2, 41, 44f, 44m	−	67	5		4	1	−
Thyroid-stimulating hormone	36[9]			1				n/a
Hemoglobin	47m	+		1	1			n/a
Fasting serum insulin	47m	−	24	2		1	1	n/a
2-h glucose tolerance test			24	1			1	n/a
Glucose, mg/dL			77m, 77f	2			2	n/a
HbA1c, %			77m, 77f	2			2	n/a
Ferritin	50m[10]	−		1		1		n/a
High-density lipoprotein (HDL) cholesterol	56m[11], 77m, 77f	+		3	3			+

Table 2 Summary of individual correlates and determinants of cardiorespiratory fitness *(Continued)*

	Related to CRF		Unrelated to CRF	Summary of associations				
	Reference numbers	Association (+/−)	Reference numbers	#	#+	#−	#0	Association (+/−)
Non-HDL cholesterol	56m[12]	+		1	1			n/a
Cholesterol	77f	−	(67, 77m)	2		1	1	n/a
Triglycerides	77m[42]		77f	2			1	n/a
Creatinine excretion	21f, 21m	+		2	2			n/a
White blood cell count			67	1			1	n/a
Homocysteine	43f	−	43m	2		1	1	n/a
Insulin-like growth factor (IGF) I			25f, 25m	2			2	n/a
IGF-binding protein 3 (IGFBP-3)			25f, 25m	2			2	n/a
IGF-I and IGF-I/IGFBP-3 ratio			25f, 25m	2			2	n/a
Nonesterified fatty acid			24	1			1	n/a
Red cell distribution width	9	−		1		1		n/a
Flow-mediated dilation			26	1			1	n/a
Nitroglycerin-mediated dilation	26[33]	+		1	1			n/a
Activity parameters								
Subjective measurements								
Overall PA								
PA index, various	11f, 11m, (12f, 59f), (12m, 59m), 33f, 33m, *37f*, *37m*, *38*, 48m, 49m, 56m, *60f*[29], *60m*[29]	+	10m, 49f, 65f, 65m, *76m*	19	14		5	+
PA level, high vs. low	*73f*[32]	+	49f, 49m	3	1		2	
Failure to meet PA recommendation			*63f*	1			1	n/a
PA times/week	23m, 47m, 66f, 66m	+		4	4			+
PA duration (hours/week)	45m	+		1	1			n/a
PA (in METS or MET minutes/week)	(14f, 67[30]), (14m, 67[30]), *38*, (45m, 47m), 68m[31], *70*	+	68f	7	6		1	+
Energy expenditure (kcal/week)	45m	+		1	1			n/a
Moderate-to-vigorous PA	30f, 30m	+		2	2			n/a
Moderate PA	39f	+	75	2	1		1	n/a
Vigorous PA	75	+		1	1			n/a
Proportion of vigorous PA/all PA	14f, 14m	+		2	2			n/a
LTPA								
Regular exercise			32m	1			1	n/a
Activity > 2 h/week	35m	+		1	1			n/a
Training time (hours/week)	16f, 16m	−		2		2		n/a
Leisure sports activities (yes vs. no)	7f, 74m	+		2	2			n/a
LTPA, quartiles	22	+		1	1			n/a

Table 2 Summary of individual correlates and determinants of cardiorespiratory fitness *(Continued)*

	Related to CRF		Unrelated to CRF	Summary of associations				
	Reference numbers	Association (+/−)	Reference numbers	#	#+	#−	#0	Association (+/−)
Intensity of LTPA (in METS)	61m	+		1	1			n/a
LTPA, duration/day			61m	1			1	n/a
Energy expenditure during active leisure time	48	+		1	1			n/a
Caloric expenditure in sports activity	16f, 16m	+		2	2			n/a
Membership in a sports club			*7m*	1			1	n/a
Past participation (years of vigorous or moderate sporting activities)			49f, 49m	2			2	n/a
Occupational PA								
Occupational PA	74m	+	45m	2	1		1	n/a
Sedentary PA								
Sedentary PA	39f	−		1		1		n/a
Other PA measures								
Satisfied with sports performance (yes)			*7f*, *7m*	2			2	n/a
Positive attitude toward swimming			*6m*	1			1	n/a
Positive attitude toward soccer and handball			*7f*, *7m*	2			2	n/a
Positive attitude toward aerobic fitness			*7f*, *7m*	2			2	n/a
Objective measurements								
Accelerometer								
PA volume			52f	1			1	n/a
PA intensity	52f	+		1	1			n/a
Step count	13f	+		1	1			n/a
Moderate-to-vigorous PA (continuous)	13f, 18, 42f, 42m	+		4	4			+
Vigorous PA (continuous)	13f	+		1	1			n/a
Vigorous PA (none vs. any)	18			1	1			n/a
Sedentary PA	42f, 42m	−		2		2		n/a
Physical fitness								
Knee extension torque			9	1			1	n/a
Handgrip strength			9	1			1	n/a
Bench press	*7m*	+	*7f*	2	1		1	n/a
Sargent jump	*6f*	+		1	1			n/a

Table 2 Summary of individual correlates and determinants of cardiorespiratory fitness *(Continued)*

	Related to CRF		Unrelated to CRF	Summary of associations				
	Reference numbers	Association (+/−)	Reference numbers	#	#+	#−	#0	Association (+/−)
Other								
Physical activity energy expenditure	24	+		1				n/a
Other health behaviors								
Smoking vs. non-smoking	*8f*, *8m*, 11f, 11m, *22*, 23m, 30m, 32m, (*37f*, *63f*), *37m*, *55m*, *60m*[22], *60f*[22]	−	14m, 16f, 16m, 24, 30f, 35m, (12f[19], 59f[21]), (12m[19], 59m[21])	22	1	13	8	−
	(14f, 67)[41]	+						
Number of cigarettes	56m[20], 68m[23]	−	68f	3		2	1	−
Alcohol	12f , 57[24]	+	12m[27]	3	2		1	+
Carbohydrates (g/day)	47m	+		1	1			n/a
Diet quality score	57f, 57m[35]	+		2	2			n/a
Meat dietary pattern	57f[26], 57m[26]	−		2		2		n/a
Fruit–vegetable dietary pattern	57m[28]	+	57f	2	1		1	n/a
Childhood television viewing	(*31*, *46*)	−		1		1		n/a
Adult television viewing	(*31*, *46*)	−		1		1		n/a
Sleep problems	62[25]	−		1		1		n/a
Other								
Commuting distance	34[34]	−		1		1		n/a
Gestational age (mother)	*64m*	+		1	1			n/a
Attachment loss (dental)			67	1			1	n/a
Probing depth (dental)			67	1			1	n/a
Preterm birth			*71*	1	1			n/a

+: positive association; –: negative association; 0: null association; n/a: summary measure not applicable because the number of independent samples investigating the relationship is less than three. The numbers in the summary table refer to the reference number for each study. f: women only; m: men only. Samples from studies with longitudinal designs are marked in italic. Separate studies drawing on the same study population and reporting redundant exposures are presented in parentheses and were counted as one unit of analysis. *CRF* cardiorespiratory fitness, *MET* metabolic equivalent, *LTPA* leisure-time physical activity, *PA* physical activity, *PWC* physical working capacity

[1]Inverse U-shaped association

[2]Negatively associated with annual change in VO_{2max}

[3]Significant association with test duration but not with work load 130

[4]Significant association with time to heart rate 130 but not with test duration

[5]Significant association with test duration but not with time to HR130

[6]Inverse U-shaped association (medium > high > low)

[7]Significant association with test duration but not with WL130

[8]Women with low CRF showed significantly higher waist circumference, compared with women with high CRF, in [77] (adjusted for "race" and age). Using the same data, in [14], women with high waist circumference did not show significantly different levels of CRF, compared with women with normal WC, after adjustment for multiple variables

[9]Lower VO_{2peak} in the second quintile than in the third quintile of thyroid-stimulating hormone

[10]Lower odds of high fitness (VO_{2max}) with elevated serum ferritin (> 300 ng/ml) vs. non-elevated serum ferritin (< 300 ng/ml)

[11]Significant association with PWC150/kg but not with PWC150, workload/heart rate, test duration, or workload

[12]Significant association with workload and workload/heart rate but not with PWC150, PWC150/kg, or test duration

[13]Higher METS with medium vs. low financial strain

[14]Higher mean VO_{2max} among white-collar workers than among blue-collar workers and farmers

[15]Significant positive association with time to heart rate 130; significant negative association with test duration

[16]Significant association with workload, workload/heart rate, PWC150, and test duration but not with PWC150/kg

[17]Significant negative association with test duration only for black women; significant positive association with WL130 only for white women

[18]Significant association with exercise test duration only for white men (not for black men)

[19]Significant negative association with test duration; significant positive association with time to heart rate 130

[20]Significant negative association with workload, test duration, and workload/heart rate; no significant association with PWC150; significant positive association with PWC150/kg

[21]Significant negative association with test duration; significant positive association with PWC130
[22]Significant negative association with test duration for black men and black women; significant negative association with WL130 for white men and black women
[23]Significant negative association with annual change in VO_{2max}
[24]Significant positive association with test duration for beer and wine but not for liquor
[25]Significant positive association of VO_{2max} with repeated awakenings and daytime sleepiness but not with sleep initiation problems or early awakening
[26]Significant negative association of test duration with meat dietary pattern for white men and women
[27]Significant negative association with test duration; significant positive association with time to heart rate 130
[28]Significant positive association of test duration with fruit–vegetable dietary pattern for white men
[29]Significant positive association with test duration for all subgroups; significant positive association with PWC130 only for white men and white women
[30]Significant positive association for high vs. none activity in METmin/week
[31]Significant positive association with VO_{2max} at first checkup
[32]Persistently active vs. persistently inactive; no significant association in other categories vs. persistently inactive
[33]Significant positive association only among non- or ex-smokers (not in current smokers)
[34]Significant negative association only for continuous measure of commuting distance and for 11–15 miles vs. 0–5 miles
[35]Significant positive association of test duration with a priori diet quality score for white men
[36]Significant positive association with time to heart rate 130; no significant association with test duration
[37]Significant positive association with test duration; no significant association with time to heart rate 130
[38]Significant higher risk of fitness decrease and lower risk of fitness persistence for medium vs. low parental education
[39]Significant higher risk of fitness persisting for high vs. low maternal education
[40]Significant lower risk of fitness persisting for medium vs. low parental education
[41]CRF was positively associated with smoking for both sexes in [67]. In [14], there was a positive association with smoking for women but not for men
[42]Significantly higher values for medium vs. high fitness but not for low vs. high fitness

Vital Parameters

Among studies investigating the relationship between vital parameters and CRF, resting HR, systolic BP, forced expiratory volume (FEV) in 1 s, and vital capacity were each studied in three or more samples. Resting HR and systolic BP showed negative associations with CRF, whereas vital capacity and FEV in 1 s were positively associated with CRF.

Biomarkers

A variety of biomarkers were investigated in a total of 22 samples. Most clearly, CRP showed a negative association with CRF. High-density lipoprotein (HDL) cholesterol was found to be positively associated with CRF in three samples. Other biomarkers were studied in fewer than three samples.

Activity Parameters

About half of the studies (39) reported at least one measure of PA. A wide range of PA measures were used, but only five of these measures were reported in at least three independent samples, allowing the calculation of a summary measure. Most studies investigating activity parameters assessed subjective PA (e.g., via the International Physical Activity Questionnaire; 34), but objective activity parameters (using an accelerometer or objective physical fitness measures) were collected in four studies. Most studies assessing subjective PA used measures of overall PA, namely customized PA indexes, dichotomous PA level (high vs. low), PA times per week, or PA in metabolic equivalents/metabolic equivalent minutes. Forms of LTPA were also often investigated, but these were too diverse for the calculation of summary measures. Other specific domains of PA (transport PA, occupational PA, or household PA) and sedentary behavior were rarely or never examined. Moderate-to-vigorous PA was the only objective measure of PA (measured using an accelerometer) reported in at least three independent samples. Almost all summarized PA exposures showed a positive association with CRF. Only dichotomous PA level (high vs. low) showed no association (based on three samples).

Other Behavioral Factors

Other than PA, smoking status was the most frequently investigated indicator of health behavior (22 samples). Overall, smoking was inversely associated with CRF. However, in a considerable number of samples, smoking status was found to be unrelated to CRF, and one study found a positive association between smoking and CRF in women. The number of cigarettes consumed, which was studied in three samples, was also inversely associated with CRF.

Alcohol consumption was examined in three samples. Whereas one mixed-sex sample showed a positive association between alcohol consumption and CRF, another study found a positive association among women but varying results depending on the CRF measure among men.

For all other investigated behavioral factors, the results could not be summarized because of a limited number of samples.

Sensitivity Analyses

No significant differences in the association with CRF were found for age, education, or WC when comparing different methods of CRF assessment (direct VO_{2max} vs. indirect VO_{2max} vs. other), different test machines used (bicycle ergometer vs. treadmill) or sex (men vs. women vs mixed samples; Additional file 2: Tables OR2.1 to OR2.19). For BMI, PA index, and smoking, we found differences in the results by the CRF measure used (p <

0.05, Fisher's exact test) but not by sex and test device. The association between CRF and BMI did not differ between samples where adjustments for body weight measures were performed, compared with samples where this adjustment was not performed.

Update Literature Search

The limited update literature search in PubMed yielded 383 records. After de-duplicating for records found in the initial search and title and abstract screening, 55 records remained for full-text screening. A total of seven records did fulfil the eligibility criteria [158–164]. Study characteristics and results of these studies can be found in Additional file 3: Table OR3.1. Overall, results from these studies are in line with the reported results from the main search and only few new potential correlates or determinants were investigated: one study analyzing caffeine consumption found a positive association with CRF among women, but not among men [162]. Another study reported a negative association between various plasma fatty acids and CRF among men, but only between arachidonic acid and CRF among women [163]. Moreover, in a further study, a negative association between anemia and CRF among women and a negative association between estimated glomerular filtration rate and CRF among men was reported [161]. As these factors were reported in two or less samples, calculation of a summary measure was not possible.

Discussion

Summary of Evidence

This systematic review aimed to give a detailed overview of the potential individual factors influencing CRF and to analyze the consistency of the results of existing research on this topic. Overall, 3016 records were identified, and 78 articles were ultimately included. We found evidence that CRF decreases with age, is lower among women than among men, and is associated with ethnicity. CRF was positively associated with SES, FEV, and vital capacity, and negatively associated with BMI, weight, WC, body fat, resting HR, systolic BP, and CRP. As expected, CRF was associated with several measures of PA. Furthermore, CRF showed a negative association with smoking and a positive association with alcohol consumption in the majority of the included studies. Age, BMI, WC, PA index, smoking, and education were the most investigated factors (≥ 10 samples). For these factors, results showed no significant sex differences. To our knowledge, this is the first comprehensive review investigating the individual determinants and correlates of CRF. A review conducted by Ortega et al. [98] summarized the relationship between fitness and CVD risk factors among children and adolescents. Another systematic review focused on studies investigating the association between genetic variants and CRF trainability [113]; however, this was beyond the scope of the present review.

Comparison with Other Studies and Interpretation of Results

Sociodemographic Characteristics

It is well established that CRF declines with age. This may be because of physiological adjustments, such as atrophy of muscle mass with biological aging, changes in lifestyle, or increasing disease burden and medication [118]. Although the decline in CRF with age is widely accepted, the causes behind this relation are not yet clearly understood [119].

The contradictory results for age found in two included samples can partially be explained by the limited age ranges of these study samples: The studies focused on young or middle-aged individuals. Because maximum CRF is usually attained between 20 and 30 years of age [37, 86, 120], linear age trends may be positive in young study populations. When the study population has an older age range, a decline in CRF with age becomes apparent—a trend that seems to be more pronounced among men than among women [22, 37, 120, 121]. However, these differences largely disappear when the decline in CRF is expressed as a percentage change rather than as an absolute value [37, 121]. Two studies used meta-analytical approaches to combine data and generate general age-specific reference values and predictive equations [99, 122]. However, because of a high level of heterogeneity in the assessment of CRF, as well as differences in methods and study population characteristics, these results should be interpreted with caution [123]. Furthermore, the effect of PA on the decline in CRF over the life course is unclear [120, 121]. Although meta-analyses of cross-sectional data have not reported evidence that increased PA levels mitigate the decline [124, 125], longitudinal studies have found that individuals with enhanced PA have less decline in CRF per decade than do sedentary individuals [120]. Independent of age, a longitudinal study among men found a greater decline in CRF over time associated with a greater risk of total mortality [157].

There is clear evidence that, overall, compared with men, women have lower CRF levels. The difference between men and women is often estimated at around 20% [20, 126–128]. Common physiological explanations for this difference are women's smaller body and organ size and higher body fat percentage, compared with men [100]. Correspondingly, Fleg et al. [22] pointed out that, when VO_{2max} is expressed relative to muscle mass (e.g., ml/kg muscle mass/min), the difference between the sexes is often eliminated. In addition to physiological explanations, there are differences in behavioral and social factors [100] (e.g., differences in PA behavior) that could partly explain the CRF differences between men and women.

Higher SES is predominantly associated with higher CRF. Although our summary measures could only be calculated for education and composite SES indicators, no inverse association was reported for the other SES indicators, which were investigated in fewer than three samples. A positive association between education and CRF was previously confirmed in a meta-analysis that included 9435 adults from four population-based studies [102]. These findings are also in line with systematic reviews investigating the association between LTPA and CRF [129]. Because aerobic LTPA is strongly associated with CRF, lower LTPA levels among lower-SES population groups may contribute to lower CRF levels in these groups. Lower SES is not only associated with lower aerobic LTPA but also with higher fat and sugar consumption, lower consumption of fruits and vegetables [130], and higher smoking prevalence [131]. In addition to unfavorable health behaviors, major NCD risk factors like obesity [132] and chronic diseases such as diabetes and CVD are more prevalent among population groups with lower SES. Thus, unfavorable health behaviors and risk factors that may be associated with CRF potentially reinforce the effect of SES on CRF. However, these associations have been confirmed mainly in high- and upper-middle-income countries, and the situation in low- or middle-income countries might be different because these countries are in earlier stages of the epidemiological transition [133]. High-SES population groups in these countries may move to the next stage before low-SES groups and therefore also adopt unfavorable health behaviors earlier. Consider, for example, the case of obesity: In low-income countries, the more affluent are more likely to be obese [134].

Anthropometric Measures and Vital Parameters

Anthropometric measures were often investigated in the included studies, showing a clear inverse association between BMI and CRF. Most samples with an inverse association between CRF and BMI used a body weight-adjusted measure of CRF (such as relative VO_{2max} in ml/kg/min) that took into account the differences in CRF because of BMI. We performed sensitivity analyses to check whether the association between CRF and BMI differed depending on the adjustment of measures for relative body weight and found no significant differences. Although CRF and BMI are related, a high BMI does not necessarily mean a low fitness level. High muscle mass can also lead to having a high BMI caused by the dense structure of muscle mass. Research suggests that, compared with the health risks of having a high BMI, having low CRF is a more important risk factor: a systematic review found that the risk for cardiovascular mortality was lower among individuals with high BMIs and high levels of CRF, compared with those with normal BMIs and low levels of CRF [135]. Furthermore, studies suggest that individuals with low CRF have higher levels of general and abdominal adiposity, as measured by WC, for example, than do individuals with moderate/high CRF, independent of BMI [136]. Thus, it is not surprising that WC was negatively associated with CRF in almost all of the included studies. Likewise, percentage of body fat was found to be negatively associated with CRF in all samples, and lean body mass (or skeletal muscle mass, which accounts for most of the lean mass) was positively associated with CRF. Again, it should be noted that the effects of these factors are strongly depending on the application and procedures (e.g., relative to body weight, relative to fat free mass, or relative to predicted weights) of data normalization for the CRF measure [165].

All of the reviewed studies demonstrated the expected associations between CRF and vital capacity parameters, most of which have been extensively studied in endurance training intervention studies and well documented in the exercise physiology literature [137]. VO_{2max} is one of many physiological parameters that improve as a result of endurance training. Increased cardiorespiratory capacities such as stroke volume and vital capacity, as well as improved muscle and blood composition, contribute to a higher maximal oxygen uptake. These adaptations lead to a more efficient supply of energy and oxygen for bodily functions and to a reduction in resting HR and BP.

Behavioral Factors

The majority of the included studies found a negative association between CRF and smoking. These findings may be explained by multiple pathways. First, tobacco smoking may trigger a cascade of modifications in the respiratory organs, which can lead to reduced pulmonary function. Limited pulmonary function, in turn, may be negatively associated with CRF [138]. Second, because CRF and PA are closely related and PA is also inversely associated with smoking, negative health behaviors such as inactivity, smoking, and alcohol consumption may often cluster together [139], and (in)activity acts as a confounder in the relation between smoking and CRF. Third, the relation between CRF and smoking also may be explained by SES because both smoking [131] and low fitness [102] seem to be associated with low SES.

Because the observed association of CRF with alcohol is based on only three samples, these findings should be interpreted with caution. One study found a direct association with some types of alcohol (e.g., wine) but not others (e.g., liquor) [57]. A recent investigation found better fitness among moderate drinkers, compared with heavy drinkers and abstainers, using data from five population-based studies [101]. Although there are potential explanations for the U-shaped relation between alcohol intake and CRF [101], it is also possible that this is a result of confounding [140].

Dietary risk factors, such as a diet high in sugar-sweetened beverages, are known to be related to cardiometabolic risk factors [141], but relatively little is known regarding the relationship between these dietary factors and CRF [57, 70]. Recent research suggests that CRF may act as a mediator of the relation between macronutrient intake relative to weight and fat mass in adolescents: individuals with a higher macronutrient intake, which may be related to engaging in more PA, may suffer from obesity less often, especially when they have high CRF levels [142].

The relation between PA and CRF has been widely discussed in the literature, and the positive impacts of PA and CRF on health are well documented [143]. CRF is influenced by several physiological traits, especially the performance of the cardiovascular system. Thus, in the relationship between PA and CRF, PA is the modifiable variable: performing PA allows individuals to reach their highest possible level of CRF, which is also determined by heredity and other factors [84, 144]. Although the nature of the association between PA and CRF is widely accepted, it cannot be ruled out that low CRF levels caused by genetic pre-conditions can lead to lower PA levels [84].

The results of this systematic review reflect the well-established relation between CRF and PA. A wide variety of objective and subjective PA measures were used in the included studies, and a majority of these studies found a significant positive association between PA and CRF. Whereas overall PA and LTPA were commonly investigated, only a few studies investigated other domains such as occupational PA. Other domain-specific types of PA may have different effects on health. For example, studies have shown that occupational PA can either have no association or be negatively associated with health outcomes, whereas LTPA affects health in a strictly beneficial way [145, 146]. While conducting this review, we found only two studies that investigated the relation between PA at work and CRF, and these studies had varying results. One study found no association between CRF and occupational PA but a significant positive association between CRF and hours of PA per week [45]. The other study found a positive association for both LTPA and occupational PA [74]. Considering their potentially varying effects on health, the associations between domain-specific types of PA and CRF should be further examined.

