Title: Relationship between handgrip strength and lung function in adults: A systematic review.

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Abstract

Background: Handgrip strength (HGS) is a functional test that has been directly associated with lung function in some healthy populations, however, inconsistent findings have been reported for populations with chronic diseases. The aim of this study was to identify the relationship between HGS and lung function in both healthy and unhealthy adults.

Method: A systematic search was conducted using six databases from their earliest inception to February 29th, 2020. Two authors reviewed and assessed methodological quality of eligible studies using the Crowe Critical Appraisal Tool (CCAT).

Results: Twenty-five studies met the inclusion criteria with 8 and 17 studies examining healthy and unhealthy populations, respectively. Reported average methodological quality of all included studies using the CCAT was 38-85% with most rated as Good to Excellent. Despite the use of heterogeneous equipment and protocols during HGS and lung function assessments, significant positive and moderate correlations and/or regression coefficients were reported for healthy populations consistently. Conversely, the reported relationships between HGS and lung function for unhealthy counterparts were variable.

Conclusion: Handgrip strength was significantly associated with lung function in most healthy adults. Future robust studies are needed to confirm the suitability of HGS to assess lung function for healthy and unhealthy adults.

Keywords: Respiratory function tests; muscle strength; relationship; adults; systematic review.

Introduction

Handgrip strength (HGS) is a functional and inexpensive test that assesses the global muscle strength of an individual (da Silva et al., 2017; Porto et al., 2019) as well as a potential indicator of overall health outcomes (McGrath, Kraemer, Snih and Peterson, 2018). Poor HGS was related to the presence of low back pain in physically inactive women aged over 50 years (Park et al., 2018), greater incidence of hip fractures in the elderly (Denk, Lennon, Gordon and Jaarsma, 2018) and associated with all-cause mortality and cardiovascular and non-cardiovascular deaths in some countries and populations (Leong et al., 2015). Collectively, HGS strength has been associated with poor indicators of health, however, its use as a monitoring tool for disease progression indices has received limited attention.

This limited focus could be attributed to the small number of studies conducted to date, which reported inconsistent relationships between HGS and measures of disease progression such as exercise capacity and lung function indices. For example, HGS was reported as an effective monitoring tool of exercise capacity in COPD patients (Kyomoto et al., 2019) and lung function (forced vital capacity, FVC; forced expiratory volume in one second, FEV_1; and peak expiratory flow rate, PEFR) in healthy and unhealthy populations (Bae et al., 2015; Martinez et al., 2017; Mgbemena et al., 2019; Son, Yoo, Cho and Lee, 2018). However, Bahat et al, (2014) reported no association between HGS and lung function in elderly men without history of pulmonary obstruction. These inconsistent findings question a reliable relationship between HGS and specifically lung function, and highlight a need to further examine such relationships accounting for different populations.

Confirmation of a consistent relationship between HGS and lung function across a range of populations would support the applicability of HGS as a simple and inexpensive assessment tool by physiotherapists and other allied health professionals. Further, the use of HGS may benefit individuals living in rural/remote regions where spirometry resources and training may be lacking (Márquez-Martín et al., 2015). Subsequently, the aim of this review was to identify the relationship between HGS and lung function (FEV_1, FVC and PEFR) in healthy and unhealthy adults. The focus on adults minimized the variation in assessments and interpretations that can occur between adults and other populations (Seed, Wilson and Coates, 2012).

METHOD

A systematic review of prior published literature was conducted (PROSPERO registration number: CRD42019122705, www.crd.york.ac.uk/prospero/) and reported using the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) protocol (Moher et al., 2009).

Search strategy and study selection

A comprehensive computerized search was carried out in six databases (Ovid MEDLINE, Ovid Emcare, CINAHL, SportDiscus, Scopus and PEDro) from their earliest inception date to February 29, 2020. The final search was conducted using explode functions (brackets to break a string into an array), truncation (to retrieve all alternative terms) and Boolean operators (connector AND/OR). Searches relating to HGS were combined with searches relating to lung function using the "AND" Boolean operator, in order to retrieve studies relating HGS with lung function. An example of the search strategy using Ovid MEDLINE is represented in Table 1. Titles of studies retrieved from the final search were initially screened with duplicates removed by the lead author (NM) using Endnote X8 (Clarivate Analytics, Philadelphia, USA). The titles and abstracts of the remaining studies were vetted by two independent reviewers (NM, AJ) using the selection criteria, with discrepancies in study

Table 1: Search strategy for Ovid MEDLINE

1	exp Hand Strength/
2	("Grasp Strength*" or "Grip Strength*" or "Hand Strength").mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
3	((hand or grip) and strength).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
4	1 or 2 or 3
5	respiratory function tests/ or exp lung volume measurements/ or exp pulmonary ventilation/ or exp spirometry/
6	("lung function test*" or "respiratory function test*" or spiromet* or "peak flow" or "peak expiratory flow" or "lung volume" or "respiratory airflow" or "Pulmonary Function" or "Lung Capacit*" or "Pulmonary Capacit*" or "Pulmonary Volume" or FRC or "Residual Capacit*" or "Reserve Volume" or "Tidal Volume*" or "volume*, tidal" or "Airflow Rate" or "flow rate*" or "Flow-Volume Curve*" or "Expiratory Volume*" or "respiratory volume*" or FEV or "Vital Capacity").mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
7	5 or 6
8	4 and 7

inclusion decided upon mutual agreement and/or by a third reviewer (AL). The full text of those studies, which addressed the selection criteria were assessed for further eligibility and subsequent inclusion for critical appraisal. The reference lists of all included studies were also reviewed to identify other studies for inclusion and completion of a comprehensive search.

The inclusion criteria for studies were: adult participants (≥18 years) who were healthy (without any chronic disease condition) or unhealthy (with any chronic disease condition e.g. chronic respiratory diseases, diabetes, cardiovascular diseases, cancer etc.) (World Health Organization, 2005); assessment of HGS via a hand dynamometer and lung function via a spirometer; and reported a relationship between HGS and lung function. Assessed lung function indices were FEV_1, FVC and PEFR. The exclusion criteria for studies were: not original research (e.g. systematic or literature reviews) and/or not published in a peer-reviewed journal (e.g. letters to the editor, editorials, comments, and conference or seminar presentations); conducted with animals or artificial models; not written in English language; where full text was unavailable; and studies that included a mixed population of healthy and unhealthy adults during analysis of relationship between HGS and lung function. No restrictions were applied to the year published or study designs of the included studies.

Data extraction

The following information was retrieved from each study: authors' names; year of publication; country where the study was done; description of study population; study sample size; study design (i.e. cohort, case-control etc.); study aims; HGS and lung function mean values [i.e. greatest volume of air expired with maximal force from a full inspiration start point – FVC; volume of air expired in the first second of an FVC manoeuvre – FEV_1 (Miller et al., 2005); greatest flow of a forceful expiration, starting without hesitation from a maximal inspiration – PEFR, (Jayapal, 2016)]; and correlation and/or regression coefficients for the relationship between HGS and lung function. Pearson correlation coefficient (r) values of 0 – 0.3 were interpreted as weak, 0.3 – 0.7 as moderate and 0.7 – 1 as strong relationship (Ratner, 2009). All correlation and regression coefficients were extracted and reported from each study as either adjusted for confounders or unadjusted values with no study reporting both formats. Mean HGS values were presented in kilograms (kg), Newtons (N) or percentage of predicted values (%Pred) using the normal values of healthy adults in the same or similar population (Nascimento et al., 2004). Results presented in Newtons were converted to kilograms (i.e. N / 9.81 = kg). Likewise, FEV_1, FVC and PEFR values were reported in Liters and Liters per second, respectively, and were presented separately from those reported as %Pred values. Percentage of predicted values were calculated by comparing actual values with previously reported reference values, based on an individual's age, sex, height and ethnicity (Stanojevic, Wade and Stocks, 2010).

Methodological quality and risk of bias

Risk of selection bias was minimized by having two independent authors review studies and agree on the eligibility of the included studies, based on the inclusion and exclusion criteria. Methodological quality and risk of bias within studies was determined using the Crowe Critical Appraisal Tool (CCAT) version 1.4 (Crowe, Sheppard and Campbell, 2012). This tool was developed on a wide number of previous critical appraisal tools, general research methods theory and reporting guidelines and reported to be a valid and reliable tool with high intra-class correlation (Crowe, Sheppard and Campbell, 2012). The CCAT consists of eight categorical items, which include; preliminaries, introduction, design, sampling, data collection, ethical matters, results and discussion (Crowe and Sheppard, 2011). Each categorical item was scored from 0 (no evidence) to 5 (high evidence) and summed to provide a total article score that was presented as a percentage (i.e. [score / 40] x 100). Resultant total scores identified the quality of the study and assisted the quality comparison of all articles included in this review (Crowe, Sheppard and Campbell, 2011). We assumed a total CCAT score of <50% as poor; ≥50% – 79% as good and ≥80% as excellent. The National Health and Medical Research Council (NHMRC) hierarchy levels of evidence were also used to rank the included studies according to the study design employed (National Health and Medical Research Council, 2009). This ranking was as follows: I – systematic reviews of level II studies; II – a randomized controlled trial (RCT); III-1 – a pseudo RCT; III-2 – cohort study, case-control study; III-3 – comparative studies without concurrent controls; and IV – case series, cross-sectional study.