Overall, health habits such as dietary, smoking, and PA behaviors are usually measured with considerable inaccuracy. This could mean that there is imprecision in the measurement of health behaviors in studies investigating these factors as correlates and determinants of CRF [47].

Strengths and Limitations

To our knowledge, this is the first systematic review investigating the individual correlates and determinants of CRF. The semi-quantitative approach used in this review made it possible to present a concise summary of the results from 78 studies and to provide a comprehensive overview of the current state of research and potential research gaps.

We acknowledge that such a comprehensive review also has limitations. The majority of the studies included in this review were cross-sectional; therefore, statements about causal relationships between exposures and outcomes are limited. Furthermore, not all studies used VO_{2max} (the "gold standard") as an outcome, diminishing the comparability of results across the studies. Although other methods for measuring CRF (e.g., exercise test duration) have been shown to be correlated with VO_{2max} [147, 148], differences in methods could lead to deviating results. It is interesting to note that the included studies that reported the associations between an exposure and various measures of CRF often found similar associations, independent of the measurement method used. Several studies also obtained CRF results using submaximal exercise-based predictive equations. Although it has been found that the results of assessed and predicted CRF can vary [111], a systematic review has demonstrated that these predictive equations are quite accurate [149]. In addition to differences in the method of measurement (indirect vs. direct), different indicators of CRF (e.g., VO_{2max} vs. others) were not taken into account when discussing the results. This could be considered a potential bias because sensitivity analyses showed significant differences in the association between directly assessed VO_{2max}, indirectly assessed VO_{2max}, and other CRF measures for some of the exposures. Variations in the methods used in the statistical analyses may also have affected the results. In this systematic review, we only analyzed the adjusted results from multivariable analyses. Because fewer variables usually reach the defined level of significance in such analyses, compared with univariate analyses [115], a bias toward null findings is possible [150]. Such a bias may be exacerbated by the use of the fully adjusted models.

Because of the wide range of correlates and determinants analyzed, as well as the significant heterogeneity in analytical methods and study samples, it was not feasible to conduct a meta-analysis. Correspondingly, we were unable to show the strength of the associations (effect measures) or to adjust the results for sample size. In addition, variation in adjustment for confounding among the studies was not considered in the interpretation of the results for each outcome, although this difference may have led to divergent results across the studies. Due to restrictions in the search strategy and the intra-study requirements to participate in CRF testing, the study populations usually consist of a relatively healthy population. However, it cannot be ruled out that some of the reported associations are influenced by underlying chronic diseases. Furthermore, the universal perspective of this review did not allow determinants, correlates, mediators, moderators, and confounders to be differentiated [151]. However, the focus of this review was to show the consistency of reported associations. Certain indicators may be underrepresented for specific reasons (e.g., underreporting or limitations of the search strategy). Existing studies have shown that correlates and determinants may differ across the life course [37, 98]. Future studies should investigate whether the results of this systematic review can be confirmed for young people and older adults. Furthermore, although this was beyond the scope of the present review, environmental and interpersonal determinants probably also play an important role in determining or moderating CRF and should be further investigated [103].

Conclusions

Our comprehensive systematic review showed that there is a broad range of individual factors associated with CRF. Whereas factors such as age, BMI, and WC showed consistent evidence of an association with CRF, other factors showed conflicting or insufficient evidence of an association. For example, few studies have investigated the relationship between CRF and behavioral factors other than PA and smoking, or the association between CRF and psychosocial factors.

Several implications for health promotion practice and for future research can be drawn from this review. First, sociodemographic factors shown to be associated with CRF in this review can be used to help identify subgroups of relatively unfit individuals (e.g., people with low education) who should be targeted for interventions. Second, the strong association between aerobic LTPA and CRF was confirmed in this review, but less is known about the relation between CRF and domain-specific PA. Thus, future studies should compare the impact of domain-specific PA on CRF. The comparability of the results was hampered by differences in the assessment of PA; therefore, the use of standardized domain-specific measures, such as the Global Physical Activity Questionnaire [152] or the European Health Interview Survey–Physical Activity Questionnaire [153], is recommended. In addition, sedentary behavior plays an important role in the global strategy to tackle NCDs, but little is known about the association of this factor with CRF in adults [154]. Third, there is some evidence that health behaviors other than PA, such as smoking, alcohol consumption, and nutrition, are also associated with CRF. Thus, multi-behavioral interventions might be an appropriate approach when implementing preventive measures to enhance health status in the general adult population [155], although the effects of these approaches have been found to be limited [156].

Future reviews could build on the results of the present systematic review by consolidating the evidence regarding the correlates and determinants of CRF in younger and older population groups, which were not included in this review. Moreover, evidence from low- and middle-income countries is needed to improve the generalizability of the results because most of the studies included in this review were conducted in high-income country settings. Notwithstanding the close association between CRF and PA and the fact that CRF is partly genetically determined, relatively little is known about the complex interplay among the potential determinants of CRF. This review can be a first step toward the development of a comprehensive model of (cardiorespiratory) fitness that integrates not only physiological aspects but also a broad set of socio-ecological factors.

Additional Files

Additional file 1: Quality Assessment. (PDF 490 kb)
Additional file 2: Sensitivity Analyses. (PDF 253 kb)
Additional file 3: Limited Search Update. (PDF 210 kb)
Additional file 4: Data extraction table. (XLSX 215 kb)

Abbreviations

BMI: Body mass index; BP: Blood pressure; CRF: Cardiorespiratory fitness; CRP: C-reactive protein; CVD: Cardiovascular disease; HDL: High-density lipoprotein; HR: Heart rate; LTPA: Leisure-time physical activity; NCD: Non-communicable disease; PA: Physical activity; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROSPERO: International Prospective Register of Systematic Reviews; SES: Socioeconomic status; VO_{2max}: Maximal oxygen consumption; VO_{2peak}: Peak oxygen consumption; WC: Waist circumference

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Authors' Contributions

JZ, NP, TK, GBMM, and JDF contributed to the conception and design of the study. JZ, KJO, NP, and JDF contributed to the acquisition, analysis, and assembly of the data. JZ, KJO, GBMM, and JDF contributed to the interpretation of the data. JZ wrote the first draft and final version of the manuscript. KJO and JDF contributed to the writing of the manuscript. All of the authors critically revised the manuscript for important intellectual content and approved the final manuscript. Additionally, all of the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Availability of Data and Materials
All data generated or analyzed during this study are included in this published article (and its supplementary information files).

Ethics Approval and Consent to Participate
Not applicable.

Consent for Publication
Not applicable.

Competing Interests
The authors, Johannes Zeiher, Katherine J. Ombrellaro, Nita Perumal, Thomas Keil, Gert B. M. Mensink, and Jonas D. Finger, declare that they have no competing interests.

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Sports Medicine - Open

SYSTEMATIC REVIEW

Open Access

Socioeconomic Correlates and Determinants of Cardiorespiratory Fitness in the General Adult Population: a Systematic Review and Meta-Analysis

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Abstract

Background: This review aims to (1) consolidate evidence regarding the association between socioeconomic status (SES) and cardiorespiratory fitness (CRF), (2) conduct a meta-analysis of the association between SES and CRF using methodologically comparable data, stratified by sex, and (3) test whether the association varies after adjustment for physical activity (PA).

Methods: A systematic review of studies from MEDLINE, EMBASE, Latin American and Caribbean Health Sciences (LILACS), Scientific Electronic Library Online (ScIELO), and Cochrane Library without time or language restrictions, which investigated associations between SES and CRF. Risk of bias within studies was assessed using a customized quality assessment tool. Results were summarized in table format and methodologically similar studies were synthesized using meta-analysis of Hedges' *g* effect sizes. Synthesized results were appraised for cross-study bias. Results were tested for the impact of PA adjustment using meta-regression.

Results: Compared to individuals with low education, both men and women showed higher CRF among individuals with high education (men 0.12 [0.04–0.20], women 0.19 [0.02–0.36]), while participants with medium education showed no significant difference in CRF (men 0.03 [– 0.04–0.11], women 0.09 [– 0.03–0.21]). Adjustment for PA did not significantly impact the association between education and CRF.

Conclusions: There is fair evidence for an association between high levels of education and increased CRF. This could have implications for monitoring, of health target compliance and of chronic disease risk among higher risk populations, to detect and prevent non-communicable diseases (NCDs) and to diminish social health inequalities.

Trial Registration: PROSPERO, CRD42017055456

Keywords: Cardiorespiratory Fitness, Socioeconomic Status, Education, Adults, Social Health Inequality, Health Monitoring, Meta-Analysis, Systematic Review

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Key Points

- Systematically reviewed studies predominantly observed a positive association between socioeconomic status and cardiorespiratory fitness among men and women.
- The meta-analysis of the most frequently reported association between education and cardiorespiratory fitness showed a significant positive association for men and women when comparing the highest with the lowest of three education groups.
- Adjustment for physical activity did not affect the association between education level and cardiorespiratory fitness in the meta-analysis.

Background

In 2005, chronic disease deaths were double the number of deaths resulting from infectious diseases (HIV/AIDS, TB, and malaria), maternal and perinatal conditions, and nutritional deficiencies combined [1]. Similarly, in 2015, 40 million or 70% of all-cause deaths globally were a result of chronic disease [2], a figure expected to increase to 52 million non-communicable disease (NCD) deaths by 2030 [3].

Socioeconomic status (SES), as defined by education, occupation, and income [4] plays a major role in the distribution of NCDs [5]. Evidence from high-income countries shows NCD burden effectively shifts to those with lower SES over time [6, 7]. Potential shift of disease burden to the poor, paired with increasing NCD and communicable disease burden on clinical and prevention resources means that individuals from lower SES groups may receive inadequate care, making them a priority for early prevention and monitoring. In fact, the World Health Organization (WHO) ranks monitoring and surveillance of risk factors as a top priority to tackle growing NCD epidemics in low-resource settings [8].

There is clear consensus in the literature that cardiorespiratory fitness (CRF), or "the ability of the circulatory and respiratory systems to supply oxygen during sustained physical activity (PA)" ([9], p. 53), measured at gold standard as maximal oxygen output, or VO_{2max} obtained during maximal treadmill or ergometer testing [10, 11], is as important as PA [12–14], if not more important [15], for the prediction of future adverse health outcomes, including adverse cardiovascular events and all-cause mortality [16]. CRF is also often an objective measure of fitness, while PA, defined as bodily movement produced by skeletal muscles that require energy expenditure [9], is often self-reported behavior. The objective nature of CRF testing makes it the most reliable test of fitness for use in large-scale, population-based studies. Furthermore, directly measured fitness is more strongly associated with a protective cardiovascular risk profile than self-reported PA level [17], helping practitioners more accurately separate individuals with high long-term risk (25 years) for NCDs from those with low long-term risk.

As clinical and preventive resources stretch to meet increasing disease burden, it becomes essential to invest in interventions for early detection and treatment of NCDs, thereby reducing the need for additional or more expensive treatment in the future, and long-term economic burden [18]. Establishment of a relationship between SES and CRF may be helpful in accurately targeting the most at-risk groups for timely NCD prevention and early detection and treatment. To our knowledge, there are currently no systematic reviews addressing the relationship between SES and CRF in the general, adult population.

The overall aim of this systematic review is to (1) review and consolidate evidence from the literature regarding the association between SES and CRF, (2) conduct a meta-analysis of the association between SES and CRF using methodologically comparable data sources, stratified by sex, and (3) test whether association varies with adjustment for PA using meta-regression. We stratify by sex because sex differences in CRF are well documented [19–21] but also because identifying and addressing gender inequality in health is a priority for international health professionals [22]. We also test for the effect of adjustment for PA, because PA partially, but not exclusively [23], leads to CRF [24–27] and may influence the relationship between SES and CRF.

Methods

Protocol and Registration

This review was conducted as part of a larger research project investigating the personal and interpersonal correlates and/or determinants of CRF in adults. It is a subset of a broader systematic review that was registered at International Prospective Register of Systematic Reviews (PROSPERO): CRD42017055456. The systematic review protocol was published elsewhere in detail [28]. Instead of all determinants and correlates of CRF, the current review focuses on the association between SES and CRF.

Literature Search and Selection Criteria

We conducted our search for journal-published articles in the MEDLINE (1965 to present), EMBASE (1947 to present), Latin American and Caribbean Health Sciences (LILACS, 1982 to present), Scientific Electronic Library Online (ScIELO, 1998 to present), and Cochrane Library literature databases. We additionally searched the Google Scholar grey literature database. In addition to electronic literature databases, the reference lists of all articles selected for full-text screening were hand searched for relevant studies not found in the electronic database search. The final database search was updated on October 30, 2017.

No date, language, article type, or text availability filters were applied. All search results were imported into the reference management software, Endnote X7 (Thomas Reuters, USA), and duplicates were removed. The current review includes quantitative observational (cohort studies, case-control studies, and cross-sectional studies) and experimental studies that report on the association between SES and CRF in the general adult population.

Eligible SES indicators were any acknowledged resource or prestige-based measure of position within a societal structure [3, 29] defined according to the MeSH (medical subject headings) term "Socioeconomic Factors" and equivalents. The Socioeconomic Factors MeSH term includes sub-headings such as educational status, employment status, income, occupation including career mobility, poverty including poverty areas (defined as city, urban, rural, or suburban areas which are characterized by severe economic deprivation and by accompanying physical and social decay), family characteristics (including family demography and family life surveys), social change, social class including social mobility and social conditions. Individual, household and area-based SES indicators as well as social mobility indicators were included.

Eligible CRF indicators were any acknowledged objective measures of CRF derived from maximal or submaximal incremental cardiopulmonary exercise testing (CPET) on a treadmill or cycle ergometer. Oxygen consumption indicators, either directly measured with spiroergometric gas exchange measurements or indirectly estimated with metabolic equations, were included. Maximal oxygen consumption (VO_{2max}) is defined as the oxygen consumption, in millimeter/(kilogram per second), during exercise, at which actual oxygen consumption reaches a maximum which cannot be increased with an increase in effort (plateau), while peak oxygen consumption (VO_{2peak}) is the highest VO_2 value obtained on a particular test, regardless of the subject's effort [30, 31]. Throughout the following, we will use the abbreviation $VO_{2max,}$ for both VO_{2max} and VO_{2peak} indicators. In addition to VO_{2max}, the following CRF indicators were included: physical working capacity in watts at variable and fixed heart rate thresholds (e.g., $PWC_{75\%,}$ PWC_{170}), time in seconds to heart-rate threshold (e.g., WL_{130}), energy expenditure in METs (metabolic equivalents), and total exercise duration in seconds.

The following exclusion criteria were applied: (1) studies measuring the impact of interventions designed to increase PA or CRF; (2) studies including only children, or adolescent participants (0–18 years) or elderly participants (90 years or older); (3) studies with sample sizes of less than 300 participants (considered too small to be representative of the general adult population [32], and the minimum sample size required for precise estimates of population mean differences [33]); (4) studies where participants were not representative of the general adult population (e.g., highly select populations, individuals from occupational groups with elevated PA, such as military groups or firefighters, symptomatic, or institutionalized individuals; (5) studies reporting only measures of childhood SES, such as family demographics and indicators found in family life surveys (because these SES measures are family based and do not always reflect an individual's own SES in adulthood); and (6) reviews, letters to the editor, commentaries, or editorials.

Two reviewers (NP, KO) independently reviewed titles and abstracts of all references identified from databases and additional literature sources. Articles that were not excluded at this stage were further reviewed for inclusion, based on the publication's full text, by reviewers (NP, KO); disagreements were resolved by a third reviewer (JF). Additional details about study selection are published elsewhere [28]. At all stages, disagreement between first and second reviewers was resolved by discussion. All studies examining the association between participant SES and CRF were included for data extraction and systematic review. In some cases, population-based studies had measured but not reported participant SES ($n = 4$). These studies were neither excluded, nor extracted, but were reserved for author follow-up. Articles based on population-based studies that were reserved for author follow-up were only included for systematic review if authors responded with supplementary data. All other studies were excluded from the systematic review. Studies included for meta-analysis were only those included for systematic review with directly comparable exposures of interest.

Data Coding and Assessment of Methodological Quality

Studies were coded for study characteristics, methods, population characteristics, exposures and outcome variables, main results including method of analysis and confounders adjusted, as well as major limitations reported by the authors.

Supplementary details about data extraction process are published elsewhere [28]. All data were extracted by two reviewers (KO and JZ). In several cases, we contacted authors requesting additional data. Additional author requests were made when studies presented insufficient measure of the association between SES and CRF, or when population-based studies that were reserved for full-text screening, measured, but did not present data on the association SES and CRF.

Risk of bias within each study was independently assessed by two reviewers (JZ, KO) using a customized version of the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies by the National Heart, Lung and Blood Institute at the National Institutes of Health, USA [34]. Risk of bias was categorized as "high" when a study reached ≤ 49% "requirement fulfilled" score, "moderate" when a study reached 50–75% "fulfillment" score, and "low" at ≥ 75% "fulfillment" score. Supplementary details about risk assessment procedure are published elsewhere [28], results of the risk of bias assessment are available in Table 1. Additional sensitivity analysis, using risk of bias score to test the effect of study quality on the association between SES and CRF, was to be conducted if methodologically similar studies, included for meta-analysis, varied in risk of bias score.

Statistical Analysis

After completion of the author requests for additional data, results of the systematic review were summarized in table and narrative format. Comparable data was only obtained for the relationship between education and CRF ($n = 3$). In order to pool results for meta-analysis, we standardized education categories across population-based studies into three main categories according to the CASMIN educational classification—high, medium, and low [35]. We also standardized the outcome measurement using VO_{2max}, in millimeter/(kilogram per second), calculated according to the American College of Sports Medicine equation: $3.5 ml \times min^{-1} \times kg^{-1} + 12.24 \times w_{max} \times bodyweight^{-1}$ [36, 37] or directly measured with Spiroergometry (ml/min). Individual study results were standardized using the Hedges' g effect size [38] calculated as ES = (((mean difference between reference and comparison categories)/(pooled and weighted standard deviation)) × correction factor (J)) to determine the overall association between education and CRF. The standardized effect sizes were then included in a random effects meta-analysis according to the DerSimonian and Laird [39] methodology; this was pre-specified due to the expected heterogeneity of outcome and exposure measurements in the underlying studies and also because it was expected that the effect of SES on CRF varies by context, and therefore that analysis would estimate the distribution of these effects, rather than estimating one true effect of SES on CRF. Our final meta-analysis model adjusted for the set of confounders adjusted for in all studies: age, PA, waist circumference (WC), body mass index (BMI), and alcohol consumption. Data analysis was performed using STATA Version 14 statistical software (Stata Corporation, College Station, TX, USA). Increases in CRF were reported as positive values and high and medium educational categories were compared to the referent low educational category so that positive CRF illustrated improvement in the comparison over the referent education category. Data are reported as mean ± 95% confidence interval (CI).

The I^2 statistic (percentage of variance in the study-specific point estimates that is attributable to true between-study heterogeneity as opposed to sampling variation) was used as an indicator of study heterogeneity or risk of bias across studies. Evidence of heterogeneity was determined by a p value < 0.1 [40], to address the low power of the statistical test resulting from limited number of studies included for meta-analysis. The meta-analysis was stratified by sex and included additional sensitivity analysis to test differences, in the synthesized association between SES on CRF, with and without adjustment for PA. Differences were tested using meta-regression. Previously mentioned additional sensitivity analyses were pre-specified. Post-hoc analysis adjusting NHANES data for race was performed.

Results

Study Characteristics

A PRISMA flowchart depicting the article selection process can be found in Fig. 1. An updated search was conducted in October 2017, resulting in no new results. A total of 3233 studies were identified from electronic databases, and 218 articles were identified from additional literature sources. After title and abstract screening, 346 articles were included for full-text screening, of which 329 were subsequently excluded. Four articles reporting data from population-based studies were reserved for author follow-up because they measured, but did not report on the association between SES and CRF. In total, 15 studies were included for systematic review and three were included for meta-analysis, resulting in four population-based studies for meta-analysis (since one study contained two independent cohorts).

In our search we did not exclude experimental studies, although it is difficult to imagine examples of experimental studies designed to modify SES, in order to improve CRF. Ultimately, however, all included studies were observational, since no experimental studies fulfilled the eligibility criteria. The associations between SES exposures and CRF found in the systematic review (positive, negative, U-shaped (all variants), and not significant), are presented in Tables 2 and 3 according to socioeconomic exposure.

Studies were cross-sectional ($n = 14$) and cohort ($n = 1$). Sample sizes ranged from 528 to 4968 participants. Studies included participants aged 16–85 years. Studies were conducted across a span of 41 years—from 1971 to 2012; four were conducted between 1971 and 1990; one study spanned from 1985 to 2006; eight were conducted

Table 1 Customized risk of bias assessment—risk of bias was categorized as high when < 49% requirements met, moderate when 50–75% requirements met, and low when > 75% requirements met

	Question	Blair [46]	Braun [44]	Sidney [48]	Ceaser [47]	Finger [52]	Shmueli [50]	Fogelholm [43]	Lindgren [53]	Thai [49]	Dyrstad [42]	Cleland [51]	Lakka [41]	MacAuley [128]	Ittermann [45]	Shishebor [54]
1	Was the research question clearly stated?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1a	Were the correlates being investigated clearly stated?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1b	Was the CRF outcome clearly stated?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2	Was the study population clearly defined?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3	Study participant selection															
3a	Was a probability-based sampling strategy used?	0	1	1	1	1	0	0	0	1	0	1	0	1	1	0
3b	Was sampling frame at a national level?	0	1	1	1	1	0	1	0	1	1	1	0	1	1	0
3c	If participants were selected from clusters, were there ≥50 clusters?	0	1	1	1	1	0	0	0	1	0	1	NA	NR	0	0
3d	Were inclusion and exclusion criteria pre-specified?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4	Was the sample size greater than 1200?	1	1	1	1	1	1	0	0	1	0	0	1	0	1	1
4a	Was sample size justification or power description provided?	0	1	1	1	1	0	0	0	1	0	0	0	NR	NR	0
5	Response rate															
5a	Was response rate of eligible participants > 50%?	NA	1	1	1	1	NA	1	0	1	1	1	1	1	1	NA
6	Loss to follow-up in cohort studies															
6a	Was loss to follow-up after baseline ≤20%?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA
7	Were correlates of CRF and potential confounders objectively measured using validated instruments?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7a	Were few exposure variables self-reported?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7b	Was the outcome variable clearly defined, valid, reliable, and reliable?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8	Was CRF measured using an objective, reliable, and validated methodology?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8a	Was CRF measured consistently for all participants?	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1
9	Were the exposure variables measured prior to measurement of the outcome variables?	1	NR	NR	NR	1	NR	1	NR	1	NR	0	NR	NR	NR	1
10	Were key potential confounding variables measured and adjusted for statistically?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Table 1 Customized risk of bias assessment—risk of bias was categorized as high when < 49% requirements met, moderate when 50–75% requirements met, and low when > 75% requirements met *(Continued)*

	Question	Blair [46]	Braun [44]	Sidney [48]	Ceaser [47]	Finger [52]	Shmueli [50]	Fogelholm [43]	Lindgren [53]	Thai [49]	Dyrstad [42]	Cleland [51]	Lakka [41]	MacAuley [128]	Ittermann [45]	Shishebor [54]
11	Did the study investigate interaction between exposure variables?	0	1	0	0	0	1	1	1	1	0	0	0	0	0	0
12	Did analysis include sensitivity analysis?	1	1	1	1	1	1	1	1	1	0	1	1	0	1	1
13	Was funding source and/or conflicts of interest reported?	0	0	1	1	1	0	1	1	1	1	1	1	1	1	0
	Final Assessment	63%	92%	92%	92%	96%	63%	73%	57%	100%	61%	77%	66%	71%	84%	63%
	Risk of Bias Evaluation	Medium	Low	Low	Low	Low	Medium	Medium	Medium	Low	Medium	Low	Medium	Medium	Low	Medium

Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies by the National Heart, Lung and Blood Institute at the National Institutes of Health, USA

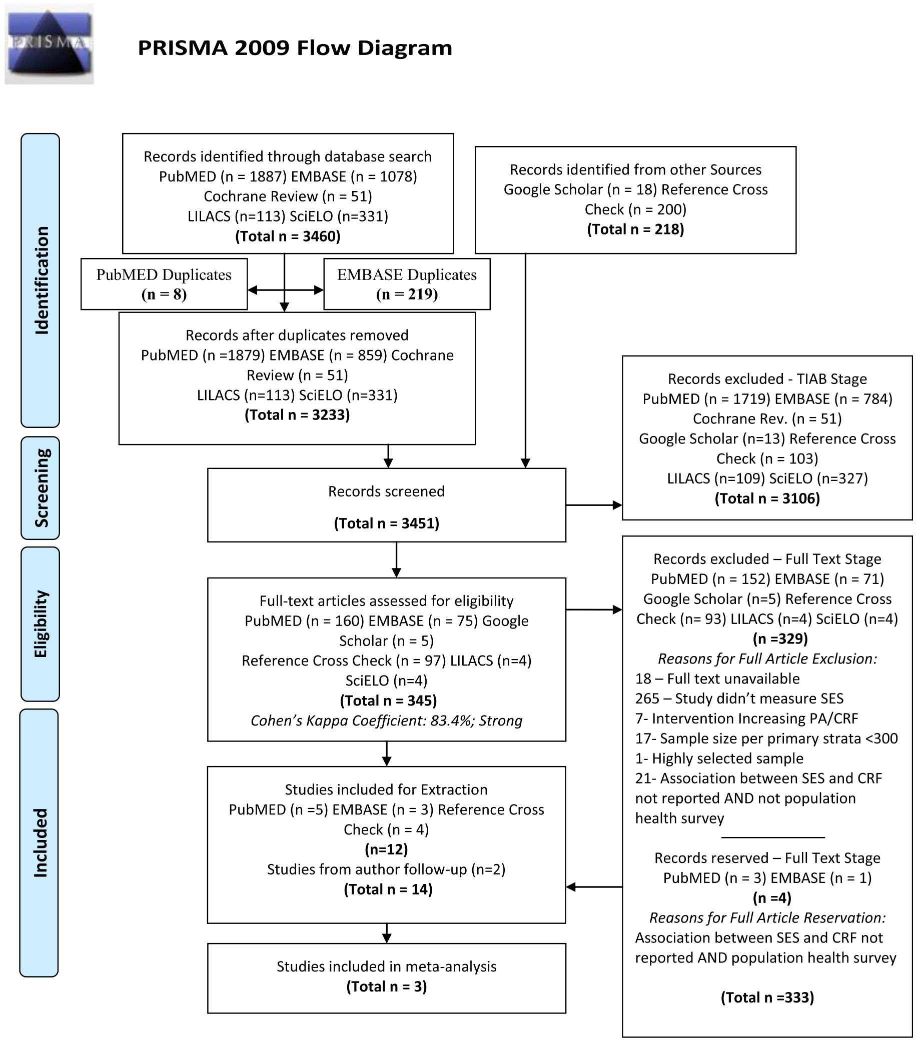

Fig. 1 Search strategy: PRISMA flow diagram. TIAB, title abstract

between 1992 and 2011; and two contained end points after 2011. Studies were from the US ($n = 6$), Finland ($n = 2$), Germany ($n = 2$), Norway ($n = 1$), Sweden ($n = 1$), Ireland ($n = 1$), Israel ($n = 1$), and Australia ($n = 1$). Most common confounders adjusted for were age, PA, alcohol consumption, BMI, and WC. One study fulfilled all methodological quality criteria, six studies had low risk of bias, and eight studies had moderate risk of bias. The major risk of bias across studies was participant selection methodology i.e. sampling method other than probability-based sampling.

Outcome: CRF

Included studies ($n = 15$) were heterogeneous with respect to measurement of CRF. CRF was measured and reported as estimated VO_{2max} (ml/kg min) in six studies, while two studies directly measured VO_{2max} using breath analysis (l/min). Three studies measured and reported CRF as exercise duration (seconds), in some cases additionally paired with a heart-rate indicator (WL_{130}). Two studies measured and reported METS (energy expenditure during treadmill testing). Indicators reported by only one study include $PWC_{75\%}$ (physical working capacity at 75% of the predicted maximal heart rate, watts) and longitudinal fitness categories constructed using PWC_{170} (watts). Specific details about CRF measurement can be found in Tables 2 and 3.

Exposure: SES Indicators

Categorical education (years), the most frequent indicator, was presented in 11 studies; 10 studies reported own education, and 1 study reported longitudinal educational mobility categories. Other SES exposures included composite measures of SES combining several indicators (high, medium, low, $n = 3$), residential area-level SES

Table 2 Results summary: education

Year	Author	Design	Country	n	Age	CRF	Measure	Association	Direction	p value	Quality
1996	Lakka et al. [41]	CRF Cross-sectional	FIN (KIHD)	Male 2280	42–61	VO_{2max} (l/min) cycle Protocol: Individual	Mean + SD	Positive gradient	+	$p < .001$	66%
2014	Ittermann et al. [45]	Cross-sectional	DE (SHIP-1) & (SHIP-Trend)	male 2074 female 2110	20–85	VO_{2max} (ml/min) cycle Protocol: Standardized (modified Jones)	β	Higher in high vs. low education (m) CRF increases with education (f)	+	$p < .009$ (m) $p < .056$ (f)	84%
2005	Dyrstad et al. [42]	CRF cross-sectional	N	Male 900	18–19	VO_{2max} (mL/kg·min) cycle Protocol: Individual	Mean + SD	8% higher fitness in high school academic vs. vocational training programs	+	$p < .01$	61%
2013	Ceaser et al. [47]	Cross-sectional	US (NHANES)	Total 3245	20–49	VO_{2max} (mL/kg·min) treadmill Protocol: Standardized (NHANES)	β	Increases with education (Hispanic Americans)	+	$p = .01$	92%
2006	Fogelholm et al. [43]	Cross-sectional	FIN	Male 891	21–43	VO_{2max} (mL/kg·min) cycle Protocol:Individual	β^a	Increases with education	+	$.01 < p < .05$	73%
2014	Thai et al. [49]	Cross-sectional	US (NHANES)	Total 2761	12–49	Low eVO_{2max} (≤ 31.98 mL/kg·min) treadmill Protocol: Standardized (NHANES)	OR	Higher odds in medium vs. low education	U	OR 95% CI (1.01–1.97)	100%
2014	Shmueli et al. [50]	Cross-sectional	IL (TAMCIS)	Total 3854	20–80	CRF in METS treadmill Protocol: Standardized (Bruce)	β	Higher mean difference in medium. vs. low education	U	$p < .05$ p trend = .002	63%
1995	Braun et al. [44]	Cross-sectional	US (CARDIA)	Total 4930	18–30	Exercise duration (sec) treadmill Protocol: Standardized (modified Balke)	β	Increases with education	+	$p < .05$	92%
						WL_{130} (sec) treadmill Protocol: Standardized (modified Balke)	β	No association	Ø	NR	
1992	Sidney et al. [48]	Cross-sectional	US (CARDIA)	Black male 1123 white male 1147 black female 1428 white female 1270	18–30	Exercise duration (sec) treadmill Protocol: Standardized (modified Balke)	β	Increases with education (black male)		$p < .05$ (black male)	92%
								Higher (white male) highest (white female)	+	$p < .001$ (white male and female)	
								No association (black female)	NS	NS (black female)	
						WL_{130} (sec) treadmill Protocol: Standardized (modified Balke)	β	WL_{130} increases with education (black male)	+	$p < .05$ (black male)	

Table 2 Results summary: education *(Continued)*

Year	Author	Design	Country	*n*	Age	CRF	Measure	Association	Direction	*p* value	Quality
1984	Blair et al. [46]	Cross-sectional	US (Cooper Center)	Female 2200	18–75	Exercise Duration (sec) treadmill Protocol: Standardized (modified Balke)	β^a	Highest with postgraduate study, some college decreases duration most	U	$p < .01$	63%
Social mobility											
2009	Cleland et al. [51]	Prospective cohort	AU (CDAH)	Total 645	26–36	Fitness Decrease (PWC_{170}) cycle Protocol: Standardized (W170)	RR	Higher risk of decrease in fitness than persistent unfit state in persistent medium vs. persistently low SES	(–)	$p < .05$	77%
						Fitness Persists (PWC_{170}) cycle Protocol: Standardized (W170)	RR	Higher risk that unfit state persists than fitness persists in persistent medium vs. persistently low SES	(–)	$p < .05$	
						Fitness Increase (PWC_{170}) cycle Protocol: Standardized (W170)	RR	Higher likelihood that fitness increases than unfit state persists in high and upwardly mobile vs. persistently low SES	+	$p < .05$	

[a]Standardized beta coefficient

Table 3 Results summary: additional socioeconomic status indicators

Year	Name	Design	Country	*n*	Age	CRF	Measure	Association	Direction	*p* value	Quality
Socioeconomic indicator: composite SES index											
2014	Shmueli et al. [50]	Cross-sectional	IL (TAMCIS)	Total 3854	20–80	CRF in METS treadmill Protocol: Standardized (Bruce)	β	CRF increases with SES	+	$p < .05$ p trend < .001	63%
1998	MacAuley et al. [128]	Cross-sectional	IE (NIHAS)	Total 528	16–74	VO_{2max} (mL/kg·min) treadmill Protocol: Individual	Mean + SD	No association	Ø	NS	71%
2013	Finger et al. [52]	Cross-sectional	DE (DEGS)	Male 1371 female 1441	18–64	High CRF (top 40% of $PWC_{75\%}$ dist.) cycle Protocol: Standardized (WHO)	OR	CRF increases with SES (f)	+	$p < .001$	96%
Socioeconomic indicator: residential area SES											
2016	Lindgren et al. [53]	Cross-sectional	S (SCAPIS)	Total 592	50–64	VO_{2max} (mL/kg·min) cycle Protocol: Standardized (SCAPIS)	median + (IQR)	Median fitness increases with area SES	+	$p < .05$	57%
2008	Shishehbor et al. [54]	Cross-sectional	US (CARDIA)	Total 2505	25–42	Impaired CRF in METs (lowest quintile per gender) treadmill Protocol: Standardized (modified Balke)	OR	Lower odds of low fitness in high SES areas	+	p trend < .001	63%
Socioeconomic indicator: occupation											
1996	Lakka et al. [41]	CRF cross-sectional	FIN (KIHD)	Male 1907	42–60	VO_{2max} (l/min) cycle Protocol: Individual	mean + SD	Higher mean fitness among white collar than blue collar workers and farmers	+	$p < .001$	66%
2014	Shmueli et al. [50]	Cross-sectional	IL (TAMCIS)	Total 3854	20–80	CRF in METS treadmill Protocol: Standardized (Bruce)	β	Fitness mean difference increases with occupation skill	+	$p < .05$ p trend < .001	63%
Socioeconomic indicator: income											
1996	Lakka et al. [41]	CRF cross-sectional	FIN (KIHD)	Male 1907	42–60	VO_{2max}(l/min) cycle Protocol: Individual	Mean + SD	Positive gradient	+	$p < .001$	66%
2014	Shmueli et al. [50]	Cross-sectional	IL (TAMCIS)	Total 3854	20–80	CRF in METS treadmill Protocol: Standardized (Bruce)	β	No Association	Ø	NS	63%
Socioeconomic indicator: employment status											
1996	Lakka et al. [41]	CRF cross-sectional	FIN (KIHD)	Male 2280	42–60	VO_{2max} (l/min) cycle Protocol: Individual	Mean + SD	Higher mean fitness when employed	+	$p < .001$	66%

(high, medium, low, $n = 2$), own occupation ($n = 2$), income based indicators ($n = 2$), and employment status (employed or unemployed, $n = 1$).

Results of Individual Studies by Exposure

Socioeconomic exposures excluded from meta-analysis generally showed a positive relationship between SES exposure and CRF measure of interest. Individual studies within the primary exposure for meta-analysis, education, generally showed a positive relationship between high education and CRF measure of interest. Three studies showed a u-shaped relationship.

Education

Four studies [41–44] observed a positive association between education and VO_{2max} ($p < 0.05$, $0.01 < p < 0.05$, $p < 0.01$, $p < 0.001$). The study [45] observed that VO_{2max} increased with education among women ($p < 0.056$), but only high education improved CRF relative to low education among men ($p < 0.009$). Exercise duration from one study [46] increased most when comparing the highest and lowest education categories ($p < 0.01$). Two studies [47, 48] presented a positive association between education and CRF that varied by ethnic subgroup. Study [47] observed a significant positive association between education and CRF, among Hispanic Americans only ($p = 0.01$). The study [48] observed higher positive association between education and exercise duration among white participants ($p < 0.001$), compared to black participants ($p < 0.05$). The increase in exercise duration with education was higher among white men and highest among white women but was non-significant among both subgroups for WL_{130}. Black males showed increase in WL_{130} with education ($p < 0.05$), while black women showed no significant associations for either measure of CRF.

Three studies [46, 49, 50] observed a u-shaped association between education and CRF. Among the studies reporting an inverted u-shaped association, study [50] observed that CRF increase was largest when comparing medium and low education level ($p < .05$). Study [49] presented an OR measure of association between education and CRF and observed that participants in medium education group had higher odds of *low* VO_{2max} (OR 1.41, 95% CI (1.01–1.97)), than participants in the high education group (OR 1.24, 95% CI (0.79–1.94)), when compared to lowest education group. This study was additionally adjusted by measures of periodontal health.

The study [51] observed an association between social mobility and longitudinal fitness. The study observed that persistently high or upwardly mobile SES status, compared to the persistently low SES status, resulted in higher likelihood of increased fitness ($p < 0.05$) than persistence of an unfit state.

All other SES Indicators

Studies [50, 52] reporting a significant association between CRF and composite socioeconomic indices presented multivariable analysis and observed a positive association ($p < 0.05$, $p < 0.001$). Results from the study [52] varied by sex; odds of high fitness were increasingly greater ($p < 0.001$) with higher SES index score, among women, while men showed non-significant results.

Studies [53, 54] reporting on the association between CRF and residential area SES conducted multivariable regression analysis and observed that median VO_{2max} increased and odds of low fitness (METs) decreased with higher residential area SES.

Both studies [41, 50] reporting the association between participant occupation and CRF observed a significant positive association between skilled occupation and CRF ($p < 0.001$ and $p < 0.05$).

While study [50] observed no significant association between financial strain and METS during treadmill exercise, study [41] identified a positive linear association between income and VO_{2max} ($p < 0.001$) using ANCOVA analysis.

Finally, the study [41] observed that VO_{2max} was higher among employed individuals ($p < 0.001$).

Direct vs. Indirect VO_{2max} Measurement

Across all exposures, studies measuring and reporting direct measures of VO_{2max} showed a strictly positive relationship between SES and CRF, while indirect measures of VO_{2max} showed a positive relationship overall. Two studies directly measured VO_{2max} through breath analysis and reported a positive association between SES and CRF. Among studies estimating VO_{2max}, four studies reported a positive association, one reported an inverted u-shaped association and one reported no association.

Synthesis of Results

Results of meta-analysis are presented in Figs. 2 and 3. Compared to individuals with low education, both men and women with high education showed significantly higher CRF (men 0.12 [0.04–0.20], women 0.19 [0.02–0.36]), while participants with medium education showed no significant difference in CRF compared to individuals with low education (men 0.03 [− 0.04–0.11], women 0.09 [− 0.03–0.21]).

Risk of Bias Across Studies: (I^2 Measure of Heterogeneity)

Our analysis standardizes both exposure and outcome to limit heterogeneity. Accordingly, among men the fully adjusted model (adjusted for age, PA, alcohol consumption, WC, and BMI) had low heterogeneity, with a non-significant p value > 0.1 (medium education: $I^2 = 0\%$, p value = 0.477; high education: $I^2 = 0\%$, p value = 0.544) while among women the fully adjusted model showed substantial heterogeneity, p value < 0.1 and I^2 value in the range 50–90% [55] (medium education: $I^2 =$

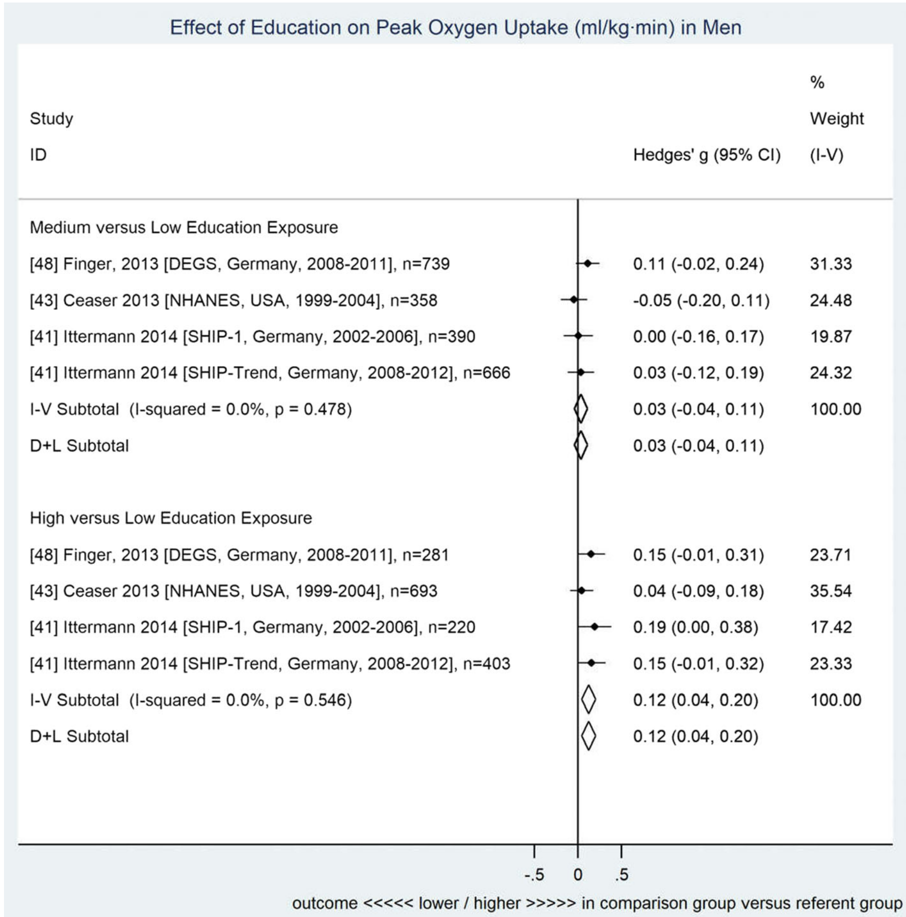

Fig. 2 Forest plot for the association between education and cardiorespiratory fitness among men. Data shown are standardized mean differences ± 95% CI (fully adjusted including physical activity, $n = 4815$). Subtotals presented for both fixed (inverse variance method) and random effects (DerSimonian and Laird) models. Reference details precede study descriptors

52.9%, p value = 0.095; high education: $I^2 = 71\%$, p value = 0.016). Presentation of the results from random effects meta-analysis adjusts for this heterogeneity within the fixed effects meta-analysis.

Additional Analysis

Meta-regression testing differences in the effect of education on CRF with adjustment for PA detected no significant differences ($p > 0.385$).

Studies from the US, that were systematically reviewed, reported differences in the association between CRF and education by ethnicity of the study sample [48], thus we performed additional post-hoc sensitivity analyses, adjusting NHANES data by "race." The measures of association between SES and CRF marginally increased, however the trend among men and women did not vary from the original meta-analysis. Studies included for meta-analysis had low risk-of-bias-score; thus, no sensitivity analysis by quality assessment score was conducted.

Discussion

In this systematic review and meta-analysis of the association between SES and CRF in adults, evidence from 15 population-based studies from 8 different countries, shows that predominately higher SES is associated with increased CRF. Socioeconomic exposures, such as SES indices, composed of various SES indicators [50, 52], and residential area SES [54], generally showed a positive relationship with CRF [41, 53]. Studies using education level as an exposure, showed either a positive relationship between education and CRF [41–45, 47, 48, 51] or a u-shaped relationship [46, 49, 50].