RESULTS

Outcomes of the search conducted in accordance with the PRISMA process is illustrated in Figure 1. The initial search returned 2207 studies from the six databases with one identified by hand searching. Removal of 975 duplicates was conducted and the resultant studies' titles and abstracts were screened with 984 excluded with reasons, yielding 249 studies for full-text review. Following full-text review and exclusions, 25 studies including healthy (n=8) and unhealthy (n=17) populations were identified for CCAT appraisal.

Critical appraisal and NHMRC Ranking

Healthy population

Scores for quality assessment of each study using the CCAT and the NHMRC hierarchy of evidence are shown in Table 2. Across these eight studies, an average CCAT score of 66% (Good) was calculated with the category items of preliminaries, introduction and discussion being the strongest while study designs and ethical matters were the weakest. During the

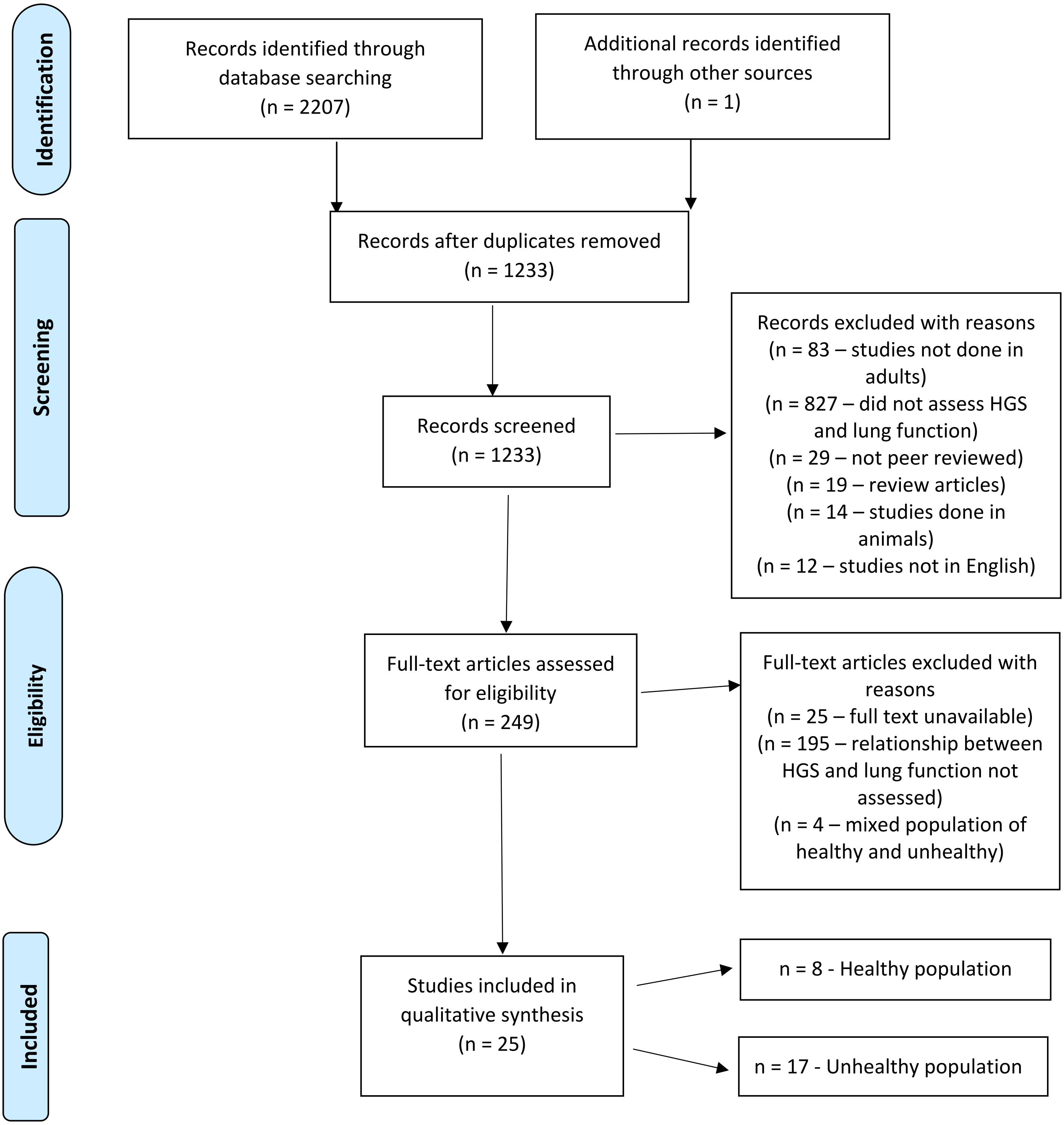

Figure 1: Flowchart of search process

Table 2: Critical appraisal of eligible articles

Author	NHMRC hierarchy score	Preliminaries	Introduction	Design	Sampling	Data collection	Ethical matters	Results	Discussion	Total score
Healthy population										
Burchfiel et al, (1997)	IV	4	5	4	3	4	1	4	5	75%
Deary, Whalley, Batty, and Starr, (2006)	III-2	2	2	3	4	3	1	3	4	55%
Holmes, Allen and Roberts, (2017)	III-2	4	4	3	4	3	4	3	4	73%
Hornby et al, (2005)	IV	4	4	3	3	3	2	3	3	63%

Author	NHMRC hierarchy score	Preliminaries	Introduction	Design	Sampling	Data collection	Ethical matters	Results	Discussion	Total score
Rozeck-Piechura et al, (2014)	IV	3	4	2	2	4	3	4	2	60%
Schweitzer et al, (2017)	IV	4	3	2	3	4	3	3	4	65%
Sillanpaa et al, (2014)	IV	4	5	4	3	4	3	4	5	80%
Zhu et al, (2020)	IV	4	2	4	3	3	1	3	4	58%
Unhealthy Population										
Barry and Gallagher, (2003)	IV	3	4	3	2	2	2	3	4	58%

Author	NHMRC hierarchy score	Preliminaries	Introduction	Design	Sampling	Data collection	Ethical matters	Results	Discussion	Total score
Cichosz, Vestergaeerd, and Hejlesen, (2018)	IV	4	4	4	4	3	1	4	5	73%
Cortopassi, Divo, Pinto-Plata, and Celli, (2011)	III-2	3	4	3	3	4	4	4	5	75%
Guler et al, (2019)	III-2	4	5	4	4	4	4	4	5	85%
Hallin et al, (2011)	IV	4	4	3	2	3	3	3	4	65%

Author	NHMRC hierarchy score	Preliminaries	Introduction	Design	Sampling	Data collection	Ethical matters	Results	Discussion	Total score
Jeong et al, (2017)	IV	3	3	3	3	2	2	3	4	58%
Kaymaz et al, (2018)	III-2	4	4	2	2	3	2	3	3	58%
Kohlbrenner et al, (2020)	III-2	5	4	3	1	4	3	4	5	75%
Kim, (2018)	IV	4	5	3	3	4	2	3	3	68%
Lopes Justo, Ferreira, and Guimaraes, (2017)	IV	4	5	4	3	4	3	3	4	75%
Ma, Liu, Wu, and Li, (2017)	III-2	4	4	3	4	4	3	4	5	76%

Author	NHMRC hierarchy score	Preliminaries	Introduction	Design	Sampling	Data collection	Ethical matters	Results	Discussion	Total score
Martinez et al, (2017)	IV	4	5	3	2	3	2	4	4	68%
Nascimento et al, (2004)	III-2	4	4	3	2	3	2	3	3	60%
Shah et al, (2013)	III-2	4	5	3	3	4	2	3	3	68%
Sirguroh et al, (2012)	III-2	2	4	2	2	2	1	1	1	38%
Strandkvist et al, (2016)	III-2	5	5	4	3	4	3	4	4	80%
Turan et al, (2018)	IV	4	3	3	4	4	2	3	2	63%

Footnotes: CCAT – Crowe critical appraisal tool; NHMRC – National health medical research council.

CCAT appraisal, all studies except two (25%) did not include the justification for their study (Deary, Whalley, Batty and Starr, 2006; Rozek-Piechura et al., 2014) as well as the strengths, limitations and overall practical usefulness of their study (Hornby et al., 2005; Rozek-Piechura et al., 2014). Two studies (25%) failed to state an ethical approval or informed consent process (Burchfiel et al., 1997; Deary, Whalley, Batty and Starr, 2006) as well as their study design and its suitability (Burchfiel et al., 1997; Zhu et al., 2020). Assessment via the NHMRC hierarchy of evidence identified that seven studies (87%) were of level IV evidence (cross-sectional studies) while one study (13%) were of level III-2 evidence (cohort study) (Table 2).