Meta-analysis of the most frequently reported association; between education and $VO_{2max,}$ was based on a sample of 9435 non-symptomatic individuals from four population-based studies. Meta-analysis showed a significant positive association between education and CRF for men and women when comparing the highest with the lowest of three education groups. To the best of our

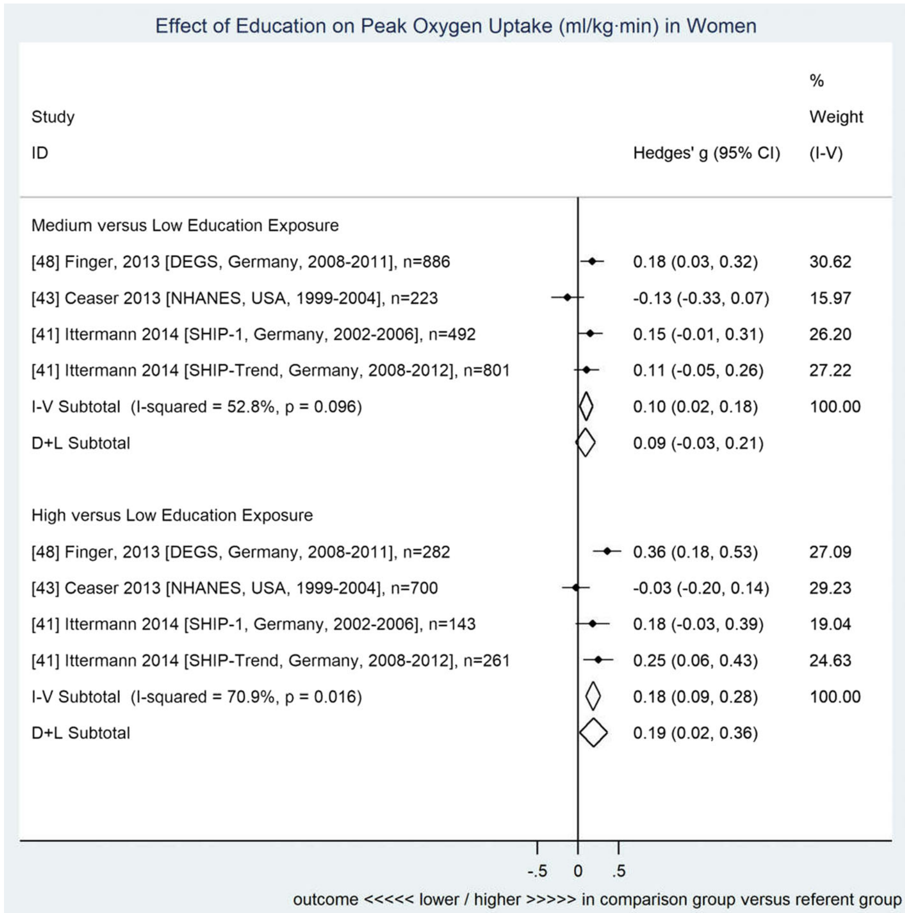

Fig. 3 Forest plot for the association between education and cardiorespiratory fitness among women. Data shown are standardized mean differences ± 95% CI (fully adjusted including physical activity, $n = 4620$). Subtotals presented for both fixed (inverse variance method) and random effects (DerSimonian and Laird) models. Reference details precede study descriptors

knowledge, this is the first systematic review conducted on the association between SES and CRF; thus, it is impossible to compare our findings with previous reviews. However, reviews on the association between SES and PA report observations in line with our findings: a positive association between SES and health-enhancing total leisure time PA [56]. Additionally, research from both the USA and Germany shows that SES is positively associated with aerobic physical activity. In 2014, the percentage of US adults, age 18 and over, who met federal guidelines for aerobic physical activity increased as family income increased [57], with 51.7% of US adults meeting the 2008 federal physical activity guidelines for aerobic activity [58]. Similar patterns can be observed among German adults in 2014; 45.3% of German adults met the WHO recommendation for aerobic activity, with higher compliance among individuals with higher education [59].

CRF inequalities across levels of SES likely stem from differences in health behavior. Lower SES is associated with health-compromising behaviors such as low levels of aerobic leisure-time PA [56, 59, 60], high sugar-rich and fat-rich food intake and low fruit and vegetable intake [52, 61, 62], and high smoking prevalence [63–66]. While the previously mentioned health-compromising behaviors are strictly negatively associated with SES, the association between SES and alcohol consumption varies by dose. Heavy episodic alcohol consumption, defined as pure alcohol intake of 60 g or more, during a single occasion, at least once per month [67], is associated with lower SES [68], while risky alcohol consumption, or consumption of 10–12 g of pure alcohol daily for women and 20–24 g for men [69, 70] is associated with higher SES [71]. Lower SES is also related to obesity [72]. These disadvantageous behaviors and conditions lead to poorer health and are primary risk factors for chronic diseases such as diabetes [73–76], cardiovascular disease (CVD) [71, 76–80], and cancer [76–78, 81, 82]. Similarly, it has been demonstrated that obesity and overweight [56], physical inactivity, and smoking are negatively associated with CRF [83]. Conversely, moderate average alcohol consumption (defined as 4–15.8 g/d) improves CRF more than non- or heavy average alcohol consumption, in an inverted u-shaped fashion [84]. Overall, it is likely that these health behaviors and conditions are underlying causes of the positive association between SES and CRF. It is also possible that the positive association between SES and CRF is explained by the negative association between high SES and chronic breathlessness: individuals with high SES are less likely to suffer from chronic breathlessness and by extension to have higher CRF [85, 86]. Consider that 15% of participants from SHIP-0 (1997–2001; $n = 4308$) and 17.7% of participants from SHIP-Trend (2008–2012; $n = 4420$) reported "shortness of breath at load" [81], demonstrating that measured fitness may have been impacted by chronic breathlessness. Apart from behavioral and health-related factors, genetic factors are also known to influence physical fitness [87–91]. However, whether the association between SES and CRF could be partly explained by genetic dispositions cannot be determined based on available evidence in the literature.

The importance of CRF for public health is reflected in the policy statement from the American Heart Association, from 2013, calling for a national registry on CRF [92]. Previous research has demonstrated that increased CRF is associated with various health benefits leading to a significant reduction in mortality rates [93]. CRF can be increased through regular PA participation [94, 95], however, not all types of PA are beneficial for CRF. Occupational PA often corresponds with muscle-strengthening activity or low-intensity tasks performed over long periods (8-h work shifts) [96] and seems to be less beneficial for CRF than aerobic sports and physical exercise activities mostly performed during leisure time [41, 97]. Adults with low SES are more likely to work in physically-demanding jobs and to show a higher total energy expenditure compared to adults with high SES who are more likely to have sedentary jobs and perform aerobic physical exercise in leisure time [59, 60, 98]. Thus, it seems that adults with low SES do not show lower CRF because they are less physically active [99], rather, because the types of PA they perform are less often aerobic and hence less beneficial for CRF and cardiovascular health [100, 101]. As a result, consideration of SES differences in working conditions is essential to address SES differences in CRF. Health interventions, striving to improve PA at the population level, mostly promote aerobic PA in leisure time, and thus fail to reach adults with low SES. The low prevalence of aerobic PA in leisure time among individuals with low SES is also illustrated by increasing social inequality in sporting activity prevalence in the adult German population over the last decade [102]. Health promotion activity delivery to individuals with low SES backgrounds remains a crucial challenge, however, workplace aerobic physical activity interventions for manual workers are a possible solution to the challenge of reaching individuals, of low SES background, for CRF improvement [103]. In 2008, the US Federal Government issued *Physical Activity Guidelines for Americans* [104], which provided science-based guidelines recommending adult aerobic PA targets for achievement of substantial health benefits [105, 106], which were adapted by the WHO in 2010. The population-based monitoring of PA guideline compliance is difficult because PA is often monitored based on self-reports, making it difficult to distinguish aerobic PA from other types of PA, and introducing the possibility of misclassification bias. Objectively measured CRF, applied for population-based health monitoring purposes, can be an important tool to accurately gauge health target compliance and prevent bias from self-reported PA. Furthermore, objectively measured CRF can be used to monitor chronic disease risk, including cardiorespiratory disease risk [107]. CRF is an important tool for population health monitoring precisely because there is a large body of evidence that CRF is a potentially stronger predictor of mortality than established risk factors such as smoking, hypertension, high cholesterol and diabetes type 2 mellitus [108]. Furthermore, the addition of CRF to traditional risk factors significantly improves the precision of risk prediction for cardiovascular morbidity and mortality [109–111] and addition of CRF to traditional CVD risk measures (such as Framingham risk score or SCORE Risk Charts) improves cardiovascular risk prediction [112]. Clinicians use measures linking CRF changes to disease decline [16] to objectively monitor individual and population health risk. Clinicians could also use CRF thresholds [113] by education status to identify low SES groups suffering health disparity for targeted, early NCD prevention, potentially reducing the need for complex, expensive treatments and long-term economic burden. Insights about the association between SES and CRF could be used to monitor, prioritize and, by extension, improve health outcomes among marginalized populations with high risk of chronic disease, whose needs may not be met by traditional health promotion activities. Monitoring and prioritization of health outcomes among marginalized populations has been established by organizations such as WHO and the Pan American Health Organization (PAHO) as a key priority for controlling NCD epidemics in low resource settings.

Limitations

Although included studies are generally population-based and not underpowered, the current meta-analysis includes only four population-based studies, due to the limited number of population-based studies reporting objective measures of CRF in the literature. Accordingly, the power of meta-analysis to detect a significant effect between SES and CRF may be limited. Ability to detect differences in effect by sex, with PA adjustment, and by ethnicity in NHANES data may also be limited by sample size of the meta-analysis. Our choice of education categories may have also affected results. The chosen education categories (high, medium, and low, based on CASMIN education classification [35]), may have limited the ability to detect subgroup differences through sensitivity analysis due to combination of disparate subgroups. Furthermore, overall results among women should be cautiously interpreted due to the high heterogeneity within this subgroup. Differences in the results of studies included for meta-analysis, and the resulting heterogeneity may be due to use of different exercise protocols for CRF measurement [114]. The association between CRF and various socioeconomic exposures was presented in the literature, but the present meta-analysis focuses on education due to issues with heterogeneity of exposure indicators used and minimum sample size required for rigorous meta-analysis. However, the omission of additional SES measures in the meta-analysis does not significantly impact overarching findings because SES indicators measuring different aspects of social position show similar association with CRF. For example, Shmueli et al. observed significantly different mean exercise capacity in higher vs. lower SES levels across education, occupation, and compiled SES indicators [50]. Similarly, Lakka et al. observed a positive dose relationship between education and income, and higher VO_{2max} with higher occupational skill [41]. Although few studies report degree of agreement between association of various SES indicators, measuring different aspects of social position, with CRF, overall agreement between indicators can also be seen for the relationship with PA [56, 115]. Studies included for review adjusted their analysis for varying sets of covariates which may impact overall result agreement. We correct for this through meta-analysis of standardized effect sizes that were derived from individual study results, which had been adjusted for a standard set of covariates. Finally, generalizability across levels of country income classification may be limited due to inclusion of only studies from high-income countries. However, inclusion of studies from only high-income countries also reduces heterogeneity within the meta-analysis by controlling the effect of country income classification on the association between SES and CRF [116, 117].

Recommendations

Systematic review of the literature revealed that few population-based studies reported SES exposures in addition to education. Population-level investigation of the effects of additional measures of SES, such as income, occupation, or composite SES indices on CRF is also necessary. Future research should include additional SES indicators in meta-analysis in order to gauge whether the relationship observed between education and CRF is generalizable to other SES indicators. Investigation of differences in the relationship between SES and CRF by outcome measure is also necessary, to compare the effect of SES on VO_{2max} (gold standard) with the effect of SES on additional CRF measures commonly cited in the literature. Adjustment for total PA did not significantly impact the results of meta-analysis, however total PA obfuscates domain specific PA. Future research should investigate the effect of adjustment for domain specific PA types that are known to be differentially correlated with SES—such as occupational physical activity (correlated with low SES) and leisure time PA (correlated with high SES) [60]. Additionally, sedentary behavior is an important determinant of CRF [118, 119], but was not included as a covariate in analyses where CRF was the outcome of interest. Future research on the association between SES and CRF might include sedentary behavior as a study covariate to strengthen results. While the patterns observed for the association between education and CRF were fairly similar among men, differences in the association between education and CRF among women from Germany and the USA should be explored. Furthermore, although sensitivity analysis showed no significant difference in the effect of SES on CRF by ethnicity, additional research regarding the effect of ethnicity on the relationship between SES and CRF would contribute to more accurate monitoring of chronic disease risk within marginalized populations [120] and help to effectively target these groups for prevention [91, 121–123]. Most studies that were systematically reviewed were cross-sectional, thus more cohort studies are required to rigorously establish an association between SES and CRF. The meta-analysis disproportionately represents populations from Germany due to data access constraints, thus inclusion of population-based studies from various countries across high-income countries would improve result quality and external validity. Included studies are from high-income countries only; future research should consider whether low- and middle-income countries reflect the association observed in high-income countries, and whether nutritional and PA transition processes [124–127] that take place during economic development influence the association between SES and CRF.

Conclusions

Despite limitations, we conclude that there is fair evidence in the literature for an association between high levels of education and increased CRF. This could have implications for monitoring, of health target compliance and of chronic disease risk among higher risk populations, to detect and prevent NCDs. In light of shifting NCD burden from adults with high SES to adults with low SES, defining CRF health targets, monitoring CRF and PA target compliance at the population level and developing tailored health promotion measures to stimulate CRF—especially among adults with low SES background—is necessary to improve cardio-metabolic health in the general adult population and to diminish social health inequalities.

Additional cohort studies are required to rigorously establish an association between SES and CRF. Furthermore, studies investigating the impact of ethnicity on the relationship between education and CRF would help improve the efficacy of targeted NCD detection and prevention among high-risk demographic subgroups.

Abbreviations

95% CI: 95% confidence interval; ANCOVA: Analysis of covariance; BMI: Body mass index; CASMIN: Comparative Analysis of Social Mobility in Industrial Nation classification; CPET: Cardiopulmonary exercise testing; CRF: Cardiorespiratory fitness; CV: Cardiovascular; CVD: Cardiovascular disease; ES: Effect size; HIV/AIDS: Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome; I^2 statistic: Percentage of variance in the study-specific point estimates that is attributable to true between-study heterogeneity as opposed to sampling variation; LILACS: Latin American and Caribbean Health Sciences; MeSH: Medical subject heading; METS: Metabolic equivalent tasks; NCD: Non-communicable disease; NHANES: National Health and Nutrition Examination Survey; OR: Odds ratio; PA: Physical activity; PAHO: Pan American Health Organization; PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analysis; PROSPERO: International Prospective Register of Systematic Reviews; PWC_{170}: Physical working capacity at a heart rate of 170 beats per minute; $PWC_{75\%}$: Physical working capacity at 75% of the predicted maximal heart rate; SciELO: Scientific Electronic Library Online; SES: Socioeconomic status; SHIP: Study of Health in Pomerania; TB: Tuberculosis; VO_{2max}: Maximal oxygen consumption; VO_{2peak}: Peak oxygen consumption; WC: Waist circumference; WHO: World Health Organization; WL_{130}: Work load 130, exercise test duration to heart rate of 130 beats per minute

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Authors' Contributions

KJO, NP, JZ, TK, GBMM, and JDF contributed to the conception and design of the manuscript. KJO, NP, JZ, TI, RE, MD, and JDF contributed to the acquisition and assembly of data. KJO, JH, TI, RE, MD, TK, GBMM, and JDF contributed to the interpretation of data. KJO, JZ, GBMM, and JDF drafted and revised the manuscript. NP, JH, TI, RE, MD, and TK revised the manuscript. KJO wrote the first draft and final version of the manuscript. All authors critically revised the manuscript for important intellectual content and approved the final manuscript. Additionally, all authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

Not applicable

Competing Interests

The authors Katherine J. Ombrellaro, Nita Perumal, Johannes Zeiher, Jens Hoebel, Till Ittermann, Ralf Ewert, Marcus Dörr, Thomas Keil, Gert B. M. Mensink, and Jonas D. Finger declare that they have no competing interests.

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Publikation III

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Individual and interpersonal correlates of cardiorespiratory fitness in adults – Findings from the German Health Interview and Examination Survey

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Cardiorespiratory fitness (CRF) is an established predictor of adverse health outcomes. The aim of this study is to investigate potential behavioral, interpersonal and socioeconomic correlates of CRF among men and women living in Germany using data from a population-based nationwide cross-sectional study. 1,439 men and 1,486 women aged 18–64 participated in the German Health Interview and Examination Survey (2008–2011) and completed a standardized sub-maximal cycle ergometer test. Maximal oxygen consumption ($\dot{V}O_2max$) in ml·min^{-1}·kg^{-1} was estimated. Mean values of VO_2max for various anthropometric, behavioral, interpersonal, and sociodemographic variables were estimated. Linear regression analyses using multiple imputations technique for missing values was performed to analyze the influence of potential correlates on CRF. Women with high alcohol consumption had higher $\dot{V}O_2max$, ($\beta = 2.20$; 95% CI 0.98 to 3.42) than women with low alcohol consumption and women with high occupational status had higher $\dot{V}O_2max$ ($\beta = 1.83$; 95% CI 0.21 to 3.44) in comparison to women with low occupational status. Among men, high fruit intake ($\beta = 1.52$; 95% CI 0.63 to 2.40), compared to low or medium fruit intake and performing at least 2.5 hours of total PA per week ($\beta = 2.19$; 95% CI 1.11 to 3.28), compared to less than 2.5 hours was associated with higher $\dot{V}O_2max$. Among both men and women, lower body mass index, lower waist circumference and higher levels of physical exercise were considerably associated with higher $\dot{V}O_2max$. Among women, those in higher age groups showed a considerably lower level of $\dot{V}O_2max$ compared with those aged 18–24. Furthermore, mean estimated $\dot{V}O_2max$ was higher among men (36.5; 95% CI 36.0 to 37.0) than among women (30.3; 95% CI 29.8 to 30.7). Despite the cross-sectional nature of the current study, we conclude that several behavioral, anthropometric, and sociodemographic factors are associated with CRF in the general adult population in Germany. These results can provide evidence to tailor prevention measures according to the needs of specific subgroups.

Cardiorespiratory fitness (CRF) is an important marker of cardiovascular health and thus a crucial factor in the prevention of non-communicable diseases. CRF, defined as the ability of circulatory, respiratory and muscular systems to supply oxygen during prolonged physical exercise[1], has a strong inverse relation to the incidence cardiovascular diseases[2], cancer[3], diabetes mellitus, depression[4] and all-cause mortality[2]. Taking into account the impact of CRF on individual health, efforts should be taken to enhance fitness in the general population. For the development of adequate interventions, knowledge about the causes of CRF, as well as population groups at elevated risk of having a low CRF, is crucial. Figure 1 shows a conceptual framework of the potential correlates

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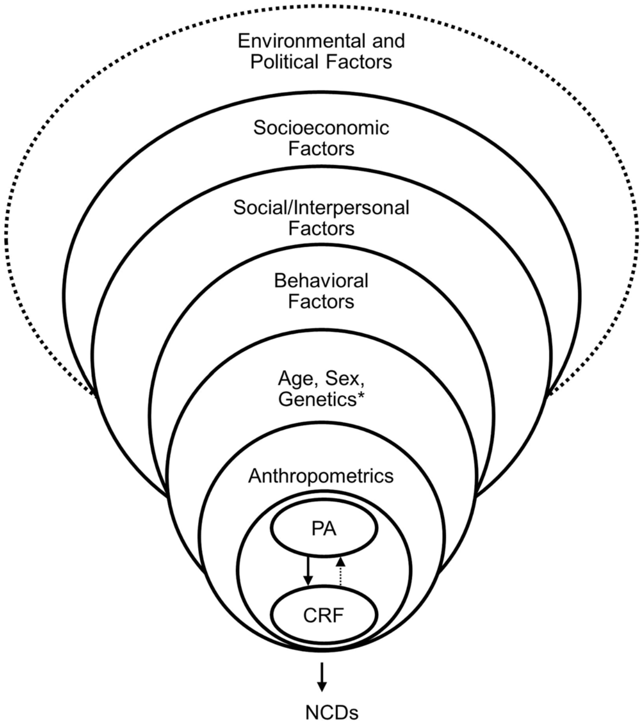

Figure 1. Schematic conceptual framework of the correlates of cardiorespiratory fitness (adapted from[5]). Solid lines: potential domains of the correlates of cardiorespiratory fitness investigated in the present study. Dotted lines: potential domains of the correlates of cardiorespiratory fitness *not* investigated in the present study. *Genetic factors were *not* investigated in the present study. *PA* physical activity, *CRF* cardiorespiratory fitness, *NCDs* non-communicable diseases.

of CRF adapted from a model proposed by Després[5]. Although CRF is partly genetically determined[6], it can be enhanced by regular endurance exercise[7], and further factors may play a role[8]. CRF has been shown to decrease with age[9,10] and is on average lower among women than men[11]. Furthermore, numerous studies have demonstrated an association between anthropometric measures, such as waist circumference (WC) or body mass index (BMI), with CRF[8]. Following explanatory ecological models on physical activity (PA)[12,13], one can postulate that further determinants and correlates of CRF on the individual, interpersonal, socioeconomic or environmental level could exist[5,8,14]. In fact, CRF has been linked to behavioral (e.g., alcohol consumption[15]), socioeconomic (e.g., education[16]) and environmental factors (e.g., commuting distance[17]). Finally, all of these factors are influenced by an environmental and political framework.

However, evidence of consistent associations between CRF and many of these factors is limited[8]. While basic sociodemographic factors such as age and sex as well as physical activity and anthropometric factors have been investigated in multiple settings, research on other health behaviors or interpersonal factors is scarce. Furthermore, to our knowledge, no study has yet examined potential influencing factors of CRF within the German general population. We therefore aimed to investigate potential behavioral, interpersonal and socioeconomic correlates of CRF among men and women living in Germany using data from a population-based nationwide cross-sectional study.

Methods

Study design. The present analysis uses cross-sectional data from the German Health Interview and Examination Survey for Adults (DEGS1). DEGS1, a nationwide population based health examination survey, is part of the Federal Health Monitoring System operated by the Robert Koch Institute[18]. The study design is described in detail elsewhere[19]. Briefly, 7,238 individuals aged 18 to 79 years participated in the physical measurements component of the DEGS1. The survey design is based on a two-stage cluster random sampling procedure. In the first step, 180 sample points were randomly selected and stratified to represent regional distributions. In the second step, within these 180 units, adults were randomly drawn from local population registries stratified by 10-year age groups. Data collection took place between November 2008 and December 2011. The response rate was 42%. All methods were performed in accordance with the relevant guidelines and regulations.

Of the total sample of 5,262 individuals aged 18 to 64 years, 3,110 subjects were categorized as test-qualified for the cycle ergometer test test. Overall, 3,030 participants completed the exercise test (97.4%). $\dot{V}O_2max$ was estimated for all participants reaching at least 75% of the age-predicted maximum heart rate. 204 (6.7%) of the participants terminated the test before reaching this heart rate. As a result, the final study sample comprised of 2,826 participants, 1,447 of whom were women and 1,379 were men (see flow diagram of participants; Supplementary Fig. 1, Additional File 1).

Outcome variable: cardiorespiratory fitness. CRF was measured in participants aged 18–64 years using a standardized, submaximal cycle ergometer test (Ergosana Sana Bike 350/450, Ergosana, Bitz, Germany). Test methodology, test protocol, and exclusion criteria are described in detail elsewhere[11,20]. The participants initially completed a modified version of the Physical Activity Readiness-Questionnaire (PAR-Q)[21,22]. In participants with contradictions reported according to PAR-Q, a physician decided whether or not such participants should be enrolled into the exercise test. CRF was assessed using the test protocol recommended by the World Health Organization (WHO)[23]: Beginning at 25 watts, the workload was incrementally increased by 25 watts every two minutes until 85% of the estimated age-specific maximal heartrate was exceeded, a maximum level of 350 watts was achieved or the test personnel terminated the test. Heart rate was monitored continuously throughout the test. The formula $208–0.7 \cdot Age$ was used to calculate the age-predicted maximum heart rate (HR_{max})[24]. To derive physical work capacity at HR_{max} ($PWC_{100\%}$), the measured heart rate (beats per minute) during the incremental phase was regressed against corresponding workload in watts for each participant. Assuming a linear relationship between heart rate and workload, $PWC_{100\%}$ was obtained by extrapolation using the individual regression equation $PWC_{100\%} = intercept + HR_{max} \cdot slope$[25]. $PWC_{100\%}$ was further converted to $\dot{V}O_2max$ using a metabolic equation provided by the American College of Sports Medicine[26]: $3.5\, ml{\cdot}min^{-1}{\cdot}kg^{-1} + 12.24{\cdot}(PWC_{100\%}){\cdot}(body\ weight^{-1})$.

Potential correlates of cardiorespiratory fitness. A comprehensive systematic literature review was performed in order to identify potential individual and socioeconomic correlates of CRF[8,14,16]. Potential interpersonal correlates of CRF were derived from evidence regarding the association of these factors and PA[12,27,28]. Based on this evidence, we developed a conceptual framework that depicts potential interrelations (Fig. 1,[8]). Corresponding covariates described below were then selected out of the DEGS1 variable list. Information on these covariates in the DEGS1 was assessed with self-administered questionnaires, physical examinations or tests by trained study personnel following standardized procedures[19].

Behavioral factors. Smoking status was classified as current (including occasional smoking), ex- or never smoking. A self-administered food frequency questionnaire was used to measure intake frequency and portion size in the last four weeks for a total of 53 food and beverage groups. This food frequency questionnaire was validated and showed reasonable validity against two 24-hour recalls[29]. We selected specific food-groups distinguishing between health enhancing ("fruits" and "vegetables") and health compromising products ("sugar rich drinks", "sugar rich foods" and "junk foods") based on evidence from the literature[30]. Quantities of intake of the food-groups were calculated by combining the frequency of intake and the portion size of the relevant food and beverage groups, and classifying them into two categories using sex-specific quintiles: low to moderate intake (quintile 1–3) and high intake (quintile 4–5). A detailed flowchart of food group selection and categorization can be found in Supplementary Fig. 2, Additional File 1. Ethanol in grams per day was estimated by multiplying the calculated quantity of each alcoholic beverage with standard ethanol content. Cumulated consumption was classified as low alcohol consumption (quintile 1), medium alcohol consumption (quintile 2–4), and high alcohol consumption (quintile 5) using sex-specific quintiles (Supplementary Fig. 2, Additional File 1).

Socioeconomic factors. Participants' need-weighted household net income (net equivalent income) was calculated based on information about estimated net income per month and number of individuals living in the household[31]. Income was then grouped into three categories: below 60%, 60–150% and above 150% of the median net household equivalent income, representing an income below the relative poverty line and an intermediate or relatively high income, respectively[32]. Educational level was assessed using the 'Comparative Analysis of Social Mobility in Industrial Nations' (CASMIN)[33] and classified into three categories (primary, secondary, and tertiary education). Occupational status was determined using the International Socio-Economic Index of Occupational Status (ISEI)[34] based on current occupation of the participants. The variable was classified into three groups: low (quintile 1), medium (quintile 2–4), high occupational status (quintile 5). Participants were further asked if they were born in Germany or abroad.

Interpersonal factors. Social support was assessed using the Oslo Three-Item Social Support Scale (OSS-3)[35] and classified as poor (3–8), moderate (9–11), and strong (12–14) social support. Marital status was grouped as single, married (while living together), and separated/divorced/widowed.

Anthropometric factors. Body weight and height was measured using portable electronic scales (SECA, Germany) and stadiometer (Holtain, UK). BMI (kg/m^2) was categorized according to the WHO guidelines[36] into underweight (BMI <18.5), normal weight ($18.5 \leq$ BMI <25), overweight ($25 \leq$ BMI <30) and obese (BMI ≥ 30). WC was measured at the smallest site between the lowest rib and the superior border of the iliac crest with flexible, non-stretchable measurement tape[37]. WC was categorized as 'normal', 'increased' and 'strongly increased' according to international guidelines[38].

Physical activity-related factors. Total PA was assessed by asking participants the number of days in an average week where they were physically active enough to start sweating or get out of breath. If they reported any PA, they were further asked about the duration of PA on such days[39]. Based on this information participants were classified into 2 groups, using the WHO recommendation as cut-off: <2.5 hours per week and ≥ 2.5 hours per week. Participants were asked "How often do you engage in physical exercise?"[39], with responses categorized into three groups: no physical exercise, <2 hours/week, ≥ 2 hours/week.

Statistical analyses. All statistical analyses were performed with Stata 15.1 (Stata Corp., College Station, TX, USA). Stata survey commands were used to adequately account for the cluster sampling design when calculating confidence intervals. Weighting factors were used, unless otherwise noted, to adjust the distribution of the sample to match those of the German population by sex, age, education and region for all calculations[40]. Scatterplots were computed to show the crude, unweighted association between age, WC and BMI with $\dot{V}O_2max$. Fractional-polynomial prediction plots with 95%-confidence intervals (95% CI) were then fitted to show the estimated associations between these variables. Mean $\dot{V}O_2max$ with 95% CI was calculated by behavioral, sociodemographic and interpersonal, anthropometric, and PA indicators. Multivariable linear regression models were computed to estimate the associations between potential correlates and estimated $\dot{V}O_2max$, stratified by sex. In Model 1 only age and behavioral factors (without total PA/ physical exercise) were included. In the next model (Model 2), sociodemographic and interpersonal factors were added. The subsequent models included the anthropometric (Model 3) and PA-related factors (Model 4). A complete case analysis would have led to a considerably reduced and less representative sample (n = 573 with missing values in at least one covariate; 20.3% of eligible cases [see Supplementary Fig. 1, Additional File 1]). Thus, we conducted multiple missing values imputation using chained equations[41] for BMI, WC, occupational status, education, migration status, marital status, total PA, physical exercise, smoking status, alcohol consumption as well as all food variables. We imputed 30 sex-specific datasets. Linear regression analyses were performed with each of the 30 datasets and the final coefficients are the results from all datasets combined. Multivariable linear regressions were performed using Stata multiple imputation commands in combination with the survey commands.

Ethics approval and consent to participate. The study protocol was approved by the Federal and State Commissioners for Data Protection and by the ethics committee of the Charité-University Medicine Berlin (No. EA2/047/08). Informed written consent was obtained from all participants.

Results

Overall, 47.4% of the included survey participants were women and the mean age of all participants was 38.4 years (95% CI: 37.9 to 38.8). CRF test participants were younger, not retired, higher educated, and reported higher levels of physical exercise than individuals who were not qualified for the test (Supplementary Table 1, Additional File 1).

Figure 2 shows the crude and fitted association between age, BMI and WC with estimated $\dot{V}O_2max$, indicating clear inverse associations between age, BMI, and WC with estimated $\dot{V}O_2max$.

Mean $\dot{V}O_2max$. Table 1 presents mean $\dot{V}O_2max$ by covariates selected for this study. Mean $\dot{V}O_2max$ (in ml·min^{-1}·kg^{-1}) was higher among men (36.5; 95% CI 36.0 to 37.0) than among women (30.3; 95% CI 29.8 to 30.7). $\dot{V}O_2max$ decreased with age in both women and men.

Further descriptive binary analyses showed that mean $\dot{V}O_2max$ was higher among women with high levels of alcohol consumption, secondary or tertiary education, high occupational status, high income, being single, having normal or underweight BMI, having a normal WC, being physically active and participating in physical exercise. Among men, mean $\dot{V}O_2max$ was higher among those with high junk food intake, being born in Germany, having secondary or tertiary education, being single, having normal or underweight BMI, having a normal WC, being physically active and participating in physical exercise.

Multivariable analyses. Multivariable analyses indicated that age, smoking, alcohol consumption, fruit intake, place of birth, WC, BMI, and physical exercise were associated with estimated $\dot{V}O_2max$ in both sexes (Table 2 and Table 3). While vegetable intake, income and occupational status were only observed to be associated with $\dot{V}O_2max$ among women, sugar-rich food intake, marital status and total PA showed a considerable association with $\dot{V}O_2max$ only among men.

The fully adjusted Model 4 showed a considerably lower level of $\dot{V}O_2max$ for women in higher age groups compared with those aged 18–24: among women aged 45 to 54 years, $\dot{V}O_2max$ decreased by $\beta = -2.08$ (95% CI -3.49 to -0.67) and in women aged 55 to 64 years by ($\beta = -4.27$; 95% CI -5.94 to -2.60), respectively (Table 2). Women with high alcohol consumption had higher $\dot{V}O_2max$, ($\beta = 2.20$; 95% CI 0.98 to 3.42) than women with low alcohol consumption. Similarly, women with high occupational status had higher $\dot{V}O_2max$ ($\beta = 1.83$; 95% CI 0.21 to 3.44) in comparison to women with low occupational status and those with increased and strongly increased WC had lower $\dot{V}O_2max$ than those with normal WC (increased WC: $\beta = -1.56$; 95% CI -2.45 to -0.68, and strongly increased WC: $\beta = -1.61$; 95% CI -2.85 to -0.38). In addition, an inverse association was observed between BMI and $\dot{V}O_2max$ among women: while underweight women had higher $\dot{V}O_2max$ compared to normal-weight women ($\beta = 3.13$; 95% CI 0.58 to 5.69), overweight ($\beta = -2.36$; 95% CI -3.26 to -1.46) and obese ($\beta = -4.88$; 95% CI -6.19 to -3.57) women showed considerably lower $\dot{V}O_2max$ compared to normal-weight women. Furthermore, among women $\dot{V}O_2max$ increased with the amount of physical exercise per week, with $\beta = 1.68$ (95% CI 0.84 to 2.52) for up to two hours and $\beta = 4.20$ (95% CI 3.10 to 5.30) for more than two hours of physical exercise per week compared to women not engaging in any physical exercise.

Among men high fruit intake was associated with higher $\dot{V}O_2max$, ($\beta = 1.52$; 95% CI 0.63 to 2.40), compared to low or medium fruit intake (Table 3). As among women, $\dot{V}O_2max$ was lower among men with increased WC ($\beta = -1.58$; 95% CI -2.71 to -0.45) and strongly increased WC ($\beta = -2.92$; 95% CI -4.23 to -1.60) in comparison to men with normal WC. Overweight ($\beta = -3.00$; 95% CI -4.00 to -1.99) and obese ($\beta = -5.79$; 95% CI -7.39 to -4.20) men had lower $\dot{V}O_2max$ compared to men with normal weight. Both total PA and physical exercise were considerably associated with $\dot{V}O_2max$ among men. Men who met the WHO PA recommendation of at least 2.5 hours of total PA per week showed higher $\dot{V}O_2max$ ($\beta = 2.19$; 95% CI 1.11 to 3.28) than men who did not

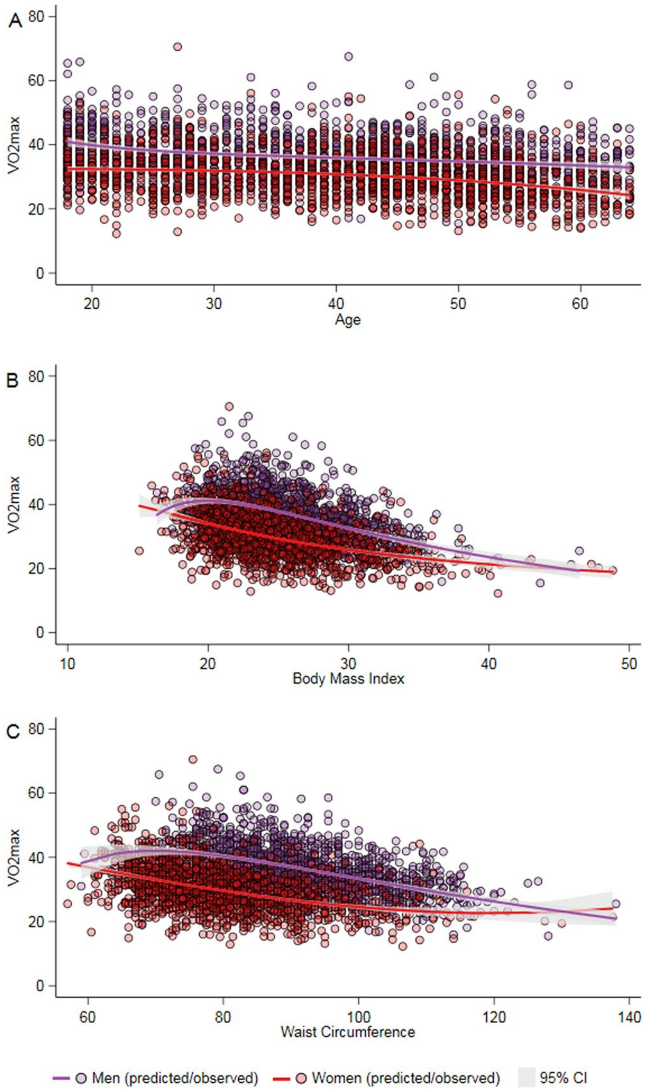

Figure 2. Association of (**A**) age, (**B**) body mass index and (**C**) waist circumference with cardiorespiratory fitness ($\dot{V}O_2max$) in men and women. $\dot{V}O_2max$ Maximal oxygen consumption; *CI* confidence interval.

meet the PA recommendation. An increasing level of $\dot{V}O_2max$ was also associated with increasing weekly hours of physical exercise participation: men with up to two hours of physical exercise per week, ($\beta = 1.99$; 95% CI 1.00 to 2.98), and men with two hours or more of physical exercise per week ($\beta = 3.74$; 95% CI 2.59 to 4.88) showed higher $\dot{V}O_2max$ compared to men who did not engage in any physical exercise.

Model comparison and additional analyses. Explained variance (R^2) increased from 13.6% in Model 1 to 35.6% in Model 4 for women and from 9.8% to 34.1% for men. Age was negatively associated with $\dot{V}O_2max$ among both sexes and indicated a strong effect size in Model 1 and Model 2. After adjustment for BMI and WC (Model 3), the effect size of age decreased for both sexes, but more strongly for men than for women. The coefficients of behavioral, interpersonal and socioeconomic factors slightly decreased after additional adjustments but the associations remained relatively stable overall. Among women, the effect size of high income on $\dot{V}O_2max$ became smaller after adjustment for BMI and WC (Model 3) and the effect sizes of fruit intake, vegetable intake and of being born outside Germany all became smaller after adjustment for PA-related factors (Model 4). Among men, the effects of being divorced, separated or widowed and being a former smoker decreased after adjustment for anthropometric measures (Model 3). After adjustment for PA-related factors (Model 4), coefficients remained relatively stable.

As additional analyses the final Model 4 for the non sex-stratified full sample using sex as an additional covariate was computed (Supplementary Table 2, Additional File 1). Even after full adjustment women showed lower levels of estimated $\dot{V}O_2max$ than men ($\beta = -6.56$; 95% CI (-7.17 to -5.94)). Furthermore, we conducted a sensitivity analysis and compared the final imputed model with a complete-case model without imputation of missing values: Despite slightly wider confidence intervals, only small deviations among the coefficients appeared (see Supplementary Figs. 3, 4, Additional File 1).

	Men		Women		Total	
	Mean $\dot{V}O_2max$	(95% CI)	Mean $\dot{V}O_2max$	(95% CI)	Mean $\dot{V}O_2max$	(95% CI)
Total (n = 2.826)	36.5	(36.0–37.0)	30.3	(29.8–30.7)	33.6	(33.1–34.0)
Age						
18–24 Years (n = 444)	39.7	(38.5–40.9)	32.1	(31.1–33.1)	36.2	(35.4–37.0)
25–34 Years (n = 579)	37.6	(36.5–38.6)	32.4	(31.4–33.4)	35.2	(34.4–36.1)
35–44 Years (n = 658)	35.8	(34.8–36.8)	30.7	(29.9–31.4)	33.3	(32.7–34.0)
45–54 Years (n = 724)	34.8	(33.8–35.7)	28.8	(28.0–29.6)	31.8	(31.1–32.5)
55–64 Years (n = 421)	34.2	(33.0–35.4)	25.9	(24.9–27.0)	30.1	(29.2–31.1)
Missing = 0						
Waist circumference						
Normal (n = 1,661)	38.8	(38.2–39.4)	32.4	(31.8–33.0)	35.9	(35.4–36.4)
Increased (n = 595)	34.3	(33.4–35.3)	28.7	(27.8–29.6)	31.4	(30.7–32.1)
Strongly increased (n = 568)	30.6	(29.6–31.6)	25.7	(25.0–26.4)	28.2	(27.5–28.8)
Missing = 2						
Body mass index						
Underweight (n = 52)	38.7	(36.9–40.4)	36.1	(33.1–39.0)	36.8	(34.6–39.0)
Normal Weight (n = 1,420)	40.0	(39.2–40.8)	32.1	(31.6–32.7)	35.5	(35.0–36.1)
Overweight (n = 982)	35.2	(34.6–35.9)	27.9	(27.1–28.8)	32.6	(32.0–33.1)
Obese (n = 364)	30.5	(29.4–31.6)	24.4	(23.5–25.2)	28.1	(27.2–28.9)
Missing = 8						
Smoking status						
Daily/ Occasionally (n = 933)	36.8	(36.0–37.5)	30.4	(29.6–31.2)	34.1	(33.5–34.7)
Former (n = 732)	34.6	(33.5–35.7)	29.3	(28.5–30.2)	32.1	(31.4–32.9)
Never (n = 1,147)	37.5	(36.6–38.3)	30.8	(30.1–31.4)	33.9	(33.3–34.6)
Missing = 14						
Alcohol consumption						
Low (n = 501)	35.7	(34.6–36.8)	28.7	(27.8–29.7)	32.4	(31.5–33.3)
Moderate (n = 1,710)	37.0	(36.4–37.6)	30.3	(29.7–30.9)	33.8	(33.3–34.3)
High (n = 586)	36.1	(34.9–37.3)	31.8	(30.7–32.9)	34.1	(33.3–34.9)
Missing = 29						
Sugar-rich foods intake						
Low/moderate (n = 1,618)	36.2	(35.5–36.9)	30.1	(29.5–30.7)	33.3	(32.7–33.8)
High (n = 1.096)	37.2	(36.4–37.9)	30.6	(29.9–31.4)	34.0	(33.4–34.6)
Missing = 112						
Sugar-rich drinks intake						
Low/moderate (n = 1,733)	36.1	(35.5–36.7)	30.5	(29.9–31.1)	33.4	(33.0–33.9)
High (n = 1.047)	37.3	(36.6–38.1)	30.1	(29.3–30.8)	33.8	(33.2–34.4)
Missing = 46						
Junk foods intake						
Low/moderate (n = 1,733)	35.9	(35.3–36.5)	29.8	(29.2–30.4)	33.0	(32.5–33.5)
High (n = 994)	37.6	(36.7–38.5)	31.0	(30.2–31.8)	34.5	(33.8–35.2)
Missing = 99						
Fruit intake						
Low/moderate (n = 1,717)	36.2	(35.6–36.8)	30.0	(29.4–30.6)	33.4	(32.9–33.9)
High (n = 1.054)	37.4	(36.5–38.3)	30.8	(30.0–31.6)	33.9	(33.3–34.6)
Missing = 55						
Vegetable intake						
Low/moderate (n = 1,680)	36.3	(35.7–36.9)	30.0	(29.4–30.5)	33.3	(32.8–33.8)
High (n = 1.073)	36.9	(36.2–37.7)	30.9	(30.1–31.6)	34.1	(33.5–34.7)
Missing = 73						
Country of birth						
Born in Germany (n = 2,508)	36.9	(36.4–37.4)	30.5	(30.0–31.0)	33.8	(33.4–34.3)
Born outside Germany (n = 273)	34.8	(33.5–36.2)	29.0	(27.7–30.4)	32.1	(31.1–33.2)
Missing = 45						
Educational classification						
Continued						

	Men		Women		Total	
	Mean $\dot{V}O_2max$	(95% CI)	Mean $\dot{V}O_2max$	(95% CI)	Mean $\dot{V}O_2max$	(95% CI)
Primary (n = 567)	34.9	(33.9–35.9)	27.7	(26.7–28.7)	32.0	(31.0–32.9)
Secondary (n = 1,667)	37.1	(36.5–37.7)	30.5	(29.9–31.0)	33.8	(33.3–34.2)
Tertiary (n = 577)	37.0	(36.0–38.1)	32.6	(31.7–33.6)	35.0	(34.2–35.7)
Missing = 15						
Occupational status						
Low (Q1) (n = 485)	35.6	(34.5–36.6)	28.0	(26.9–29.2)	32.3	(31.4–33.3)
Medium (Q2-Q4) (n = 1,512)	36.5	(35.7–37.2)	29.9	(29.3–30.5)	33.1	(32.6–33.6)
High (Q5) (n = 525)	37.2	(36.2–38.3)	33.0	(31.8–34.3)	35.5	(34.6–36.3)
Missing = 304						
Income (% of median-income)						
<60% (n = 479)	36.6	(35.3–37.9)	29.1	(27.8–30.4)	33.2	(32.2–34.3)
60 –<150% (n = 1,690)	36.2	(35.6–36.8)	29.9	(29.3–30.5)	33.2	(32.7–33.6)
≥150% (n = 657)	37.2	(36.2–38.2)	32.3	(31.4–33.2)	34.9	(34.2–35.6)
Missing = 0						
Social support						
Poor support (n = 244)	36.4	(34.8–38.0)	28.9	(27.0–30.7)	33.4	(32.0–34.8)
Moderate support (n = 1,394)	36.3	(35.6–37.0)	29.6	(29.0–30.2)	33.3	(32.7–33.8)
Strong support (n = 1,171)	36.8	(35.9–37.7)	31.1	(30.5–31.8)	33.9	(33.3–34.4)
Missing = 17						
Marital status						
Single (n = 994)	38.2	(37.4–39.0)	31.9	(31.1–32.6)	35.6	(35.0–36.2)
Married, living together (n = 1,565)	35.0	(34.3–35.6)	29.6	(29.0–30.1)	32.2	(31.7–32.7)
Separated/Divorced/Widowed (n = 240)	36.9	(34.8–39.0)	28.8	(27.4–30.2)	32.4	(30.9–33.9)
Missing = 27						
Total physical activity per week						
<2.5 hours (n = 2,124)	35.2	(34.5–35.8)	29.9	(29.4–30.4)	32.5	(32.0–32.9)
≥2.5 hours (n = 643)	39.6	(38.7–40.5)	32.2	(31.2–33.3)	37.0	(36.2–37.8)
Missing = 59						
Physical exercise per week						
No physical exercise (n = 672)	33.0	(32.2–33.9)	27.6	(26.8–28.4)	30.4	(29.7–31.1)
<2 hours (n = 1,249)	36.1	(35.4–36.7)	30.0	(29.3–30.6)	32.9	(32.3–33.4)
≥2 hours (n = 869)	39.5	(38.5–40.4)	33.4	(32.6–34.2)	37.0	(36.4–37.7)
Missing = 36						

Table 1. Bivariate associations between $\dot{V}O_2max$ and potential correlates. $\dot{V}O_2max$: maximal oxygen consumption; CI: confidence intervals.