Unhealthy population

Similar to the healthy population studies, an average score of 67% (Good) was reported for the unhealthy population studies using the CCAT, with the category items of preliminaries, introduction and discussion being the strongest while study designs and ethical matters were the weakest. All studies justified their study, six studies (35%) did not explain the strengths (Kim, 2018; Lopes, Justo, Ferreira and Guimaraes, 2017; Nascimento et al., 2004; Shah, Nahar, Vaidya and Salvi, 2013; Sirguroh et al., 2012; Turan et al., 2019) while four studies (24%) did not explain practical usefulness of their study (Barry and Gallagher, 2003; Guler et al., 2019; Kaymaz et al., 2018; Strandkvist et al., 2016). One study (6%) failed to state an ethical approval or informed consent process (Cichosz, Vestergaard and Hejlesen, 2018). Seven studies (41%) described their sampling method and its suitability (Guler et al., 2019; Jeong et al., 2017; Lopes, Justo, Ferreira and Guimaraes, 2017; Ma, Liu, Wu and Li, 2017; Shah, Nahar, Vaidya and Salvi, 2013; Sirguroh et al., 2012; Strandkvist et al., 2016), while nine studies (53%) stated their study design and its suitability (Cichosz, Vestergaard and Hejlesen, 2018; Cortopassi, Divo, Pinto-Plata and Celli, 2011; Kohlbrenner et al., 2020;

Lopes, Justo, Ferreira and Guimaraes, 2017; Martinez et al., 2017; Shah, Nahar, Vaidya and Salvi, 2013; Sirguroh et al., 2012; Strandkvist et al., 2016; Turan et al., 2019). Using the NHMRC hierarchy of evidence, eight studies (47%) were of level IV evidence, while nine (53%) were of level III-2 evidence (Table 2).

Participant characteristics

Healthy population

Five studies (63%) reported participants' mean age of ≥65years (Burchfiel et al., 1997; Deary, Whalley, Batty and Starr, 2006; Holmes, Allen and Roberts, 2017; Schweitzer et al., 2017; Sillanpää, Stenroth, Bijlsma and et al, 2014) while three studies (37%) reported a mean age of <65 years (Hornby et al., 2005; Rozek-Piechura et al., 2014; Zhu et al., 2020). Six studies (75%) were conducted in Europe (Deary, Whalley, Batty and Starr, 2006; Holmes, Allen and Roberts, 2017; Hornby et al., 2005; Rozek-Piechura et al., 2014; Schweitzer et al., 2017; Sillanpää et al., 2014), one (13%) in Asia (Zhu et al., 2020) and one in North America (Burchfiel et al., 1997) (Table 3).

Unhealthy population

Among the 17 studies retrieved, 10 studies (58%) examined patients with COPD (Cortopassi, Divo, Pinto-Plata and Celli, 2011; Hallin et al., 2011; Jeong et al., 2017; Kaymaz et al., 2018; Kohlbrenner et al., 2020; Martinez et al., 2017; Shah, Nahar, Vaidya and Salvi, 2013; Sirguroh et al., 2012; Strandkvist et al., 2016; Turan et al., 2019), two studies (12%) involved patients with diabetes (Cichosz, Vestergaard and Hejlesen, 2018; Ma, Liu, Wu and Li, 2017) and the remaining studies (6%) examined separately, patients with cystic fibrosis (CF) (Barry and Gallagher, 2003), idiopathic lung disease (ILD) (Guler et al., 2019), stroke (Kim, 2018), chronic kidney disease (CKD) (Nascimento et al., 2004) and systemic sclerosis (SSc) (Lopes,

Table 3: Study characteristics of eligible articles reported according to study population, disease condition and study design

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
Healthy population									
Burchfiel et al. (1997)	USA	Japanese-American men who completed spirometry in the 4th examination of the Honolulu Heart Foundation.	3 111	Cross sectional study	All: 77.2(4.3) (71-93)	All males	Equipment and protocol not reported	Water-sealed spirometer with test guidelines from ATS. Calibration of spirometer not reported.	Identification of factors associated with lung function
Hornby et al. (2005)	United Kingdom	Healthy adults who were invited from all areas of the hospital	98	Cross sectional study	All: 45.9	46 (M) 52 (F)	Portable strain-gauge dynamometer Lying in bed at 30°, elbow at 90°, mean of 3 trials	A miniature Wright peak flow meter with test done in lying at 30° and an average of 3 readings was the accepted value. Calibration of	Relationship between HGS and PEFR

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
								spirometer not reported.	
Rozeck-Piechura et al. (2014)	Poland	Participants were selected from rural farmers who stayed on a 3-week rehabilitation camp.	116	Cross sectional study	Males 49.26(5.86) Females 47.52(6.17)	29 (M) 87 (F)	Hydraulic hand dynamometer, protocol and accepted value not reported	Flowscreen spirometer with test was done in sitting, but number of trials was not reported. Calibration of spirometer not reported.	Relationship between respiratory function and PA levels and body composition
Schweitzer et al. (2017)	Germany	Participants were selected from healthy Caucasians between the ages of 65-81 years in 2014.	40	Cross sectional study	Males 72.6(4.3) Females 71.8(4.3)	20 (M) 20 (F)	Saehan hand dynamometer SH5001, sitting position with	Spirometer Vmax with test done in standing but number of trials was not reported. Calibration	Relationship between body composition and lung function

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
							elbow at 90º, highest of 3 trials	of spirometer not reported.	
Sillanpaa et al. (2014)	Finland United Kingdom France	Participants were socially active and healthy elderly individuals aged from 69-81 years old that were recruited from the MyoAge project,	135	Cross sectional study	Males 75.0(3.6) Females 74.4(3.1)	61 (M) 74 (F)	Jamar handgrip dynamometer, standing position with elbow extended, highest of 3 trials	Three different types of spirometers with test guidelines from ATS/ERS. Calibration of spirometer was reported.	Association between HGS, lung function and mobility
Zhu et al. (2020)	China	On-going survey of Chinese adults (≥ 18 years) without COPD, who undertook	380	Cross sectional study	All: 43.7(14.3) Males 43.0(14.3)	187 (M) 193 (F)	Takei dynamometer, standing with arms extended to	Pneumoscreen II spirometer with test guidelines from ATS/ERS. Calibration of	Association between HGS and cardiopulmonary function

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
		pulmonary function tests; conducted from the beginning of 2013 in five provinces.			Female 44.3(14.2)		the side, highest of two trials	spirometer not reported.	
Holmes, Allen and Roberts (2017)	United Kingdom	Subjects were patients aged ≥70 years admitted to acute older people's wards at a university hospital in the UK.	50	Cross sectional study	Males 86.3(4.9) Females 87.5(4.8)	20 (M) 30 (F)	Jamar dynamometer Sitting position with elbow at 90°, highest of 3 trials	Microlab portable spirometer with best of 5 measurements recorded in sitting position. Calibration of spirometer was reported.	Relationship between lung function and HGS

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
Deary, Whalley, Batty, and Starr (2006)	United Kingdom	Generally healthy surviving participants of the Scottish Mental Survey of 1932.	460	Retrospective cohort	79 years	188 (M) 272 (F)	Jamar hydraulic hand dynamometer Position not reported. Highest of 3 trials	Microspirometer with test position not reported and best of 3 trials was the accepted value. Calibration of spirometer not reported.	Association between physical fitness and cognitive aging
Unhealthy population									
Martinez et al. (2017)	U.S.A.	Participants with COPD selected from the NIH-funded Genetic epidemiology of	272	Cross sectional study	All: 64.7(8.0)	151 (M) 121 (F)	Jamar dynamometer Position not reported, highest of 3 trials	EasyOne Spirometer with test position and number of trials not reported. Calibration of spirometer not reported.	Association between HGS, SAT, imaging characteristics and lung function

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
		COPD Study, COPDGene.							
Hallin et al. (2011)	Sweden	Patients with moderate to severe COPD who were recruited from an exercise study from September 2002 to March 2004.	49	Cross sectional study	All: 66	14 (M) 35 (F)	Grippit Type G 100 (AB Detector) Position not reported. Mean of 3 trials	Jaeger master piece spirometer with test guidelines from ATS. Calibration of spirometer not reported.	Relationship between physical capacity, nutrition, inflammation and COPD severity
Jeong et al. (2017)	Republic of Korea	Participants (≥40 years) who had COPD were selected from the Korea National Health and Nutrition	421	Cross sectional study	All: 65.4(8.8)	317 (M) 104 (F)	Digital hand grip dynamometer (Takei), Standing position with elbow	Spirometry system (SensorMedics) with test guidelines from ATS/ERS. Calibration of	Evaluate the clinical relevance of HGS in patients with COPD