Discussion

In this study we were able to replicate the well-established relationships in the literature between anthropometric measures (BMI and WC), total PA and physical exercise, and estimated $\dot{V}O_2max$ using data from a nation-wide, population-based cross-sectional health examination survey among adults in Germany. In addition, we demonstrated associations between a range of additional individual and interpersonal factors and CRF. Among women, high levels of alcohol consumption, high occupational status, lower BMI, smaller WC and higher physical exercise level were associated with higher $\dot{V}O_2max$. Among men, lower age, high intake of fruits, lower BMI, smaller WC, at least 2.5 hours of PA per week and higher physical exercise level were associated with higher $\dot{V}O_2max$.

Sex and age differences. The observation that men have a higher CRF than women has been reported in a number of previous studies, both internationally and in Germany[8,11,42,43]. In the current study, women had 17% lower $\dot{V}O_2max$ than men, which is comparable to an often reported sex difference in CRF of about 20%[8,11]. Lower fitness among women compared to men is commonly explained by women's smaller organ and body size and higher percentage of body fat on average and lower skeletal muscle mass[7,44]. Additional analyses with sex as an additional covariate showed that sex differences are not mediated by the anthropometric, behavioral, sociodemographic and interpersonal factors used in the fully adjusted model.

Our finding of decreasing $\dot{V}O_2max$ with increasing age corresponds with evidence from both cross-sectional and cohort studies[8–10]. Potential explanations are physiological adjustments during the aging process, such as muscle mass atrophy, increasing burden of disease, and onset of physical limitations. Although, the use of coronary drugs and cardiovascular diseases were contraindications for test participation in this study, other illnesses and medications could affect the results[20]. Therefore, our study-sample consists of a relatively healthy population aged <65 years.

	Model 1		Model 2		Model 3		Model 4	
	β	(95 % CI)	β	(95 % CI)	β	(95 % CI)	β	(95 % CI)
Age								
18–24 Years	(ref.)		(ref.)		(ref.)		(ref.)	
25–34 Years	0.44	(−0.87–1.76)	−0.36	(−1.71–1.00)	0.13	(−1.10–1.36)	0.89	(−0.33–2.12)
35–44 Years	**−1.53**	**(−2.71–−0.35)**	**−2.34**	**(−3.82–−0.86)**	−1.12	(−2.55–0.31)	−0.28	(−1.64–1.08)
45–54 Years	**−3.27**	**(−4.41–−2.12)**	**−4.00**	**(−5.46–−2.53)**	**−2.79**	**(−4.27–−1.31)**	**−2.08**	**(−3.49–−0.67)**
55–64 Years	**−6.53**	**(−7.98–−5.09)**	**−7.04**	**(−8.79–−5.30)**	**−4.98**	**(−6.74–−3.22)**	**−4.27**	**(−5.94–−2.60)**
Smoking status								
Never	(ref.)		(ref.)		(ref.)		(ref.)	
Daily/Occasionally	−0.89	(−1.93–0.15)	−0.61	(−1.66–0.44)	−0.15	(−1.11–0.81)	0.12	(−0.80–1.04)
Former	−0.85	(−1.83–0.12)	**−1.01**	**(−1.95–−0.06)**	−0.54	(−1.45–0.36)	−0.67	(−1.55–0.20)
Alcohol consumption								
Low	(ref.)		(ref.)		(ref.)		(ref.)	
Moderate	**1.88**	**(0.86–2.90)**	**1.11**	**(0.13–2.09)**	0.81	(−0.09–1.72)	0.75	(−0.13–1.62)
High	**3.69**	**(2.27–5.11)**	**2.79**	**(1.46–4.12)**	**2.42**	**(1.13–3.71)**	**2.20**	**(0.98–3.42)**
Sugar-rich foods intake								
Low/moderate	(ref.)		(ref.)		(ref.)		(ref.)	
High	0.75	(−0.16–1.66)	0.71	(−0.17–1.59)	0.57	(−0.24–1.37)	0.44	(−0.34–1.22)
Sugar-rich drinks intake								
Low/moderate	(ref.)		(ref.)		(ref.)		(ref.)	
High	−0.85	(−1.78–0.08)	−0.68	(−1.56–0.20)	−0.75	(−1.56–0.05)	−0.73	(−1.48–0.03)
Junk foods intake								
Low/moderate	(ref.)		(ref.)		(ref.)		(ref.)	
High	0.080	(−0.89–1.05)	0.23	(−0.63–1.10)	0.52	(−0.29–1.32)	0.75	(−0.01–1.51)
Fruit intake								
Low/moderate	(ref.)		(ref.)		(ref.)		(ref.)	
High	**1.04**	**(0.04–2.04)**	**0.91**	**(0.004–1.81)**	**1.06**	**(0.30–1.82)**	0.65	(−0.08–1.37)
Vegetable intake								
Low/moderate	(ref.)		(ref.)		(ref.)		(ref.)	
High	**0.82**	**(0.02–1.63)**	**0.79**	**(0.03–1.55)**	**0.96**	**(0.28–1.65)**	0.62	(−0.06–1.30)
Place of birth								
Born in Germany			(ref.)		(ref.)		(ref.)	
Born outside Germany			**−2.19**	**(−3.59–−0.79)**	**−2.01**	**(−3.42–−0.60)**	−1.34	(−2.70–0.03)
Education								
Primary			(ref.)		(ref.)		(ref.)	
Secondary			0.89	(−0.15–1.92)	0.59	(−0.33–1.52)	0.80	(−0.12–1.71)
Tertiary			1.46	(−0.11–3.02)	0.78	(−0.76–2.32)	0.90	(−0.58–2.37)
Occupational status								
Low			(ref.)		(ref.)		(ref.)	
Medium			**1.46**	**(0.25–2.67)**	**1.28**	**(0.13–2.43)**	0.94	(−0.15–2.02)
High			**2.76**	**(0.97–4.55)**	**2.42**	**(0.67–4.18)**	**1.83**	**(0.21–3.44)**
Income (% of median income)								
<60 %			(ref.)		(ref.)		(ref.)	
60 to <150%			0.82	(−0.54–2.19)	0.67	(−0.63–1.97)	0.52	(−0.75–1.79)
>=150%			**2.40**	**(0.66–4.15)**	1.57	(−0.09–3.22)	1.24	(−0.37–2.86)
Social support								
Poor			(ref.)		(ref.)		(ref.)	
Moderate			0.13	(−1.67–1.94)	−0.33	(−1.93–1.27)	−0.50	(−2.03–1.03)
Strong			0.79	(−0.99–2.58)	0.58	(−0.95–2.12)	0.08	(−1.42–1.58)
Marital status								
Married, living together			(ref.)		(ref.)		(ref.)	
Single			−0.33	(−1.54–0.88)	−0.59	(−1.77–0.58)	−0.59	(−1.72–0.55)
Separated/Divorced/Widowed			−0.02	(−1.33–1.29)	−0.38	(−1.69–0.92)	−0.31	(−1.53–0.91)
Waist circumference								
Normal					(ref.)		(ref.)	
Increased					**−1.73**	**(−2.66–−0.79)**	**−1.56**	**(−2.45–−0.68)**
Strongly increased					**−1.83**	**(−3.11–−0.54)**	**−1.61**	**(−2.85–−0.38)**

Continued

	Model 1		Model 2		Model 3		Model 4	
	β	(95 % CI)	β	(95 % CI)	β	(95 % CI)	β	(95 % CI)
Body mass index								
Underweight					**2.95**	**(0.38–5.52)**	**3.13**	**(0.58–5.69)**
Normal Weight					(ref.)		(ref.)	
Overweight					**−2.21**	**(−3.18–−1.24)**	**−2.36**	**(−3.26–−1.46)**
Obese					**−5.14**	**(−6.43–−3.85)**	**−4.88**	**(−6.19–−3.57)**
Total physical activity per week								
<2.5 hours							(ref.)	
≥2.5 hours							0.45	(−0.53–1.43)
Physical exercise per week								
No physical exercise							(ref.)	
<2 hours							**1.68**	**(0.84–2.52)**
≥2 hours							**4.20**	**(3.10–5.30)**
Constant	**30.0**	**(28.5–31.6)**	**28.0**	**(25.1–30.9)**	**29.8**	**(27.2–32.5)**	**27.9**	**(25.2–30.6)**
N	1,447		1,447		1,447		1,447	
R^2	0.136		0.199		0.310		0.356	

Table 2. Correlates of $\dot{V}O_2max$ in women. Coefficients and 95 % CI and shown in bold: 95 % CI does not include 0. $\dot{V}O_2max$: maximal oxygen consumption; β: linear regression coefficient; CI: confidence intervals.

After adjustment for total PA and physical exercise (Model 4), there was no considerable age-effect among men. According to the literature, the effect of PA on the decline in CRF over the life course is inconclusive[45,46]. While longitudinal studies found that individuals with enhanced PA levels had a smaller decline in CRF than sedentary individuals[46], there was no evidence for the mitigation of the effect by PA in meta-analyses of cross-sectional data[47,48].

Behavioral factors. Former smokers demonstrated lower fitness compared to non-smokers in bivariate analyses and Model 2, but the effect decreased when controlling for anthropometric and PA-related factors. Most studies investigating the association between smoking and CRF have found lower fitness levels among smokers compared with non-smokers, but some other studies have not found such association[8]. Two studies with NHANES data, adjusted for multiple variables, even observed higher fitness levels among young to middle-aged adult current smokers in both sexes[49] or in the male subsample[50]. While all studies observing no or a positive association had a cross sectional design, all longitudinal studies observed lower CRF levels among smokers compared with non-smokers[51–55]. Thus, in a cross-sectional study design, the effect of smoking on CRF might be hidden due to confounding, e.g. by age, as especially ex-smokers are usually older than current or never smokers. They may also have quit smoking because of health problems. In our analysis, the adequate elucidation of the effect of smoking on CRF could be hampered by the use of smoking status instead of quantitative measures of smoking (e.g., pack years).

We observed higher CRF among women with high levels of alcohol consumption. A study investigating the association between alcohol consumption and CRF based on five independent population-based studies from the US and Germany (including DEGS1) found an inverse u-shaped association with higher fitness levels among moderately drinking men and women[15]. However, these findings are in line with the results of our study, as Baumeister *et al.* observed a maximum of the curve at a very high level of consumption among women (ca. 35 g/d). In DEGS1, few women (<2%) reach this high level of consumption and correspondingly most women in the high consumption category consume less alcohol per day. Higher levels of fitness among individuals who consume alcohol are consistent with research on PA and alcohol intake. Studies in the past found that moderate or even high alcohol consumption is associated with higher levels of PA[56]. However, the mechanisms behind this relation are not fully understood. One possible explanation is that both PA and alcohol consumption work as rewarding stimuli and have overlapping effects in individuals stress regulation mechanisms[56]. Another possible explanation could be that specific personality characteristics like extroversion might correlate with both alcohol consumption (opportunities) and physical exercise (with others). Finally, confounding has to be considered as a possible explanation, as alcohol consumption is more common among higher educated women in Germany[57,58] who are practicing a lifestyle that includes more physical exercise[39,59] translating into higher CRF.

We observed higher CRF among men with high fruit intake. This is in line with results from the CARDIA-Study, where higher CRF was observed among men with a relative high level of fruit and vegetable intake[60]. Although in the final model of our study none of the other food groups (sugar-rich foods, sugar-rich drinks, junk food, vegetables) showed association with $\dot{V}O_2max$, for most food groups a tendency toward higher CRF among participants with high intake could be observed. The food frequency questionnaire used in DEGS1 included a limited number of food groups of which some are relatively broad. Therefore, we did not adjust for overall energy intake[29]. Thus, higher CRF among participants with high intake of any food- and beverage group could be related to a higher energy requirement. However, the inclusion of physical activity as well as body mass index may partly adjust for energy needs.

	Model 1		Model 2		Model 3		Model 4	
	β	(95 % CI)	β	(95 % CI)	β	(95 % CI)	β	(95 % CI)
Age								
18–24 Years	(ref.)		(ref.)		(ref.)		(ref.)	
25–34 Years	**−1.96**	**(−3.52–−0.41)**	**−1.84**	**(−3.45–−0.23)**	−0.46	(−1.94–1.01)	0.37	(−1.06–1.80)
35–44 Years	**−3.74**	**(−5.28–−2.21)**	**−3.32**	**(−5.23–−1.41)**	−1.17	(−2.96–0.63)	−0.10	(−1.86–1.66)
45–54 Years	**−4.59**	**(−6.09–−3.08)**	**−4.09**	**(−6.12–−2.05)**	**−1.94**	**(−3.80–−0.08)**	−0.96	(−2.80–0.87)
55–64 Years	**−5.37**	**(−7.12–−3.62)**	**−4.99**	**(−7.30–−2.67)**	−2.09	(−4.27–0.08)	−1.39	(−3.50–0.72)
Smoking status								
Never	(ref.)		(ref.)		(ref.)		(ref.)	
Daily/Occasionally	−0.61	(−1.73–0.50)	−0.35	(−1.52–0.82)	0.027	(−1.04–1.09)	0.38	(−0.62–1.38)
Former	**−2.14**	**(−3.55–−0.73)**	**−1.85**	**(−3.22–−0.49)**	−0.79	(−2.01–0.44)	−0.57	(−1.80–0.65)
Alcohol consumption								
Low	(ref.)		(ref.)		(ref.)		(ref.)	
Moderate	**1.48**	**(0.29–2.67)**	0.95	(−0.20–2.11)	0.80	(−0.23–1.83)	0.86	(−0.13–1.86)
High	1.34	(−0.27–2.94)	0.92	(−0.72–2.57)	0.80	(−0.60–2.20)	0.96	(−0.37–2.29)
Sugar-rich foods intake								
Low/moderate	(ref.)		(ref.)		(ref.)		(ref.)	
High	0.91	(−0.12–1.94)	**1.02**	**(0.01–2.03)**	0.74	(−0.19–1.66)	0.66	(−0.18–1.51)
Sugar-rich drinks intake								
Low/moderate	(ref.)		(ref.)		(ref.)		(ref.)	
High	0.30	(−0.65–1.25)	0.30	(−0.67–1.27)	0.65	(−0.23–1.52)	0.35	(−0.52–1.21)
Junk foods intake								
Low/moderate	(ref.)		(ref.)		(ref.)		(ref.)	
High	−0.001	(−1.20–1.20)	0.042	(−1.12–1.20)	0.23	(−0.78–1.25)	0.23	(−0.73–1.19)
Fruit intake								
Low/moderate	(ref.)		(ref.)		(ref.)		(ref.)	
High	**1.77**	**(0.73–2.81)**	**1.84**	**(0.81–2.88)**	**1.77**	**(0.82–2.72)**	**1.52**	**(0.63–2.40)**
Vegetable intake								
Low/moderate	(ref.)		(ref.)		(ref.)		(ref.)	
High	0.38	(−0.52–1.29)	0.15	(−0.73–1.03)	0.43	(−0.38–1.25)	0.36	(−0.43–1.15)
Place of birth								
Born in Germany			(ref.)		(ref.)		(ref.)	
Born outside Germany			**−1.70**	**(−3.29–−0.12)**	−1.35	(−2.71–0.01)	−1.28	(−2.59–0.04)
Education								
Primary			(ref.)		(ref.)		(ref.)	
Secondary			0.65	(−0.62–1.93)	0.65	(−0.50–1.80)	0.35	(−0.71–1.42)
Tertiary			1.20	(−0.72–3.12)	0.19	(−1.49–1.88)	−0.076	(−1.63–1.48)
Occupational status								
Low			(ref.)		(ref.)		(ref.)	
Medium			0.71	(−0.64–2.05)	0.31	(−0.87–1.48)	0.16	(−0.98–1.30)
High			0.90	(−0.98–2.77)	0.53	(−1.06–2.11)	0.31	(−1.22–1.84)
Income (% of median income)								
<60 %			(ref.)		(ref.)		(ref.)	
60 to <150%			−0.15	(−1.54–1.25)	−0.18	(−1.45–1.09)	−0.42	(−1.64–0.80)
>=150%			0.42	(−1.21–2.04)	0.52	(−0.91–1.94)	0.11	(−1.26–1.49)
Social support								
Poor			(ref.)		(ref.)		(ref.)	
Moderate			−0.12	(−1.76–1.52)	−0.76	(−2.11–0.59)	−0.61	(−1.84–0.61)
Strong			0.073	(−1.65–1.80)	0.055	(−1.41–1.52)	−0.10	(−1.45–1.25)
Marital status								
Married, living together			(ref.)		(ref.)		(ref.)	
Single			0.97	(−0.48–2.43)	0.04	(−1.33–1.41)	−0.34	(−1.67–0.99)
Separated/Divorced/Widowed			**2.34**	**(0.42–4.26)**	1.38	(−0.48–3.25)	0.98	(−0.76–2.72)
Waist circumference								
Normal					(ref.)		(ref.)	
Increased					**−2.08**	**(−3.26–−0.91)**	**−1.58**	**(−2.71–−0.45)**
Strongly increased					**−4.04**	**(−5.42–−2.67)**	**−2.92**	**(−4.23–−1.60)**

Continued

	Model 1		Model 2		Model 3		Model 4	
	β	(95 % CI)	β	(95 % CI)	β	(95 % CI)	β	(95 % CI)
Body mass index								
Underweight					−1.14	(−3.28–1.01)	−0.84	(−3.26–1.59)
Normal Weight					(ref.)		(ref.)	
Overweight					**−2.90**	**(−3.95–−1.84)**	**−3.00**	**(−4.00–−1.99)**
Obese					**−5.35**	**(−7.01–−3.69)**	**−5.79**	**(−7.39–−4.20)**
Total physical activity per week								
<2.5 hours							(ref.)	
≥2.5 hours							**2.19**	**(1.11–3.28)**
Physical exercise per week								
No physical exercise							(ref.)	
<2 hours							**1.99**	**(1.00–2.98)**
≥2 hours							**3.74**	**(2.59–4.88)**
Constant	**38.0**	**(36.2–39.7)**	**36.5**	**(33.2–39.7)**	**38.7**	**(35.7–41.7)**	**35.7**	**(32.8–38.6)**
N	1,379		1,379		1,379		1,379	
R^2	0.098		0.123		0.279		0.341	

Table 3. Correlates of $\dot{V}O_2max$ in men. Coefficients and 95% CI and shown in bold: 95% CI does not include 0. $\dot{V}O_2max$: maximal oxygen consumption; β: linear regression coefficient; CI: confidence intervals.

Socioeconomic and interpersonal factors. In the multivariable analyses, fitness was not associated with education or income, but we observed considerably higher fitness among women with high occupational status. While a previous study found that for other health indicators (e.g., smoking and obesity), education showed stronger effect sizes than occupational status, this was not the case for PA[61]. Other studies showed mixed results regarding the association between CRF and education, with a tendency for higher fitness levels among the highly educated[16]. A meta-analysis of four population-based studies (including DEGS1) found a positive association between education and CRF, but no relation after adjustment for PA[16]. While this meta-analysis adjusted for important confounders, no other measures of SES, such as occupational status or income were included. This may explain the differences with the results found in our study.

Higher fitness among individuals with high occupational status is in line with previous research[16], although studies investigating the effect of occupational status on fitness are scarce. It is possible that lower occupational status is associated with higher levels of occupational PA[62,63]. Described as the 'physical activity paradox'[64], recent research suggests that there are no positive health effects of occupational PA. In fact, the effects of occupational PA might be inverse[65–67]. One hypothesized explanation for this paradox is that occupational PA is usually of too low intensity or too long duration without recovery time to improve CRF[68]. In addition, individuals with high occupational status tend to be more active during leisure time, improving their CRF[61,69,70].

We found no evidence that interpersonal factors (social support and marital status) are strongly correlated with individual fitness. Overall, research on this topic is scarce. To our knowledge, there is no study that has investigated this association of social support with CRF so far. Regarding the relation of social support and PA, there is inconclusive evidence that social support is higher among more active individuals[12,71].

Marital status was not considerably associated with CRF in our analysis, but, in contrast to women, divorced men tended to have higher fitness on average than married men. A longitudinal study from the US found that changes in marital status influence fitness status in men and women differently, supporting our observations: among men, the transition to being married was associated with a decrease in $\dot{V}O_2max$, while being divorced was associated with a modest non-significant increase. In contrast, no clear patterns were observed among women[72].

Anthropometric factors. We observed strong associations between the anthropometric measures BMI and WC and $\dot{V}O_2max$. In fact, the anthropometric factors showed the largest association among all behavioral, interpersonal and socioeconomic factors investigated, with the exception of PA-related variables.

Consistent with the findings of other studies, women and men with overweight or obesity had lower $\dot{V}O_2max$ than individuals with a normal BMI[73–76]. Furthermore, our results indicated a higher CRF for underweight women, but no relation between underweight and $\dot{V}O_2max$ was observed in men. Compared with the large number of studies that have investigated the association between continuous BMI or overweight or obesity (as measured by BMI), and CRF[8], we are aware of only one study examining the association between underweight (defined by BMI) and CRF in adults. The study, conducted in a population-based sample from Taiwan reported lower CRF in underweight men, but not in women[77]. The strong relation between $\dot{V}O_2max$ and BMI may be generated by the definition of $\dot{V}O_2max$ as being relative to body weight[75]. Nevertheless, a study investigating $\dot{V}O_2max$ relative to fat-free mass also showed a negative association with obesity, as measured by BMI, in both men and women[78].

Independent of BMI, increased WC was strongly associated with lower CRF in men and women. This is in line with previous findings investigating the association between abdominal obesity measured by WC and CRF[8,79,80]. It has been hypothesized that for specific health outcomes, a low CRF attenuates the health risk of obesity as measured by BMI[81]. Simultaneously, studies have shown that higher CRF is associated with less abdominal fat and visceral adipose tissue[82]. Thus, it can be argued that the larger health effects of CRF compared to BMI may be mediated by the reduced abdominal adiposity in individuals with higher fitness levels[82].