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
		Examination Survey (KNHANES)					extended, mean of 3 trials	spirometer not reported.	
Turan et al. (2019)	Turkey	Participants with acute exacerbated COPD registered in pulmonary rehabilitation medical records between January 2010 and December 2014.	101	Cross sectional study	All: 68.3(9.1)	75 (M) 26 (F)	Handheld Vigorimeter, sitting position with elbow at 90º, the highest of three trials	Sensormedics Vmax Series, with test guidelines from ERS. Calibration of spirometer not reported.	Relationship between HGS and factors in COPD exacerbation
Cortopassi, Divo, Pinto-Plata, and Celli (2011)	USA	Patients with moderate to severe COPD from St Elizabeth's Medical	33	Case control study	COPD group All: 64.3(9.7) Control group	Not reported	Jamar dynamometer Done in sitting position, elbow at	Equipment not reported with test guidelines from ATS/ERS.	Relationship between HGS and oxygen pulse

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
		Centre between July 2008- January 2009 and age-matched control participants.			All: 61.6(7.7)		90º. Mean of 3 trials	Calibration of spirometer not reported.	
Shah, Nahar, Vaidya, and Salvi (2013)	India	Participants included COPD patients attending Respiratory medicine outpatient at Sasson General Hospital and controls were healthy hospital workers from March	86	Case control study	COPD group Males 56.9(8.5) Females 61.7(6.9) Control group Males 54.9(8.3) Females 59.4(7.8)	46 (M) 40 (F)	Handgrip dynamometer, sitting position with elbow at 90º, highest of 3 trials	Turbine flow-sensor based MIR Spirolab with test guidelines from ATS/ERS. Calibration of spirometer not reported.	Association between lung function and upper limb muscle strength

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
		2009 to August 2010.							
Sirguroh and Ahmed (2012)	India	Patients with COPD admitted in the respiratory medicine ward of Sassoon General Hospital, Pune and age-matched controls	60	Case control study	COPD group All: 58.1(11.7) Control group All: 58.1(11.7)	Not reported	Jamar dynamometer, sitting position with elbow at 90°, the highest of three trials.	Wright's peak flow meter, with test guidelines from ATS. Calibration of spirometer not reported.	Relationship between HGS and PEFR
Strandkvist et al. (2016)	Sweden	Participants included subjects with or without COPD that were recruited from a COPD study from 2009 to 2010.	1 011	Case control study	COPD group Males 68.3(9.0) Females 69.5(9.7)	561 (M) 450 (F)	Handheld dynamometer, sitting position with elbow at 90°, highest of 3 trials	Dry volume spirometer with test guidelines from ATS/ERS. Calibration of	Relationship between HGS and COPD severity

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
					Control group Males 67.8(10.2) Females 67.8(10.3)			spirometer not reported.	
Kohlbrenner et al. (2020)	Switzerland	Patients with mild to very severe COPD from seven pulmonary outpatient clinics from October 2010 to April 2016	194	Prospective cohort	Median age of 64	127 (M) 68 (M)	Digital dynamometer, sitting with elbow at 90º, the highest of three trials	Equipment not reported, with test guidelines from ATS/ERS. Calibration of spirometer not reported.	Course of HGS and possible predictors of the changes in HGS
Kaymaz et al. (2018)	Turkey	Patients with diagnosed COPD who were admitted	88	Retrospective cohort	All: 64.2(8.7)	79 (M) 9 (F)	Jamar hydraulic hand dynamometer,	Vmax 229 series, Sensormedics with test guidelines from	Relationship between HGS with lung function,

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
		to Pulmonary Rehabilitation centre					sitting position with elbow at 90º, highest of 3 trials	ATS/ERS. Calibration of spirometer not reported.	exercise capacity, quality of life and dyspnoea
Guler et al. (2019)	Canada	Consecutive adults who attended an interstitial lung disease (ILD) clinic from January 2016 to December 2017.	115	Prospective cohort	Males 69(10) Females 66(9)	71 (M) 44 (F)	HiRes Hydraulic hand dynamometer Done in sitting with elbow at 90º, highest of 3 trials	Equipment nor reported but ATS/ERS guidelines were used. Calibration of spirometer not reported.	Importance of body composition, muscle strength and physical performance
Barry and Gallagher (2003)	Ireland	Outpatient department at the National Referral	23	Cross sectional study	All: 23.3(5.1) (18–39)	13 (M) 10 (F)	Compufet system Assessment protocols not reported	Vitalograph with test guidelines from ATS. Calibration of	Relationship between muscle strength, spirometry and nutrition

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
		Centre for adult cystic fibrosis						spirometer not reported.	
Lopes Justo, Ferreira, and Guimaraes (2017)	Brazil	Patients with systemic sclerosis who were followed at the Pedro Ernesto University Hospital, Rio de Janeiro between October 2015 and August 2016.	28	Cross sectional study	Median age of 51.2	2 (M) 26 (F)	Saehan hand dynamometer SH5001, sitting position with elbow at 90°, highest of 3 trials	Spirometer with test guidelines from ATS. Calibration of spirometer not reported.	Relationship between HGS and lung function
Cichosz, Vestergaeerd , and	USA	Data of known diabetics in the US from the National Health and Nutrition	233	Cross sectional study	All: 54.3(11.1) (20-80)	126 (M) 107 (F)	Handgrip dynamometer. Position not reported.	Spirometer with test done in standing and number of trials not reported. Calibration	Muscle strength as a predictor for reduced lung function

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
Hejlesen (2018)		Examination Survey (NHANES) 2011-2012					Sum of the largest result from each hand	of spirometer not reported.	
Ma, Liu, Wu, and Li (2019)	China	Chinese adults with diabetes aged 45 years and older from the China Health and Retirement Longitudinal Study (CHARLS) from May 2011 to March 2012.	1 636	Prospective cohort study	Not reported	Not reported	Hand dynamometer, Standing position with elbow at 90º, mean of 4 measures from both hands	Peak flow meter with test done in standing with an average of 3 readings as the accepted value. Calibration of spirometer not reported.	Relationship between HGS and PEFR
Kim, (2018)	Korea	Participants were patients over 50 years of age who had	51	Cross sectional study	All: 68.69(10.40)	21 (M) 30 (F)	Hydraulic hand dynamometer, position not	Spirometer (Pony FX) with test guidelines from ATS.	Relationship between HGS and lung function and

Author	Country	Study population	Sample	Study design	Age Mean (SD) or median in years	Sex	HGS assessment	Lung function assessment	Aim of the study
		their first episode of unilateral stroke with hemiparesis during the previous 12 months.					reported, elbow at 90º, mean of 3 trials	Calibration of spirometer not reported.	respiratory muscle strength
Nascimento et al. (2004)	Sweden	Participants were Chronic Kidney Disease (stage 5) patients selected from an ongoing prospective study.	109	Prospective cohort study	All: 53(12)	68 (M) 41 (F)	Harpenden dynamometer, position not reported, highest of 3 trials	Spirolab with test position not reported but best of 3 readings was the accepted value. Calibration of spirometer not reported.	Relationship between lung function, nutrition and malnutrition

Footnotes: M – Males; F – Females; PA – Physical activity, SAT – Subcutaneous adipose tissues.

Justo, Ferreira and Guimaraes, 2017). Out of sixteen studies (94%) that stated the age of their participants, a mean age of ≥65years was reported in nine (53%) studies (Cortopassi, Divo, Pinto-Plata and Celli, 2011; Guler et al., 2019; Hallin et al., 2011; Jeong et al., 2017; Kaymaz et al., 2018; Kim, 2018; Martinez et al., 2017; Strandkvist et al., 2016; Turan et al., 2019) while seven studies (41%) reported a mean age of <65 years (Barry and Gallagher, 2003; Cichosz, Vestergaard and Hejlesen, 2018; Kohlbrenner et al., 2020; Lopes, Justo, Ferreira and Guimaraes, 2017; Nascimento et al., 2004; Shah, Nahar, Vaidya and Salvi, 2013; Sirguroh et al., 2012). More studies (41%) were conducted in Europe (Barry and Gallagher, 2003; Hallin et al., 201; Kaymaz et al., 2018; Kohlbrenner et al., 2020; Nascimento et al., 2004; Strandkvist et al., 2016; Turan et al., 2019) than in Asia (29%) (Jeong et al., 2017; Kim, 2018; Ma, Liu, Wu and Li, 2017; Shah, Nahar, Vaidya and Salvi, 2013; Sirguroh et al., 2012), North America (24%) (Cichosz, Vestergaard and Hejlesen, 2018; Cortopassi, Divo, Pinto-Plata and Celli, 2011; Guler et al., 2019; Martinez et al., 2017) and South America (6%) (Lopes, Justo, Ferreira and Guimaraes, 2017) (Table 3).