Physical activity-related factors. We observed strong associations between physical exercise as well as total PA and CRF among men and between physical exercise and CRF among women. It is empirically well documented that most people respond to regular physical exercise and training with short- and long-term physiological adaptations, which improve the CRF[83,84]. Greater activity amounts and intensities result, in general, in greater improvement of CRF[7]. Our results confirm this dose-response relationship with further increases of CRF with higher amounts of physical exercise per week. However, not all types of PA have the same beneficial effects for CRF, which could explain the differences for total PA compared with physical exercise found in our study. For example, occupational PA might be either of too low intensity or of too long duration to improve CRF. This might be the reason why total PA showed smaller effects sizes than physical exercise[67,85].

Practical implications. In Germany, there is great potential to increase the CRF of the general population[11,86]. The results of our study provide evidence to tailor interventions or prevention measures according to the needs of specific subgroups. For example, women with a low occupational position should be enabled to perform sufficient physical exercise to enhance their fitness levels. The suggested measures of the Global Action Plan on Physical Activity by the World Health Organization[87] can be a good reference when planning measures to enhance the activity level of the population. Following the recommendations of the WHO, such measures should not solely focus on the individual, but also address the environment. In the case of women with low occupational status, this can for example translate into support for active transport to work or political measures to reconcile work and family life to enable more time for recreational PA. Furthermore, the association of $\dot{V}O_2max$ and consumption of specific foods might be an indication that different favorable health behaviors should not necessarily be seen separately, but rather be addressed at the same time. Again, such measures should focus on improvements of the living environment to foster individuals to make healthy choices.

Strengths and limitations. Strengths of this study include the large population-based sample and its comprehensive nature, allowing for the investigation of a broad range of behavioral, interpersonal, and socioeconomic factors as potential correlates of CRF. Nonetheless, due to the cross-sectional design of the present study, no conclusions regarding causality can be drawn and there may have been potential bias related to reverse causality. The study sample consisted of a relatively healthy population that was rated as being test-qualified according to the PAR-Q screener, which could compromise the generalizability of the results. Another strength of the present study is that the measurement of CRF is based on a highly standardized and quality assured survey procedure[20,88]. In this study, as in most epidemiological studies investigating large populations[7,8], we did not assess $\dot{V}O_2max$ directly via breath gas analyses, but estimated $\dot{V}O_2max$ based on a submaximal ergometer test. However, previous validation studies have shown that directly measured $\dot{V}O_2max$ in a maximal test and estimated $\dot{V}O_2max$ in a submaximal test are highly correlated[89]. Furthermore, the exposure variable physical exercise included information about the weekly duration but not about intensity which can have great impact on CRF[7]. Even though DEGS1 includes a wide range of health-related variables, some known correlates of CRF which were investigated in previous studies, e.g. caffeine consumption[90], were not considered due to lacking information in the DEGS1 data set. Major efforts during the study process were made to reduce potential sources of bias[19]. Nevertheless, as most of the covariates were based on self-reporting by participants, reporting bias cannot be ruled out. Despite the various measures that were taken to enhance the willingness to participate, to account for unequal sampling probabilities and to adjust the distribution of the sample to the official population statistics, it cannot be ruled out that the relatively low response rate could have contributed to a potential selection bias. Although we used weighting factors, specific population groups, such as those with lower education status and individuals with migration background, may be underrepresented in our study.

Conclusions

Despite the cross-sectional nature of the current study, we conclude that several factors at different domains of the conceptual framework are associated with CRF in the general adult population in Germany. These results can provide evidence to tailor prevention measures according to the needs of specific subgroups. Such measures should not solely focus on the individual, but also include actions on the environmental and political level.

Data availability

Datasets of DEGS1 are available as Public Use File: https://www.rki.de/EN/Content/Health_Monitoring/Public_Use_Files/application/application_node.html.

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Author contributions
G.B.M.M. and J.D.F. were involved in the design and conduct of DEGS1, J.D.F. in particular for the ergometer testing. J.Z., N.P. and J.D.F. conceptualized the current study. J.Z. conducted the present analysis and drafted the manuscript. G.B.M.M. and T.K. contributed to the analysis plan and interpretation of the results. K.M., B.K., N.P., T.K., G.B.M.M. and J.D.F. critically revised it. K.M. and J.D.F. contributed to the writing of the manuscript. All authors contributed to the interpretation of findings, reviewed, edited and approved the final manuscript.

Competing interests
The authors declare no competing interests.

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BMJ Open

Domain-specific physical activity patterns and cardiorespiratory fitness among the working population: Findings from the cross-sectional German Health Interview and Examination Survey

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ABSTRACT

Objectives This study aimed to investigate associations between occupational physical activity patterns (physical work demands linked to job title) and leisure time physical activity (assessed by questionnaire) with cardiorespiratory fitness (assessed by exercise test) among men and women in the German working population.

Design Population-based cross-sectional study.

Setting Two-stage cluster-randomised general population sample selected from population registries of 180 nationally distributed sample points. Information was collected from 2008 to 2011.

Participants 1296 women and 1199 men aged 18–64 from the resident working population.

Outcome measure Estimated low maximal oxygen consumption ($\dot{V}O_2max$), defined as first and second sex-specific quintile, assessed by a standardised, submaximal cycle ergometer test.

Results Low estimated $\dot{V}O_2max$ was strongly linked to low leisure time physical activity, but not occupational physical activity. The association of domain-specific physical activity patterns with low $\dot{V}O_2max$ varied by sex: women doing no leisure time physical activity with high occupational physical activity levels were more likely to have low $\dot{V}O_2max$ (OR 6.54; 95% CI 2.98 to 14.3) compared with women with ≥2 hours of leisure time physical activity and high occupational physical activity. Men with no leisure time physical activity and low occupational physical activity had the highest odds of low $\dot{V}O_2max$ (OR 4.37; 95% CI 2.02 to 9.47).

Conclusion There was a strong association between patterns of leisure time and occupational physical activity and cardiorespiratory fitness within the adult working population in Germany. Women doing no leisure time physical activity were likely to have poor cardiorespiratory fitness, especially if they worked in physically demanding jobs. However, further investigation is needed to understand the relationships between activity and fitness in different domains. Current guidelines do not distinguish between activity during work and leisure time, so specifying leisure time recommendations by occupational physical activity level should be considered.

Strengths and limitations of this study

- ► This is among the first studies to examine the association between leisure time and occupational physical activity patterns and cardiorespiratory fitness in Germany.
- ► We used a large nationally representative population-based sample of the resident adult working population, to allow our findings to be generalised.
- ► Leisure time physical activity was assessed by self-reports, which may be prone to recall and social desirability bias.

BACKGROUND

Physical activity is crucial for health and the unfavourable effects of an increasingly sedentary lifestyle are acknowledged as a major public health challenge.[1 2] Physical activity is defined as all bodily movement produced by skeletal muscles that require energy expenditure.[3] It has a positive influence on physical and mental health and contributes to the prevention of non-communicable diseases and premature mortality.[1] It can also take different forms and happen in different domains of individual daily routines and life courses. For example, people may participate in sports during their leisure time (leisure time physical activity) or be active at work (occupational physical activity). To date, physical activity in any form and setting has been considered beneficial and recent recommendations do not distinguish between domains. The current WHO guideline recommends

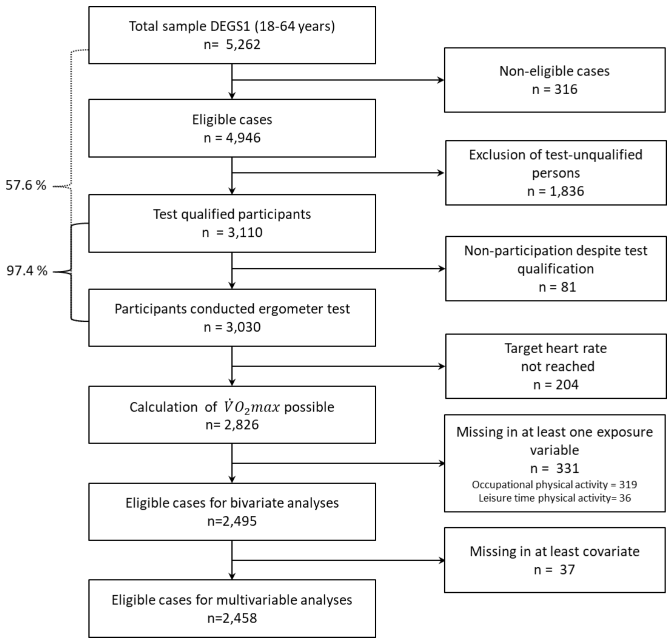

Figure 1 Flow diagram of participants. DEGS1, German National Health Interview and Examination Survey for Adults; $\dot{V}O_2max$, maximal oxygen consumption

at least 150 min of moderate intensity aerobic physical activity per week, stating that "[…] Physical activity includes leisure time physical activity, transportation (eg, walking or cycling), occupational (ie, work), household chores, play, games, sports or planned exercise, in the context of daily, family, and community activities".([3], p8)

Manual and physically demanding occupations have been declining for decades, but occupational physical activity still accounts for a large part of many people's daily activity.[4] The beneficial effects of leisure time physical activity are well established, but the effect of occupational physical activity is inconclusive. Studies in the past often argued that occupational physical activity should also be considered to improve health,[5] but recent studies suggest that it is not health enhancing and may even have the opposite effect.[6,7] As a possible explanation for this 'health paradox', the domain-specific effects of physical activity on cardiorespiratory fitness have come to attention.[8,9] Defined as the ability of circulatory, respiratory and muscular systems to supply oxygen during prolonged physical exercise,[3] cardiorespiratory fitness can be enhanced by regular endurance exercise[10] and is a strong predictor of adverse health outcomes.[11] It has been argued that occupational physical activity rarely has the adequate intensity, duration and volume to increase cardiorespiratory fitness.[8,9,12,13]

However, research on the association between different activity domains and cardiorespiratory fitness in Germany is limited. In particular, the interplay between different domains has not yet been analysed for cardiorespiratory fitness. This study therefore aimed to investigate the associations between leisure time and occupational physical activity with cardiorespiratory fitness among the German working population. Furthermore, in addition to the direct effects of the domain-specific physical activity, their interactional effects on cardiorespiratory fitness are investigated. The analyses were stratified by sex because men and women may vary in their exposure to physical demands at work,[14] type of occupations[15] and response to physical activity.[16]

METHODS

Study design

We used data from the nationwide cross-sectional German Health Interview and Examination Survey for Adults (Studie zur Gesundheit Erwachsener in Deutschland; DEGS1). DEGS1 is part of the Federal Health Monitoring System administered by the Robert Koch Institute.[17] In detail, the study design is described elsewhere.[18] Briefly, the study is based on a two-stage cluster randomised sampling procedure. First, 180 sample points were sampled from a list of German communities stratified to represent the regional distribution. Second, within these units, adult individuals were randomly drawn from local population registries stratified by 10-year age groups. The response rate was 42%. A total of 5262 participants aged 18–64 years took part in the physical measurements component from November 2008 to December 2011. Of these, 3110 individuals were test qualified for the exercise test (figure 1).

Overall, 3030 participants completed the exercise test (participation rate 97.4%). $\dot{V}O_2max$ was estimated for all participants reaching at least 75% of the age-predicted maximum heart rate (HR_{max}). In total, 204 participants terminated the test before reaching this heart rate, so $\dot{V}O_2max$ could be calculated for 2826 participants. Further cases were excluded from this analysis because of missing physical activity data. Overall, valid information on $\dot{V}O_2max$ and occupational and leisure time physical activity was available for 1296 women and 1199 men. Table 1 shows demographic, anthropometric and health behaviour variables from this representative sample of the adult working population of Germany. Women made up 48.0% of the sample, and the mean age of the participants was 39.6 years (range 18–64 years). The unweighted and weighted percentages did not differ substantially, although weighting led to a slightly smaller proportion of participants in the older age groups and a smaller proportion in the high socioeconomic status group.

Patient and public involvement

This research was done without patient involvement. Patients were not invited to comment on the study design and were not consulted to develop patient-relevant outcomes or interpret the results. Patients were not invited to contribute to the writing or editing of this document for readability or accuracy.

Outcome variable

Cardiorespiratory fitness was measured using a standardised, submaximal cycle ergometer test (Ergosana

Table 1 Characteristics of study participants in German Health Interview and Examination Survey for Adults

	Men			Women			Total		
	n	%*	%†	n	%*	%†	n	%*	%†
$\dot{V}O_2max$									
Low	494	41.2	41.2	546	42.1	40.5	1040	41.7	40.9
Intermediate/high	705	58.8	58.8	750	57.9	59.5	1455	58.3	59.1
Missing	0	0.0	–	0	0.0	–	0	0.0	–
LTPA									
No	297	24.8	24.9	309	23.8	24.7	606	24.3	24.8
<2 hours	492	41.0	39.8	647	49.9	49.9	1139	45.7	44.7
≥2 hours	410	34.2	35.3	340	26.2	25.3	750	30.1	30.5
Missing	0	0.0	–	0	0.0	–	0	0.0	–
OPA									
Low	750	62.6	59.7	895	69.1	67.0	1645	65.9	63.2
High	449	37.4	40.3	401	30.9	33.0	850	34.1	36.8
Missing	0	0.0	–	0	0.0	–	0	0.0	–
Age									
18–24 Years	137	11.4	11.3	138	10.6	11.8	275	11.0	11.5
25–34 Years	277	23.1	26.4	250	19.3	22.5	527	21.1	24.5
35–44 Years	287	23.9	26.8	338	26.1	27.7	625	25.1	27.2
45–54 Years	308	25.7	23.2	369	28.5	25.8	677	27.1	24.5
55–64 Years	190	15.8	12.3	201	15.5	12.3	391	15.7	12.3
Missing	0	0.0	–	0	0.0	–	0	0.0	–
Waist circumference									
Normal	719	60.0	61.7	702	54.2	57.0	1421	57.0	59.4
Increased	256	21.4	20.1	289	22.3	22.5	545	21.8	21.3
Strongly increased	224	18.7	18.2	303	23.4	20.5	527	21.1	19.3
Missing	0	0.0	–	2	0.2	–	2	0.1	–
Body mass index									
Underweight	9	0.8	0.8	32	2.5	2.8	41	1.6	1.8
Normal weight	467	38.9	37.7	748	57.7	58.1	1215	48.7	47.5
Overweight	548	45.7	46.1	348	26.9	27.1	896	35.9	37.0
Obese	171	14.3	15.4	164	12.7	11.9	335	13.4	13.7
Missing	4	0.3	–	4	0.3	–	8	0.3	–
Smoking status									
Daily	349	29.1	31.3	268	20.7	23.2	617	24.7	27.4
Occasionally	106	8.8	8.2	96	7.4	7.6	202	8.1	7.9
Former	323	26.9	26.9	354	27.3	25.8	677	27.1	26.3
Never	420	35.0	33.7	576	44.4	43.4	996	39.9	38.3
Missing	1	0.1	–	2	0.2	–	3	0.1	–
Alcohol consumption									
Low	180	15.0	16.7	151	11.7	12.3	331	13.3	14.6
Moderate	760	63.4	64.3	821	63.3	64.8	1581	63.4	64.6
High	245	20.4	19.0	314	24.2	22.9	559	22.4	20.9
Missing	14	1.2	–	10	0.8	–	24	1.0	–
Socioeconomic status									

Continued

Table 1 Continued

	Men			Women			Total		
	n	%*	%†	n	%*	%†	n	%*	%†
Low	151	12.6	14.7	113	8.7	9.6	264	10.6	12.3
Medium	702	58.5	61.4	800	61.7	63.5	1502	60.2	62.4
High	346	28.9	23.9	382	29.5	26.8	728	29.2	25.3
Missing	0	0	–	1	0.1	–	1	0.0	–

Values shown are frequencies in percentages.
*Percentage of the sample (unweighted).
†Weighted percentage (weighting factors were used to adjust the distribution of the sample to match the German population for sex, age, education and region).
LTPA, leisure time physical activity; OPA, occupational physical activity; $\dot{V}O_2max$, maximal oxygen consumption.

Sana Bike 350/450 (Ergosana, Germany), heart rate monitor (Polar, Finland), blood pressure cuffs (Ergosana, Germany), a heart rate transmitter (Oregon Scientific, USA) and a notebook with ergometer software (Dr Schmidt GmbH, Germany)). Test methodology, protocol and exclusion criteria have been described elsewhere.[19 20] DEGS1 participants were included in the ergometer test if they were aged 18–64 years, gave informed consent and were test qualified based on a modified German version of the Physical Activity Readiness Questionnaire (PAR-Q).[21 22] If any PAR-Q contraindications were reported, the participant was seen by a physician, who decided whether they should be enrolled into the exercise test. Cardiorespiratory fitness was assessed using the test protocol recommended by WHO.[23] Beginning at 25 W, the workload was increased by 25 W every 2 min until 85% of the estimated age-specific maximal heart rate was exceeded, a maximum level of 350 W was achieved or the study staff terminated the test. Heart rate was monitored continuously throughout the test. The formula *208–0.7×Age* was used to calculate the age-predicted maximum heart rate.[24] To derive physical work capacity at HR_{max} ($PWC_{100\%}$), the measured heart rate (beats/min) during the incremental phase was regressed against corresponding workload in watts for each participant. Assuming a linear relationship between heart rate and workload, $PWC_{100\%}$ was obtained by extrapolation using the individual regression equation $PWC_{100\%}=intercept + HR_{max} \times slope$.[25] $PWC_{100\%}$ was converted to $\dot{V}O_2max$ using a metabolic equation provided by the American College of Sports Medicine: $3.5\ mL/min/kg+12.24 \times (PWC_{100\%}) / (body\ weight)$.[26] Estimated $\dot{V}O_2max$ was categorised into low (sex-specific quintiles 1–2) and intermediate to high (quintiles 3–5).

Exposure variable

Occupational physical activity: a physical work demands index

To assess occupational physical activity, we used an indirect method and computed specific job exposure matrices to distinguish participants' occupation by level of physical demand. These matrices are an established methodological tool to allow inclusion of specific occupational exposure in analyses, drawing on studies that assess information about job titles. They are constructed using available secondary data to determine exposure profiles for each occupation. These profiles are matched to primary data using standardised job classifications. In our case, such matrices were constructed using data from a large-scale representative study on working conditions of 20 000 employees in Germany,[27 28] which was part of the European Working Conditions Survey regularly conducted in member states of the European Union. The overall job index and specific indexes have been described and applied elsewhere.[29–31] In this study, we used a specific subindex of perceived physical work demands. To construct the index, we used data on the frequency of lifting and carrying heavy loads (men≥20 kg, women≥10 kg). The item was assessed with a frequency scale with four answer categories: 'often', 'sometimes', 'rarely' and 'never'.[27 28] The physical demand index was assigned to the occupations based on hierarchic multilevel analyses adjusted for sex, age, job experience and part time employment. In contrast to the use of occupation-specific means, this procedure allows adjustment for other variables besides the specific occupation that could also influence the level of demand (eg, the sex ratio or the level of part-time employment). The levels for the multilevel estimation were defined by the 2-digit, 3-digit and 4-digit codes of the International Classification of Occupations of 1988 (ISCO-88) classification. These matrices were then classified into deciles. Occupations with the lowest level of physical work demands had a value of 1 (first decile), and those with the highest level had a value of 10 (tenth decile). Using the ISCO-88, the matrices were matched to DEGS1. To create a combined physical activity variable, this index was then dichotomised into low (index values 1–6) and high occupational physical activity (index values 7–10). A list of the most frequent occupations in DEGS1 by occupational physical activity level for men and women is shown in online supplementary table S1.

Leisure time physical activity: physical exercise

Leisure time physical activity was assessed by asking participants 'How often do you engage in physical exercise?'[32] Leisure time physical activity usually refers to all physical activity in freely disposable time, but sport and exercise are the main elements[33] so were used in this study.

Responses were on a five-point scale of 'no physical exercise', 'less than 1 hour a week' and 'regularly 1–2 hours a week', 'regularly up to 4 hours' and 'regularly more than 4 hours', and were categorised into three groups: no physical exercise, <2 hours/week and ≥2 hours/week.

Combined occupational and leisure time physical activity

To analyse the combined relationship of occupational and leisure time physical activity on cardiorespiratory fitness, we generated a combined variable by grouping no, <2 hours, and ≥2 hours leisure time physical activity with each of low and high occupational physical activity, giving six possible categories.

Covariates

Relevant covariates were selected from the literature.[34 35] Age was categorised into five groups: 18–24 years, 25–34 years, 35–44 years, 45–54 years and 55–64 years. Smoking was grouped into daily, occasionally, former and never. Alcohol intake was estimated by multiplying the calculated quantity of each alcoholic beverage, assessed by a food frequency questionnaire, with standard ethanol content (beer: 4.8%; wine: 11%, spirits: 33%) and classified into low (quintile 1), medium (quintile 2–4) and high (quintile 5) alcohol consumption using sex-specific quintiles. Body mass index and waist circumference have been shown to be independently related to cardiorespiratory fitness,[34 35] so we included both parameters as covariates. Body height and weight were measured by standardised procedures using portable electronic scales (SECA, Germany) and stadiometer (Holtain, UK). Body mass index (kg/m^2) was categorised using WHO guidelines.[36] Waist circumference was measured at the smallest site between the lowest rib and the superior border of the iliac crest with flexible, non-stretchable measurement tape (Sibner Hegner, Switzerland) and categorised as 'normal', 'increased' and 'strongly increased' using international guidelines.[37] Socioeconomic status was determined using a composite additive index, based on information about participants' education, occupational position and net equivalent income.[38]

Statistical analyses

Leisure time and occupational physical activity were cross tabulated to show the association of the domain-specific activity levels. Prevalence and 95% CIs of low $\dot{V}O_2max$ were calculated by occupational and leisure time physical activity and covariates. Multivariable logistic regression models were computed to estimate the associations between domain-specific physical activity (exposure) and low $\dot{V}O_2max$ (outcome). In a first step, the main effects of occupational and leisure time physical activity were investigated; in a second step, the combined activity variable was used. In both steps, we fitted an age-adjusted model and one adjusting for age, body mass index, waist circumference, smoking, alcohol intake and socioeconomic status. Finally, we computed predicted margins[39] from the fully adjusted logistic regression model investigating

Table 2 Association of leisure time and occupational physical activity among male and female German Health Interview and Examination Survey for Adults participants

	Low OPA		High OPA	
	%	(95% CI)	%	(95% CI)
Men				
No LTPA	24.0	(20.1 to 28.3)	26.2	(21.4 to 31.5)
<2 hours LTPA	39.4	(35.2 to 43.7)	40.4	(34.9 to 46.2)
≥2 hours LTPA	36.6	(32.7 to 40.7)	33.4	(27.7 to 39.7)
Women				
No LTPA	21.6	(17.9 to 25.9)	31.1	(25.6 to 37.3)
<2 hours LTPA	49.6	(44.8 to 54.3)	50.6	(44.9 to 56.4)
≥2 hours LTPA	28.8	(25.1 to 32.8)	18.2	(14.4 to 22.9)

Values shown are frequencies in percentages with 95% CIs.
LTPA, leisure time physical activity; OPA, occupational physical activity.

the combined physical activity variable to plot adjusted prevalence of low $\dot{V}O_2max$ by domain-specific physical activity. All analyses were performed separately for men and women to identify sex-specific physical activity patterns associated with cardiorespiratory fitness and to detect potential effect modification by sex. Analyses were performed with Stata V.15.1 (Stata Corp.). To enhance the external validity of the results, weighting factors were used to adjust for distribution of the sample by sex, age, education and region, to match the German population. Stata's survey procedures were applied to account for the clustered sampling design.