Handgrip assessment

Healthy population

Disparities in assessment protocols were identified for this population as two studies (25%) conducted HGS assessment during sitting with elbow flexed to 90º and wrist in neutral position (Holmes, Allen and Roberts, 2017; Schweitzer et al., 2017), two studies (25%) conducted their assessment during standing with elbow fully extended (Sillanpää et al., 2014; Zhu et al., 2020), one study (13%) assessed HGS in the lying position (Hornby et al., 2005) while the remaining three studies (37%) did not report their protocol (Table 3). Further, determination of the HGS results varied across studies with five (62%) reporting the highest of two or three trials (Deary, Whalley, Batty and Starr, 2006; Holmes, Allen and Roberts, 2017; Schweitzer et al., 2017; Sillanpää et al., 2014; Zhu et al., 2020), one (13%) reporting the mean of two or three trials (Hornby et al., 2005), while two (25%) did not report how their measure was determined (Burchfiel et al., 1997; Rozek-Piechura et al., 2014) (Table 3). Different types of dynamometers were used during HGS assessments; six studies (74%) reported the use of hydraulic dynamometers (with Jamar and Saehan dynamometers reported in two studies, respectively) (Deary, Whalley, Batty and Starr, 2006; Holmes, Allen and Roberts, 2017; Hornby et al., 2005; Rozek-Piechura et al., 2014; Schweitzer et al., 2017; Sillanpää et al., 2014), one study (13%) used an electronic/digital dynamometer (Zhu et al., 2020) while one study (13%) did not report the type of dynamometer used (Burchfiel et al., 1997) (Table 3). All studies reported HGS in kilograms except one, which reported HGS in Newtons (Rozek-Piechura et al., 2014). Studies including HGS results that also documented the sex of participants reported that males had greater values than females (Table 4).

Unhealthy population

Assessment protocols for these populations were also varied, as 10 studies (59%) reported HGS assessment during sitting with elbow flexed to 90º and wrist in neutral position (Cortopassi, Divo, Pinto-Plata and Celli, 2011; Guler et al., 2019; Kaymaz et al., 2018; Kim, 2018; Kohlbrenner et al., 2020; Lopes, Justo, Ferreira and Guimaraes, 2017; Shah, Nahar, Vaidya and Salvi, 2013; Sirguroh et al., 2012; Strandkvist et al., 2016; Turan et al., 2019), two (12%) during standing with elbow fully extended (Jeong et al., 2017; Ma, Liu, Wu and Li, 2017) while the remainder (29%) did not report their assessment protocols (Barry and Gallagher, 2003; Cichosz, Vestergaard and Hejlesen, 2018; Hallin et al., 2011; Martinez et al., 2017; Nascimento et al., 2004). Determination of the HGS measure ranged from adopting the highest of three trials (65%) (Cichosz, Vestergaard and Hejlesen, 2018; Guler et al., 2019; Kaymaz et al., 2018; Kohlbrenner et al., 2020; Lopes, Justo, Ferreira and Guimaraes, 2017;

Table 4: Study results of eligible articles reported according to study population, disease condition and type of analysis

Authors	Statistical test for relationship	Handgrip strength Mean (SD)	Lung function assessed Mean (SD)	Results for test of relationship
Healthy population				
Burchfiel et al. (1997)	Pearson correlation after adjustment of FEV_1 and FVC for age and height	HGS(kg) 27.9(5.9)	FEV_1(L) 2.11(0.48) FVC(L) 2.93(0.58)	FEV_1 & HGS; r = 0.31; p<0.001 FVC & HGS; r = 0.35; p<0.001
Schweitzer et al. (2017)	Pearson correlation after adjustment of FEV_1 and FVC for height	HGS (kg) Males Females 40.1(6.6) 26.3(5.0) p<0.05	FEV_1 (L) Males Females 2.9(0.7) 2.1(0.4); p<0.05 FVC (L) Males Females 4.1(0.7) 3.0(0.5); p<0.05 FEV_1 (%Pred) Males Females 95.4(20.2) 97.8(19.7); p>0.05 FVC (%Pred) Males Females 103.5(11.4) 106.2(15.2); p>0.05	FEV_1 & HGS; r = 0.61; p<0.05 FVC & HGS; r = 0.60; p<0.05
Deary, Whalley, Batty, and Starr (2006)	Pearson correlation after adjustment of FEV_1 and HGS for age and sex	HGS (kg) Males Females 34.6(7.4) 20.5(4.5)	FEV_1 (L) Males Females 2.33(0.62) 1.55(0.39)	FEV_1 & HGS; r = 0.26; p<0.01
Rozeck-Piechura et al. (2014)	Pearson correlation	HGS (N) Males Females 438.9(104.2) 282.5(86.2)	FEV_1 (L) Males Females 3.65(0.67) 2.81(0.50); p<0.05	FEV_1 & HGS r = 0.62; p<0.05 (Males) r = 0.34; p<0.05 (Females)

Authors	Statistical test for relationship	Handgrip strength Mean (SD)	Lung function assessed Mean (SD)	Results for test of relationship
		44.7(10.6)kg 28.8(8.8)kg	FVC (L)	FVC & HGS
		$p<0.05$	Males Females	$r = 0.61$; $p<0.05$ (Males)
			4.23(0.77) 3.21(0.62); $p<0.05$	$r = 0.33$; $p<0.05$ (Females)
			PEFR (L/s)	PEFR & HGS
			Males Females	$r = 0.46$; $p<0.05$ (Males)
			7.25(1.65) 4.87(1.33); $p<0.05$	$r = 0.33$; $p<0.05$ (Females)
			FEV_1 (%Pred)	FEV_1(%Pred) & HGS
			Males Females	$r = 0.53$; $p<0.05$ (Males)
			102.14(11.83) 106.63(15.40)	$r = 0.22$; $p<0.05$ (Females)
			$p = 0.15$	
			FVC (%Pred)	FVC(%Pred) & HGS
			Males Females	$r = 0.53$; $p<0.05$ (Males)
			96.45(11.10) 104.29(16.95)	$r = 0.23$; $p<0.05$ (Females)
			$p<0.05$	
			PEFR (%Pred)	PEFR(%Pred) & HGS
			Males Females	$r = 0.37$; $p<0.05$ (Males)
			82.79(16.49) 75.79(20.02)	$r = 0.28$; $p<0.05$ (Females)
			$p = 0.09$	
Hornby et al. (2005)	Pearson correlation	DHGS NDHGS	PEFR (L/min)	PEFR & DHGS
		Males 41.2 39.2 kg	Males Females	$r = 0.51$; $p<0.001$
		Females 26.7 25.1 kg	516.6 402.9	PEFR & NDHGS
			$p<0.001$	$r = 0.54$; $p<0.001$
Sillanpaa et al. (2014)	Linear regression after adjustment for age, sex,	HGS (kg)	FEV_1 (L)	FEV_1 & HGS
		Males Females	Males Females	$\beta = 0.24$; $p<0.05$

Authors	Statistical test for relationship	Handgrip strength Mean (SD)	Lung function assessed Mean (SD)	Results for test of relationship
	total fat mass, height and site of enrolment	40.9(8.1) 25.2(4.6)	2.8(0.6) 2.0(0.4) FVC(L) Males Females 3.7(0.6) 2.6(0.4) FEV_1 (%Pred) Males Females 97.4(18.7) 101.9(16.0) FVC (%Pred) Males Females 98.4(13.9) 102.5(14.9)	95% CI (0.053, 0.424) FVC & HGS β = 0.22; p<0.05 95% CI (0.038, 0.408)
Zhu et al. (2020)	Linear regression after adjustment for age, BMI, SBP, DBP, muscle mass, smoking and drinking status	HGS (Kg) Males Females 36.9(7.0) 21.5(5.2) p<0.001	FEV_1 (L) Males Females 3.4(0.6) 2.5(0.4) p<0.001	FEV_1 & HGS β = 0.02; p<0.001 (Males) 95% CI (0.014, 0.032) β = 0.02; p<0.001 (Females) 95% CI (0.010, 0.028)
Holmes, Allen and Roberts (2017)	Linear regression after adjustment for age, height and weight	HGS (kg) Males Females 19.5(7.21) 12.4(3.73) p = 0.03	FEV_1 (L) Males Females 1.7(0.5) 1.0(0.3); p = 0.02 FVC (L) Males Females 2.1(0.7) 1.4(0.4); p = 0.01 PEFR (L/min) Males Females 262.1(102.5) 148.1(57.5)	FEV_1 & HGS β = 0.04; p = 0.06 (Males) β = 0.02; p = 0.27 (Females) FVC & HGS β = 0.06; p = 0.07 (Males) β = 0.02; p = 0.35 (Females) PEFR & HGS β = 6.60; p = 0.15 (Males) β = 6.94; p<0.02 (Females)

Authors	Statistical test for relationship	Handgrip strength Mean (SD)	Lung function assessed Mean (SD)	Results for test of relationship
			p = 0.004	
Unhealthy population				
Martinez et al. (2017)	Pearson correlation	Not reported	FEV_1(L) 1.70(0.77) FEV_1(%Pred) 59.0(22.5)	FEV_1(L) & HGS; r = 0.47; p<0.001
Turan et al. (2019)	Pearson correlation	COPD group DHGS NDHGS (bar) 0.47(0.2) 0.44(0.2) Control group DHGS NDHGS 0.55(0.16) 0.52(0.16)	COPD group FEV_1%Pred 38.9(14.6)	FEV1 & HGS r = - 0.07; p=0.51
Shah, Nahar, Vaidya and Salvi (2013)	Pearson correlation	HGS (kg) COPD group Males Females 21.8(4.7) 19.2(3.4) Control group Males Females 31.2(4.3) 23.0(1.9)	COPD group FEV_1%Pred Males Females 35.6(0.3) 37.6(6.1) FVC (%Pred) Males Females 54.3(10.9) 53.2(9.7) PEFR (%Pred) Males Females 25.9(11.2) 25.2(7.0) Control group FEV_1 (%Pred) Males Females	FVC%Pred & HGS (COPD group) r = 0.57; p<0.05 (Males) FEV_1%Pred & HGS (COPD group) r = 0.45; p<0.05 (Females)

Authors	Statistical test for relationship	Handgrip strength Mean (SD)	Lung function assessed Mean (SD)	Results for test of relationship
			88.5(6.9) 84.1(4.4) FVC (%Pred) Males Females 90.5(9.7) 83.2(5.4) PEFR (%Pred) Males Females 78.6(12.3) 84.1(10.1)	
Kaymaz et al. (2017)	Spearman correlation	HGS (kg) 30.8(7.9)	FEV_1 (%Pred) 34.2(15.2) FVC (%Pred) 53.2(16.9)	FEV_1 (%Pred) & HGS r = 0.09; p = 0.395 FVC (%Pred) & HGS r = 0.17; p = 0.114
Cortopassi et al. (2011)	Pearson correlation	HGS (kg) COPD Control 37.8(7.5) 55.0(2.8) p<0.001	FEV_1(L) COPD Control 1.51(0.73) 3.02(0.67) FEV1 (%) COPD Control 44.8±20.4 99.0±16.8	FVC & HGS; r = 0.42; p>0.001
Sirguroh and Ahmed (2012)	Pearson correlation	COPD group (kg) 17.4(4.49) Control group 28.4(8.35)	Not reported	PEFR & HGS r = -0.15; p=0.42
Strandkvist et al. (2016)	Linear regression after adjustment for sex	HGS (kg) COPD group Males Females	COPD group FEV_1%Pred Males Females	FEV_1%Pred & HGS β= 0.05; p<0.05 (All) 95% CI (0.01, 0.09)

Authors	Statistical test for relationship	Handgrip strength Mean (SD)	Lung function assessed Mean (SD)	Results for test of relationship
		45.9(9.9) 25.8(5.9) Control group Males Females 46.3(10.5) 26.9(6.7)	74.6(15.7) 80.1(16.6) Control group FEV_1%Pred Males Females 93.7(13.3) 97.2(14.3)	β= 0.07; p<0.05 (Males) 95% CI (0.01, 0.14) β= 0.02; p=0.29 (Females) 95% CI (-0.02, 0.07)
Kohlbrenner et al. (2020)	Multivariate mixed effect modelling after adjustment for baseline HGS	HGS(kg) Median is 35.3(28.2, 44.4)	FEV_1%Pred Median is 46 (34, 65)	FEV_1%Pred & ΔHGS β= -0.01; p = 0.30 95% (-0.03, 0.01)
Hallin et al. (2011)	Linear regression after adjustment for age, sex and FEV_1	HGS (N) FFMI Low FFMI Normal 202(64) 272(96)	FEV_1 (%Pred) FFMI Low FFMI Normal 31(9) 32(10)	FEV_1% & HGS β = 1.2 p = 0.23
Jeong et al. (2017)	Linear regression after adjustment for age, sex and height	HGS (kg) 33.3(9.1)	FEV_1 (L) 2.35(0.64) FEV_1 (%Pred) 79.9(15.3) FVC (L) 3.68(0.91) FVC (%Pred) 91.1(14.2)	FEV_1 & HGS β = 0.11; p = 0.24 FVC & HGS β = 0.04; p = 0.70

Authors	Statistical test for relationship	Handgrip strength Mean (SD)	Lung function assessed Mean (SD)	Results for test of relationship
Guler et al. (2019)	Pearson correlation	DHGS (kg) Male Female 40.2(9.6) 25.6(5.7) NDHGS (kg) Male Female 37.5(9.3) 24.2(6.4)	FVC (%Pred) Male Female 77(17) 72(22)	FVC(%Pred) & HGS r = 0.17; p = 0.16 (Male) r = -0.13; p = 0.41 (Female)
Barry and Gallagher (2003)	Pearson correlation	HGS (%Pred) 67.9(12.2)	FEV_1 (%Predicted) 48.7(24)	HGS(%Pred) & FEV_1(%Pred) r = 0.23; p>0.01
Lopes, Justo, Ferreira, and Guimaraes (2017)	Spearman correlation	HGS (kg) Median 19 (13-22)	Median FEV_1 (%Pred) 73 (62-86.4) Median FVC (%Pred) 75 (66.3-87)	FEV_1 (%Pred) & HGS r = 0.33; p = 0.10 FVC (%Pred) & HGS r = 0.22; p = 0.27
Cichosz, Vestergaard, and Hejlesen (2018)	Pearson correlation	HGS (kg) Males Females 80.7(17.3) 55.1(10.3)	FEV_1(L) Males Females 3.0(0.7) 2.1(0.4) FVC (L) Males Females 3.9(0.9) 2.6(0.5)	FVC & HGS; r = 0.70; p<0.001
Ma, Liu, Wu, and Li (2019)	Pearson correlation	Not reported	Not reported	PEFR & HGS; r = 0.49; p<0.0001
Kim, (2018)	Pearson correlation	HGS (kg) 22.3(8.5)	FEV_1 (L) 1.57(0.48) FVC (L) 1.96(0.49) PEFR (L/s) 2.87(1.40)	FEV_1 & HGS; r = 0.61; p<0.01 FVC & HGS; r = 0.69; p<0.01 PEFR & HGS; r = 0.49; p<0.01

Authors	Statistical test for relationship	Handgrip strength Mean (SD)	Lung function assessed Mean (SD)	Results for test of relationship
Nascimento et al. (2004)	Spearman correlation	HGS (%Pred) Males Females 71(22) 81(32); $p = 0.09$	FEV_1 (%Pred) Males Females 75(19) 78(28); $p = 0.58$ FVC (%Pred) Males Females 76(18) 80(26); $p = 0.55$ PEFR (%Pred) Males Females 67(24) 63(30); $p = 0.26$	FEV_1 & HGS; $r = 0.49$;$p<0.05$ FVC & HGS; $r = 0.50$; $p<0.05$

Footnotes: L – Liters; L/s – Liters per second; L/min – Litres per minute; N – Newtons; %Pred – percentage of predicted; HGS – handgrip strength; NDHGS – Non-dominant handgrip strength; DHGS – Dominant handgrip strength; FFMI – Fat free mass index; Kg – Kilogram; p – significance level; r – correlation coefficient; β – regression coefficient; FEV_1 – Forced expiratory volume in 1 second; FVC – Forced vital capacity; PEFR – Peak expiratory flow rate; BMI – Body mass index; SBP – Systolic blood pressure; DBP – Diastolic blood pressure; Δ – change; 95% CI – 95% confidence intervals.

Martinez et al., 2017; Nascimento et al., 2004; Shah, Nahar, Vaidya and Salvi, 2013; Sirguroh et al., 2012; Strandkvist et al., 2016; Turan et al., 2019), mean of two or three trials (29%) (Cortopassi, Divo, Pinto-Plata and Celli, 2011; Hallin et al., 2011; Jeong and et al., 2017; Kim, 2018; Ma, Liu, Wu and Li, 2017) to non-reporting the number of trials conducted (6%) (Barry and Gallagher, 2003). Hydraulic dynamometers (Jamar and Saehan) were cited in seven studies (41%) and the most commonly used type (Cortopassi, Divo, Pinto-Plata and Celli, 2011; Guler et al., 2019; Kaymaz et al., 2018; Kim, 2018; Lopes, Justo, Ferreira and Guimaraes, 2017; Martinez et al., 2017, Sirguroh et al., 2012). Electronic and mechanical dynamometers were used in four (24%) (Barry and Gallagher, 2003; Hallin et al., 2011; Jeong et al., 2017; Kohlbrenner et al., 2020) and two studies (11%) (Nascimento et al., 2004; Turan et al., 2019), respectively, while four studies (24%) did not report the type of dynamometer used (Cichosz, Vestergaard and Hejlesen, 2018; Ma, Liu, Wu and Li, 2017; Shah, Nahar, Vaidya and Salvi, 2013; Strandkvist et al., 2016) (Table 3). Reporting HGS in kilograms was the most common method for 13 studies (76%), bars was reported in one study (6%) (Turan et al., 2019), while Newtons and %Pred values were reported in one (6%) (Hallin et al., 2011) and two (12%) studies (Barry and Gallagher, 2003; Nascimento et al., 2004), respectively (Table 4).