RESULTS

Occupational and leisure time physical activity levels

Prevalence of high occupational physical activity was 40.3% among men and 33.0% among women (table 1). In total, 24.9% of men and 24.7% of women engaged in no leisure time physical activity, 39.8% and 49.9% in less than 2 hours per week, and 35.3% and 25.3% in 2 hours or more per week. Leisure time physical activity did not vary with occupational physical activity level among men, but women with high occupational physical activity were less likely to engage in 2 hours or more leisure time physical activity per week than women with low occupational physical activity (table 2).

Low

Overall, the prevalence of estimated low $\dot{V}O_2max$ was 41.2% (95% CI 37.6 to 44.8) for men and 40.5% for women (95% CI 37.1 to 44.0). Table 3 shows the prevalence of low $\dot{V}O_2max$ by domain-specific physical activity and sociodemographic, health behaviour and anthropometric variables. Binary analyses showed that men and women with higher leisure time activity levels had substantially lower prevalence of low $\dot{V}O_2max$. There were no relevant differences in low $\dot{V}O_2max$ by occupational physical activity among men, but women with high occupational

Table 3 Prevalence and 95% CIs of low estimated $\dot{V}O_2max$ by domain-specific physical activity, health behavioural, anthropometric and sociodemographic characteristics among male and female German Health Interview and Examination Survey for Adults participants

	Men		Women	
	%	(95% CI)	%	(95% CI)
Total	41.2	(37.6 to 44.8)	40.5	(37.1 to 44.0)
LTPA				
No	63.2	(56.4 to 69.4)	56.1	(49.1 to 62.9)
<2 hours	42.2	(36.5 to 48.0)	41.2	(36.6 to 45.9)
≥2 hours	24.7	(19.8 to 30.5)	24.1	(19.0 to 30.1)
OPA				
Low	41.5	(36.8 to 46.4)	37.2	(33.0 to 41.6)
High	40.8	(35.0 to 46.8)	47.4	(41.5 to 53.4)
OPA/LTPA				
No LTPA, low OPA	68.5	(59.2 to 76.4)	48.0	(39.7 to 56.3)
No LTPA, high OPA	56.0	(44.9 to 66.5)	67.7	(56.7 to 77.0)
<2 hours LTPA, low OPA	42.6	(35.8 to 49.7)	39.3	(33.5 to 45.5)
<2 hours LTPA, high OPA	41.6	(32.3 to 51.5)	44.9	(37.5 to 52.5)
≥2 hours LTPA, low OPA	22.8	(17.1 to 29.6)	25.4	(19.0 to 33.0)
≥2 hours LTPA, high OPA	28.0	(19.1 to 39.0)	19.9	(11.6 to 32.1)
Age				
18–24 Years	28.0	(19.9 to 37.7)	25.8	(17.9 to 35.7)
25–34 Years	36.0	(28.9 to 43.8)	29.2	(23.3 to 35.9)
35–44 Years	41.9	(34.9 to 49.2)	36.1	(30.3 to 42.3)
45–54 Years	47.2	(40.9 to 53.7)	48.5	(42.1 to 55.1)
55–64 Years	51.9	(42.3 to 61.4)	68.7	(60.2 to 76.1)
Waist circumference				
Normal	27.1	(23.2 to 31.4)	26.9	(23.0 to 31.1)
Increased	54.6	(46.2 to 62.8)	46.4	(38.5 to 54.6)
Strongly increased	74.2	(66.7 to 80.4)	72.5	(66.3 to 77.9)
Body mass index				
Underweight	19.8	(3.3 to 64.1)	18.9	(7.7 to 39.4)
Normal weight	21.7	(16.9 to 27.4)	27.1	(23.4 to 31.2)
Overweight	47.5	(42.3 to 52.8)	53.7	(46.4 to 60.8)
Obese	71.1	(62.4 to 78.4)	83.1	(75.3 to 88.8)
Smoking status				
Daily	40.7	(34.9 to 46.8)	38.8	(31.6 to 46.7)
Occasionally	31.7	(22.3 to 42.9)	33.5	(22.9 to 46.0)
Former	49.6	(42.3 to 56.9)	46.7	(40.0 to 53.6)
Never	37.5	(31.4 to 44.0)	39.0	(34.0 to 44.3)
Alcohol consumption				
Low	45.7	(38.0 to 53.7)	50.2	(40.8 to 59.5)
Moderate	39.1	(34.9 to 43.6)	41.1	(36.6 to 45.8)
High	43.4	(35.1 to 52.2)	33.2	(26.7 to 40.5)
Socioeconomic status				
Low	39.9	(30.7 to 49.8)	56.3	(45.8 to 66.3)
Medium	43.3	(38.7 to 48.1)	43.4	(39.3 to 47.5)
High	36.8	(30.8 to 43.2)	28.2	(22.4 to 34.9)

LTPA, leisure time physical activity; OPA, occupational physical activity; $\dot{V}O_2max$, maximal oxygen consumption.

Table 4 Domain-specific physical activity and low estimated $\dot{V}O_2max$ among male and female German Health Interview and Examination Survey for Adults participants

	Men				Women			
	OR*	(95% CI)	OR†	(95% CI)	OR*	(95% CI)	OR†	(95% CI)
Main effects model								
OPA								
Low OPA	(Ref.)		(Ref.)		(Ref.)		(Ref.)	
High OPA	1.05	(0.75 to 1.46)	0.95	(0.64 to 1.42)	1.71	(1.23 to 2.36)	1.06	(0.75 to 1.49)
LTPA								
No LTPA	4.97	(3.47 to 7.13)	4.46	(2.89 to 6.89)	4.96	(3.26 to 7.54)	4.65	(2.90 to 7.45)
<2 hours LTPA	2.17	(1.48 to 3.19)	2.04	(1.32 to 3.15)	2.49	(1.72 to 3.62)	2.13	(1.44 to 3.14)
≥2 hours LTPA	(Ref.)		(Ref.)		(Ref.)		(Ref.)	
OPA/LTPA model								
No LTPA, low OPA	4.92	(2.56 to 9.46)	4.45	(2.14 to 9.23)	4.37	(2.02 to 9.47)	6.54	(2.98 to 14.3)
No LTPA, high OPA	2.86	(1.47 to 5.58)	2.34	(1.08 to 5.07)	11.1	(5.15 to 24.1)	10.5	(4.39 to 24.9)
<2 hours LTPA, low OPA	1.69	(0.94 to 3.06)	1.54	(0.77 to 3.06)	2.84	(1.39 to 5.78)	3.52	(1.75 to 7.09)
<2 hours LTPA, high OPA	1.70	(0.91 to 3.17)	1.54	(0.75 to 3.16)	4.01	(1.90 to 8.49)	3.69	(1.80 to 7.60)
≥2 hours LTPA, low OPA	0.67	(0.35 to 1.27)	0.64	(0.32 to 1.27)	1.37	(0.64 to 2.92)	1.93	(0.90 to 4.13)
≥2 hours LTPA, high OPA	(Ref.)		(Ref.)		(Ref.)		(Ref.)	
n	1199		1181		1296		1277	

Different adjustment criteria were used in multivariable logistic regression analyses.
*Adjusted for age.
†Adjusted for age, waist circumference, body mass index, smoking status, alcohol consumption and socioeconomic status index.
LTPA, leisure time physical activity; OPA, occupational physical activity; $\dot{V}O_2max$, maximal oxygen consumption.

physical activity had a higher prevalence of low $\dot{V}O_2max$ than women with low occupational physical activity.

Multivariable analyses (table 4) showed that women in jobs with high levels of occupational physical activity were more likely to have a low estimated $\dot{V}O_2max$ when adjusting only for age (OR 1.71; 95% CI 1.23 to 2.36). This association disappeared when controlling for leisure time physical activity and other covariates (OR 1.06; 95% CI 0.75 to 1.49). Neither model showed any association between low $\dot{V}O_2max$ and occupational physical activity for men (OR 1.05; 95% CI 0.75 to 1.46 and OR 0.95; 95% CI 0.64 to 1.42).

Men and women who did no or less than 2 hours leisure time physical activity per week were more likely to have a low $\dot{V}O_2max$ than participants who did 2 hours or more. The effect size did not change considerably when adjusting for occupational physical activity and other controls.

Multivariable analyses of the combined physical activity variable (fully adjusted model) showed that less-active men were more likely to have a low $\dot{V}O_2max$ with ORs of 4.45 (95% CI 2.14 to 9.23) for no leisure time/low occupational physical activity, 2.34 (95% CI 1.08 to 5.07) for no leisure time/high occupational physical activity, 1.54 (95% CI 0.77 to 3.06) for <2 hours leisure time/low occupational physical activity, 1.54 (95% CI 0.75 to 3.16) for <2 hour leisure time/high occupational physical activity and 0.64 (95% CI 0.32 to 1.27) for ≥2 hours leisure time/low occupational physical activity compared with men with ≥2 hours leisure time/high occupational physical activity. The corresponding ORs for women were 6.54 (95% CI 2.98 to 14.3), 10.5 (95% CI 4.39 to 24.9), 3.52 (95% CI 1.75 to 7.09), 3.69 (95% CI 1.80 to 7.60) and 1.93 (95% CI 0.90 to 4.13), indicating women were most likely to have a low fitness if they worked in physically demanding jobs and did not engage in leisure time physical activity.

Based on the final model with the combined variable, we plotted predicted probabilities of having a low $\dot{V}O_2max$ to show these different patterns for men and women (figure 2).

DISCUSSION

Summary of results

This cross-sectional study showed a strong association between low leisure time physical activity and low estimated $\dot{V}O_2max$, but not between occupational physical activity and $\dot{V}O_2max$. The association between domain-specific physical activity and low $\dot{V}O_2max$ also varied by sex. After adjustment for potential confounding, women working in physically demanding occupations who did not participate in leisure time physical activity had the highest likelihood of having a low $\dot{V}O_2max$. However, the men with the highest risk of low $\dot{V}O_2max$ were those who did not engage in leisure time physical activity and were not working in physically demanding occupations.

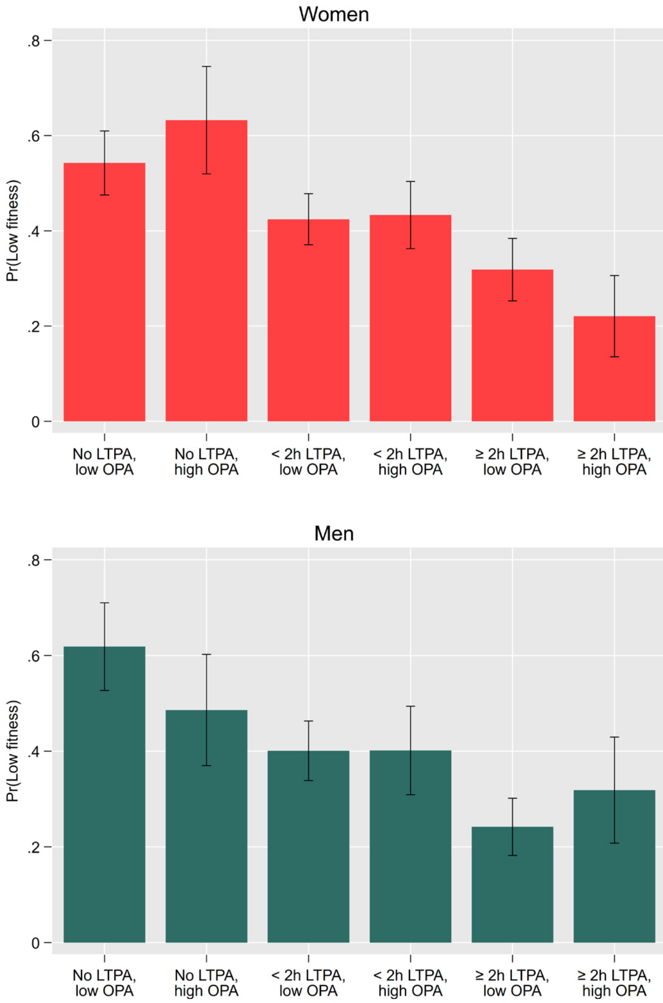

Figure 2 Figure 2Predicted probabilities (with 95% CIs) of low $\dot{V}O_2max$ by domain-specific physical activity among men and women who participated in the nationwide German Health Interview and Examination Survey for Adults. Adjusted for age, waist circumference, body mass index, smoking status, alcohol consumption and socioeconomic status index. LTPA, leisure time physical activity; OPA, occupational physical activity.

Comparison with other studies

The strong association between leisure time physical activity and cardiorespiratory fitness has been shown in numerous studies.[34] However, evidence of the association between occupational physical activity and cardiorespiratory fitness is inconclusive. Historically, occupational physical activity has been seen as a way to improve health in behavioural medicine, but as a potential health hazard in occupational medicine.[6 40] Recent studies agree that occupational physical activity does not lead to increased cardiorespiratory fitness.[41–44] A Swiss study among adults reported no association between the amount of objectively assessed steps during work-time and $\dot{V}O_2max$, and a lower $\dot{V}O_2max$ among participants doing manual work than those doing sedentary work (according to reported job title), while controlling for leisure time physical activity and various other covariates.[41] A cross-regional study in Germany also found higher levels of $\dot{V}O_2max$ among participants with high levels of leisure time physical activity, but $\dot{V}O_2max$ was lower among participants with higher levels of occupational physical activity (assessed by questionnaire).[43] A study among the Danish working population observed that self-reported work and leisure sitting time had different associations with $\dot{V}O_2max$: there was a strong negative association between sitting leisure time and $\dot{V}O_2max$, but no similar association with sitting time at work.[45] However, a study among male workers in Japan found higher levels of $\dot{V}O_2max$ among those with self-reported high occupational physical activity than low[46] and a study from Finland found a positive association between cardiorespiratory fitness and self-reported occupational physical activity even after adjustment for leisure time physical activity among young men.[47]

Occupational physical activity has been linked to negative health outcomes: in a meta-analysis, Li *et al*[6] found evidence that it might increase the risk of cardiovascular disease, although leisure time physical activity considerably reduced the risk. Another meta-analysis found that men with high occupational physical activity had an increased risk of preliminary mortality, but women did not.[7] In particular, the combination of high occupational physical activity with low cardiorespiratory fitness seems to be associated with a higher risk of adverse cardiovascular outcomes.[48 49]

Potential mechanisms

Regular aerobic exercise induces biological changes, such as increased stroke volume and decreased venous oxygen content, both of which lead to increased individual cardiorespiratory fitness.[10] To increase $\dot{V}O_2max$, exercise should ideally be performed with sufficient intensity at ≥50% of the maximal aerobic capacity for untrained individuals.[10] Cardiorespiratory fitness is determined by the cardiac output and arteriovenous oxygen difference, so it can be enhanced by an increase in stroke volume, oxygen difference or both.[10] Leisure time physical activity, especially sport, is usually relatively short duration but high intensity, and provides sufficient recovery time between occasions. This is important, because this type of activity can achieve a training effect of the myocardium. This reduces the heart rate, the heart muscle remains longer in diastole and the stroke volume increases.[50] In contrast, physical activity without recovery leads to prolonged elevation of heart rate and blood pressure.[51] This can result in erosion of the endothelium, which can provoke atherosclerosis.[52] This prolonged activity is typically observed in occupational physical activity, where workers also have limited control of work speed and duration.[9 50] Sufficient recovery is therefore not possible, because individuals are unable to decide for themselves how to perform their work, and when to pause. Assuming average occupational physical activity as a constant, monotonous but low intensity activity, it has also been proposed that its intensity might be too low to increase individual fitness.[9] However, this might not hold true for all occupations. Studies among blue-collar workers found that directly assessed intensity of physical activity was higher during work than leisure time,[53] especially among those with low fitness levels.[54]

Differences between men and women

The results suggest that the association between domain-specific physical activity and cardiorespiratory fitness is different for men and women. High occupational physical activity was associated with lower fitness among women doing low levels of leisure time physical activity. Online supplementary table S1 shows that men in physically demanding occupations mainly worked in manual and technical professions (eg, electricians, plumbers and mechanics), and women in physically demanding jobs worked mainly in the service sector (eg, nursing/care, catering and cleaning). These service jobs are particularly affected by limited work control and higher job strain, which may be a possible explanation for these sex-specific patterns. For example, healthcare workers in Germany reported very high levels of job demands compared with the average level for all occupations, and also had low decision-making autonomy.[55 56] This is particularly concerning because high-strain jobs can lead to lower leisure time physical activity[57] and high occupational stress in combination with low cardiorespiratory fitness considerably increases the cardiovascular risk.[58] These potential physiological mechanisms hold especially true for the most common high activity demand professions for women. For example, cleaners often work continuously for long periods, but at insufficient intensity to increase fitness, and this is coupled with a high relative workload.[13]

Recommendations for further research and practical implications

To take into account the observed sex differences, it is recommended that future studies should investigate men and women separately. It is generally assumed that high levels of leisure time physical activity increase individual cardiorespiratory fitness and are also beneficial for general health. However, some studies have found that a moderate-to-high level of leisure time physical activity was associated with adverse health outcomes among those exposed to high occupational physical activity levels.[59 60] Thus, the inter-relationships between occupational and leisure time physical activity remain unclear and further research is needed to explain these potentially contradictory results. Furthermore, much of the research on this topic is based on self-reported physical activity with high heterogeneity among the instruments used. Future studies should investigate the domain-specific effects of physical activities using objective measures.[61]

When recommending higher levels of leisure time physical activities, it is important to consider the embedded and dependent relationship of the different domains of physical activity. Occupational and leisure time activity are not the only areas of physical activity. Transportation and domestic activities are also relevant. This is important because both these domains can also be described as non-discretionary time[62] with limited individual autonomy. Second, physical activity in all these domains depends on structures at the societal, environmental and individual level.[63] Individuals face obstacles in engaging in more leisure time physical activity, such as cultural temporal structures (eg, public transport timetables) or individual responsibilities (eg, parenthood). Thus, measures and policies to create an activity-friendly environment are needed, rather than blaming individuals for lack of exercise.[1] Finally, we recommend that policy-makers and public health experts involved in the development of physical activity recommendations consider specifying these recommendations by level of occupational physical activity, because recent guidelines do not make this distinction.

Strengths and limitations

A major strength of this study is its use of a large population-based nationally representative sample of the non-institutionalised, resident adult working population. This allows the findings to be generalised. Significant efforts were made to reduce potential sources of bias in DEGS1,[64 65] but our study still needs to be interpreted in the context of some limitations. First, the study's cross-sectional design does not permit any causal inferences to be drawn about the observed relationship between physical activity patterns and cardiorespiratory fitness. It is well known that regular physical activity can increase cardiorespiratory fitness, but reversed causality cannot be ruled out: for example, individuals who have inherited a lower cardiorespiratory fitness may tend to be less active.[66] We therefore cannot conclude that a higher cardiorespiratory fitness can be traced to higher leisure time physical activity levels. Second, due to the use of the PAR-Q screening questionnaire, our sample consists of a relatively healthy study-population. This implies the exclusion of most study participants using cardiorespiratory-related medication. However, it is possible that the use of other medications (eg, psychotropic or antidiabetic drugs) may act as a source of bias. The use of a relatively healthy study population may also have hampered the generalisability of our results. The results might also be affected by the so-called healthy worker effect, a specific form of selection bias where more healthy individuals are more likely to work in physically demanding occupations. Third, as in most large-scale epidemiological studies,[10 34] $\dot{V}O_2max$ was estimated using a submaximal ergometer test in a highly standardised and quality-assured procedure[19] and not directly assessed by breath gas analysis. Fourth, self-reports on physical activity levels are prone to recall and social desirability bias.[67 68] We cannot exclude the possibility that the level of physical activity was over-reported or under-reported. This is also true for most of the studies cited. Leisure time physical activity was assessed based on information about the duration per week, but not intensity, although intensity may have an additional impact on cardiorespiratory fitness.[10] In the case of occupational physical activity, self-reports are restricted to specific task, such as lifting of heavy loads. In contrast, objectively measured activity levels usually include general activities at work. This is particularly important, because this type of task influences cardiorespiratory fitness in a different way from general activities. Fifth, occupational physical activity was assessed indirectly via job exposure matrices. These were based on a very large sample and the use of hierarchical linear regression models, controlling for age, sex, working hours and job experience, reduced the likelihood of confounding. However, they are generally not able to account for variability of exposure within jobs.[69] If the prevalence of high physical demands within occupations varied widely, this could have led to biased results on observed occupational physical activity levels, which would reduce the magnitude of the observed associations.

CONCLUSIONS

This study showed a strong association between patterns of physical activity during leisure time and work and cardiorespiratory fitness among men and women in the working population in Germany. For example, women doing little or no leisure time physical activity were likely to have low cardiorespiratory fitness, especially if they worked in physically demanding jobs. These findings therefore contribute to the increasing body of evidence about different domain-specific effects of physical activity on health outcomes. They also emphasise the importance of considering different domains of physical activity in future studies. Current guidelines do not distinguish between work and leisure time physical activity, and it may be helpful to specify leisure time physical activity recommendations by occupational physical activity levels. Further research is needed to understand the pathways through which different domains of physical activity lead to divergent health effects and to confirm these findings with objective measures of physical activity.

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Publikationen

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Gesamt:	**14.809**
Zeiher, J., Duch, M., Kroll, L. E., Mensink, G. B. M., Finger, J. D., & Keil, T. (2020). Domain-specific physical activity patterns and cardiorespiratory fitness among the working population. Findings from the cross-sectional German health interview and examination survey. BMC Public Health, 10(4). 10.1136/bmjopen-2019-034610	**2.496**
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Lebenslauf

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