Lung function assessment

Healthy population

Type of spirometer used and the position adopted during assessment varied among studies. No two studies reported the use of the same type or model of spirometer. Assessment in the sitting position was the most adopted protocol and reported in four studies (50%) (Burchfiel et al., 1997; Holmes, Allen and Roberts, 2017; Rozek-Piechura et al., 2014; Sillanpää et al., 2014). One study (12%) reported assessment during standing (Schweitzer et al., 2017) and lying positions (30^{o} recumbent) (Hornby et al., 2005) respectively, while positioning was not stated in two studies (25%) (Deary, Whalley, Batty and Starr, 2006; Zhu et al., 2020). Reporting the highest value of three trials, in accordance with the American Thoracic Society (ATS) and/or European Respiratory Society (ERS) guidelines, was cited in two studies (25%) (Burchfiel et al., 1997; Sillanpää et al., 2014) while the number of trials was unreported in three studies (38%) (Rozek-Piechura et al., 2014; Schweitzer et al., 2017, Zhu et al., 2020). Other studies reported using the highest of five trials (12%) (Holmes, Allen and Roberts, 2017), three trials (12%) (Deary, Whalley, Batty and Starr, 2006) and an average of three trials (12%) (Hornby et al., 2005). Only two studies (25%) reported to have conducted routine calibration of the spirometer prior to assessment (Holmes, Allen and Roberts, 2017; Sillanpää et al., 2014) (Table 3). Further, 88% of studies reported lung function indices (FEV_1, FVC & PEFR) according to sex with males exhibiting greater lung function than females. All studies reported lung function measures in Liters (FVC, FEV_1), and Liters/second or Liters/minute ((PEFR) with three studies (Rozek-Piechura et al., 2014; Schweitzer et al., 2017; Sillanpää et al., 2014) also reporting their %Pred values (Table 4).

Unhealthy population

Apart from two studies, which used the Vmax Sensormedics spirometer (Kaymaz et al., 2018; Turan et al., 2019), others used different types of spirometer while the assessment positions adopted were inconsistent. Ten studies (59%) adopted a sitting position during assessment (Barry and Gallagher, 2003; Cortopassi, Divo, Pinto-Plata and Celli, 2011; Guler et al., 2019; Hallin et al., 2011; Jeong, Kang, Song and et al, 2017; Kaymaz et al., 2018; Kim, 2018; Lopes, Justo, Ferreira and Guimaraes, 2017; Shah, Nahar, Vaidya and Salvi, 2013; Strandkvist et al., 2016), two studies (12%) assessed lung function during standing (Cichosz, Vestergaard and Hejlesen, 2018; Ma, Liu, Wu and Li, 2017) while the remaining five (29%)

did not report the position adopted during assessment (Kohlbrenner et al., 2020; Martinez et al., 2017; Nascimento et al., 2004; Sirguroh et al., 2012; Turan et al., 2019). Reporting of lung function was stated as the highest of three trials according to ATS/ERS criteria in 14 studies (82%), while the remaining studies utilized either the highest of three trials (6%) (Nascimento et al., 2004), or unstated number of trials (12%) (Cichosz, Vestergaard and Hejlesen, 2018; Martinez et al., 2017). None of the included studies reported routine calibration of the spirometer before assessment (Table 3). Six studies (35%) presented FVC and FEV_1 in Liters and PEFR in Liters/seconds or Liters/minutes, ten studies (59%) presented these variables as %Pred values while one study (6%) did not report lung function values of their participants (Sirguroh and Ahmed, 2012) (Table 4).

<u>Relationship between handgrip strength and lung function</u>

Healthy population

Total sample size reported for this population was 4 390 with study sample sizes ranging from 40 to 3 111 (Table 3). Six studies (75%) (Holmes, Allen and Roberts, 2017; Hornby et al., 2005; Rozek-Piechura et al., 2014; Schweitzer et al., 2017; Sillanpää et al., 2014; Zhu et al., 2020) reported a fixed aim of examining the relationship between lung function and HGS (usually as an indirect measure of muscle mass) with clearly reported results, while the remaining studies (Burchfiel et al., 1997; Deary, Whalley, Batty and Starr, 2006) reported this relationship as additional information in their results. Correlation and regression coefficients, levels of significance and 95% confidence interval (if available) were reported for this population (Table 4). Analysis of the association between HGS and lung function was reported using Pearson product-moment correlation coefficients in five studies (63%) (Burchfiel et al., 1997; Deary, Whalley, Batty and Starr, 2006; Hornby et al., 2005; Rozek-Piechura et al., 2014; Schweitzer et al., 2017) while regression analysis was conducted in three studies (37%) (Holmes, Allen and Roberts, 2017; Sillanpää et al., 2014; Zhu et al., 2020). All reported Pearson correlation coefficients (r) were statistically significant, with one study (13%) reporting a weak correlation (r = 0.26) (Deary, Whalley, Batty and Starr, 2006) while three studies (38%) reported moderate correlations between HGS and FEV_1 (r = 0.31, r = 0.62, r = 0.61), and HGS and FVC (r = 0.35, r = 0.61, r = 0.60) (Burchfiel et al., 1997; Rozeck-Piechura et al., 2014; Schweitzer et al., 2017). Similarly, two studies (25%) reported moderate correlations (r = 0.33, r = 0.51) between HGS and PEFR (Hornby et al., 2005; Rozeck-Piechura et al., 2014) (Table 4). Through regression analysis, HGS was reported as a significant predictor of FEV_1 for 908 middle-aged (~42 years) (Zhu et al., 2020) and 135 elderly (~75 years) (Sillanpaa et al., 2014) healthy males and females. Likewise, HGS was reported as a significant predictor of FVC for elderly (~75 years) males and females (Sillanpaa et al., 2014). In contrast, HGS was not a significant predictor of any lung function variable in 50 elderly (~87 years) males and females (Holmes, Allen and Roberts, 2017). When considering confounders within analyses, only six studies (75%) adjusted for confounders with three utilizing Pearson correlations (Burchfiel et al., 1997; Deary, Whalley, Batty and Starr, 2006; Schweitzer et al., 2017) while three utilized linear regression analyses (Holmes, Allen and Roberts, 2017; Sillanpaa et al., 2014; Zhu et al., 2020). Participants' age, height and sex were reported as the most common confounders applied to the analyses (Table 4).

Unhealthy population

Total sample size reported from the included studies for this population was 4 510 with study sample sizes ranging from 23 to 1 636 (Table 3). Twelve studies (70%) reported a fixed aim of evaluating the relationship between lung function and HGS in a chronic disease condition while the other five studies reported this relationship as additional information (i.e. no direct aim to examine relationships between HGS and lung function). Likewise, variable correlation and/or regression coefficients, levels of significance and 95% confidence intervals (if available) were reported for unhealthy populations (Table 4). Thirteen studies (76%) analyzed the association between HGS and one/two lung function measures using Pearson product-moment correlation coefficients while four studies (24%) analyzed this relationship using linear regression. Two studies that involved patients with diabetes reported significant moderate correlations between HGS and FVC ($r = 0.70$) (Cichosz, Vestergaard and Hejlesen, 2018), and PEFR ($r = 0.49$) (Ma, Liu, Wu and Li, 2017). Out of six studies that involved patients with COPD, two reported significant weak ($r = 0.20$) to moderate correlations ($r = 0.47$) between HGS and FEV_1 (Martinez et al., 2017; Shah, Nahar, Vaidya and Salvi, 2013). Of the four studies that involved patients with COPD and regression analysis, two reported insignificant but positive relationships between FEV_1 and HGS (Hallin et al., 2011; Jeong et al., 2017). Correlation or regression analyses in the remaining six studies indicated varied strengths of association between HGS and lung function for patients with other disease conditions (Table 4). Studies that involved patients with stroke (Kim, 2018) and CKD (Nascimento et al., 2004) reported significant moderate associations ($r = 0.49 – 0.69$) while those examining adults with SSc (Lopes, Justo, Ferreira and Guimaraes, 2017), ILD (Guler et al., 2019) and CF (Barry and Gallagher, 2003) identified positive but insignificant relationships. Only four studies (24%), which involved COPD patients, adjusted analyses for confounders. Three studies used linear regression analysis (Hallin et al., 2011; Jeong et al., 2017; Strandkvist et al., 2016) while one utilized multivariate mixed modelling (Kohlbrenner et al., 2020) with participants' age and sex reported as the common confounders (Table 4).

Discussion

This review examined the relationship between HGS and lung function in healthy and unhealthy adults across 25 screened studies. Sex of the participant was a substantial determinant of HGS and lung function with males exhibiting greater values than females in healthy and unhealthy populations. Significant heterogeneity in the equipment and protocols utilized during HGS and lung function assessments was observed in both populations with average quality of included studies being good. Despite this assessment heterogeneity, significant and consistent weak-moderate associations between HGS and lung function indices (FEV_1, FVC & PEFR) were identified in healthy adults for the majority (87%) of studies. In contrast, the relationship between HGS and lung function was more variable for unhealthy adults with weak-moderate associations reported for some (52%), but not all populations.

Relationship between handgrip strength and lung function

Healthy population

Significant positive and moderate relationships between HGS and lung function (FEV_1, FVC & PEFR) were predominantly reported for healthy populations despite adoption of different assessment protocols and equipment. Previously, a positive association between HGS and respiratory muscle strength, which are both reliant upon skeletal muscle tissue, was reported in healthy older individuals (Shin et al., 2017). Respiratory muscle strength was reported as a partial determinant of lung function with the activation of skeletal muscle during respiration leading to contraction of respiratory muscles (e.g. diaphragm, external intercostals), increased intrathoracic expansion and greater lung volume (Park et al., 2018). Consequently, HGS may indirectly represent overall skeletal muscle strength that contributes to lung function (Bohannon, 2015; Wind, Takken, Helders, & Engelbert, 2010). In this review, moderate correlations were reported by most studies that had a dominance of Caucasian adults, which may bias the results and limited the applicability of these relationships (Woo et al., 2014). To the best of our knowledge, no study has looked at a specific ethnic comparison for HGS and lung function relationships with future work needed to elaborate upon the current results. An additional factor that may influence this relationship could be an individual's physical activity level, which was reported to affect lung function (Roman, Rossiter and Casaburi, 2016). Holmes and colleagues, (2017) reported an insignificant relationship between HGS and lung function in elderly males living in a nursing home and likely to experience substantially low physical activity levels (Parry, Chow, Batchelor and Fary, 2019). Many included studies (75%) adjusted their analyses for common confounders (e.g. age, sex, height) and reported similar associations between HGS and lung function, despite involving large sample sizes. Therefore, common confounders such as age, sex and height may have minimal effect on the relationship between HGS and lung function in healthy adults. Further, the average CCAT score for studies that specifically examined the relationship between HGS and lung function (67%) was similar to those studies that incidentally reported these relationships (65%). This finding suggests that the aim of these studies did not affect the quality of studies or the strength of the identified relationships with both sub-groups reporting weak to moderate relationships. Given the diversity in reported relationships between HGS and lung function, further studies are needed to confirm HGS as an indirect indicator of lung function in healthy adults.

Unhealthy population

A major finding in the unhealthy population was the varied level of relationship reported between HGS and lung function. This heterogeneity could be explained by factors such as: the underlying disease and its severity, and effects of inflammation on muscle and lung tissues (Byun et al., 2017; Lima et al., 2018). Since more than half (53%) of the included studies had a mean age of ≥65 years, age-related muscle weakness (Sarcopenia) may have also been a likely contributing factor (Cruz-Jentoft et al., 2018; Kaymaz et al., 2018). Weak respiratory muscles during aging reduces the ability of the lungs to inflate and deflate maximally and is also a risk factor for notable respiratory-related diseases like COPD, pulmonary fibrosis and lung cancer (Meiners, Eickelberg and Königshoff, 2015).

Chronic obstructive pulmonary disease was the most cited condition in the current review, possibly due to COPD being one of the global leading causes of morbidity and mortality (World Health Organization, 2016) and/or the frequent lung function assessments of these patients. Significant weak to moderate associations (r = 0.20-0.47) were identified between HGS and lung function in three COPD studies (Martinez et al., 2017; Shah et al., 2013; Strandkvist et al., 2016) that could reflect the interplay of aging and systemic inflammation, which concurrently affect muscle and lung tissues (Lima et al., 2018). Greater presence of inflammatory biomarkers (e.g. interleukin-6) has been associated with increased muscular dysfunction (Byun et al., 2017). However, these effects are not restricted to limb muscles only and can affect respiratory muscle tissue as well, leading to reduced lung function (Byun et al., 2017). Similarly, distortion of chest wall configuration, reduction in elastic tissues of the lungs, number of alveoli and blood capillaries during aging, result in carbon dioxide retention, reduced blood oxygenation and weaker skeletal muscles (Ito and Mercado, 2014). Further, the reported increase in sympathetic neural activity for COPD could cause vasoconstriction of blood vessels to the peripheral muscle tissues, which leads to decreased muscle strength and subsequently, reduced lung function when respiratory muscles are affected (Andreas et al., 2014). These interlinked mechanisms, acting either independently or combined, could ultimately lead to decreased lung function, weaker limb muscles and HGS in COPD patients. Despite reported significant associations between HGS and lung function in three COPD studies, non-significant associations were reported in seven studies of COPD patients including three that adjusted analyses for confounders (age, sex, height, HGS, FEV_1). These results highlight the inconsistent relationship between HGS and lung function in COPD with future studies encouraged to consider factors such as inflammation, COPD severity and presence of other comorbidities (Raherison et al., 2018).

Significant moderate associations (r = 0.49-0.70) between HGS and lung function were also identified for diabetic patients with inflammation, insulin resistance, collagen glycosylation of lung parenchyma and neuropathy of peripheral and respiratory muscles (Kinney et al., 2014, Lee et al., 2018) as potential mechansims for the relationship. Recently, Lee et al, (2018) reported that HGS was associated with the risk of Type 2 diabetes with an inflammatory biomarker, high sensitive-C-reactive protein, mediating this association. Inflammation was also suggested to contribute to the reported significant association between HGS and lung function for patients with CKD and stroke (Kim, 2018; Nascimento et al., 2004). In contrast, no relationship was reported in patients with CF, ILD and SSc, despite previous reports of distinct and persistent inflammatory processes in these conditions (Furue et al., 2017; King et al., 2014; Rahman et al., 1999). Therefore, the degree of inflammation, which has been positively associated with disease severity and reduced lung function, may be an important factor when considering the relationship between HGS and lung function in unhealthy adults (Baines et al., 2015; Moldoveanu et al., 2009). Further, the inconsitent relationships for CF, ILD and SSc patients may be a resultant of underpowered studies with larger studies needed to confirm these results.

The current review included studies across a range of disease conditons comprising respiratory based and/or those with marked neurological or endocrinological factors (e.g. diabetes, stroke and CKD). Subsequently, the current review also undertook an impromptu sub-analysis of the relationship between HGS and lung function in a subgroup of 13 studies involving lung-related disease conditions (COPD, ILD, CF and SSc). This sub analysis indicated weaker relationships in lung-related than in non-lung related conditions (r = 0.20-0.47 vs. r = 0.49-0.70) with similar quality of studies (67% vs. 69% average CCAT score) observed in both conditions. In addition, the methodological design (i.e. focused aim to examine HGS and lung function relationship; utilization of the ATS/ERS protocol for lung function assessment) was similar for studies involving lung-related or non-lung related conditions. Therefore, the variable relationship between HGS and lung function in unhealthy populations may be due to the degree of inflammation, as well as the type (lung-related or not) and severity of disease condition.

This review has demonstrated variable relationships between HGS and lung function in unhealthy populations. Further studies are required to clarify the relationship between HGS and lung function for a range of chronic conditions with consideration of inflammation, disease type and severity, aging or larger sample sizes desirable. The use of HGS may be a simple and valid indicator of lung function in *some* chronic conditions and not in others with more research needed.

Methodological quality

Using the CCAT, the average methodological quality of all included studies was Good (67%). Despite this rating, several studies scored poorly for some category items with results to be considered with a degree of caution. For example, none of the studies reported sample size calculations nor the rationale for the sample size. Further, there was heterogeneity in the equipment utilized during assessments of HGS and lung function. However, the majority (84%) of the studies followed a well described protocol that would enable replication. Researchers are encouraged to consider involving and reporting suitable study designs, sample sizes, sampling methods and ethical matters in their studies. Consideration of a tool like the CCAT during study development would ensure the robustness of the study and its results.

Study limitations and strengths

To our knowledge, this review has produced the most thorough analysis of HGS and lung function using six large databases with a comprehensive selection of search terms across a range of populations. The limitless year of publication during the search enabled the accessibility of available data, which increased the robustness of the search strategy. Further, the use of two independent authors during data extraction and critical appraisal of included studies helped in reducing bias to a minimum level. While an extensive review was undertaken, the selection criteria were pre-defined and limited the inclusion of some studies for this review. Studies conducted in patients with CF, ILD and SSc were weakly powered due to small sample sizes that may have resulted in insignificant associations between HGS and lung function that require further follow-up.

Clinical implications

An easy-to-use and inexpensive tool like HGS could be a timely indicator of lung function in healthy adults, but its use for unhealthy populations requires further investigation. Physiotherapists and other allied health practitioners are encouraged to use calibrated/standard equipment and follow well-reported protocols during HGS and lung function assessments to enable valid comparison with other datasets, avoid misdiagnosis and poor monitoring of health and disease conditions.

Conclusion

Handgrip strength was positively and moderately associated with lung function in most healthy adults while similar relationships were variable for unhealthy adults, especially COPD patients. The assessment of HGS may provide a potentially simpler and indirect marker of lung function when assessing and monitoring healthy adults. Future longitudinal studies using valid, reliable equipment with well-defined assessment protocols, will confirm the relationship between HGS and lung function in healthy and unhealthy states and its potential to monitor disease progression.

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