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Meta-analyses

Handgrip strength measurement protocols for all-cause and cause-specific mortality outcomes in more than 3 million participants: A systematic review and meta-regression analysis

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SUMMARY

Background & aims: Handgrip strength is a strong predictor of the risk of mortality. The objective of this systematic review was to analyse handgrip strength measurement protocols used in all-cause and cause-specific mortality studies.
Method: A systematic search of PubMed/MEDLINE, Web of Science and Scopus was conducted from inception to February 2022. Prospective cohort studies with objective measures of handgrip strength were included. Studies had to report at least one all-cause, cancer, or cardiovascular mortality outcome. The quality of the included studies was assessed using the Newcastle Ottawa Scale. Meta-regression was used to quantify the bias associated with handgrip strength values in relation to the use of different measurement protocols.
Results: Forty-eight studies with a total of 3,135,473 participants (49.6% women) were included. Half of the studies controlled body position, 39.6% arm position, 33.3% elbow position, 12.5% wrist position, 13% handgrip duration, 23% hand-adjustment to dynamometer and 12.5% verbal encouragement. The number of measurements, the laterality of the hand tested, and the estimation method of the handgrip strength value varied considerably between the study protocols. The spline regression model showed a non-linear inverse association between the values of handgrip strength and the number of protocol items controlled. Handgrip strength was higher when the number of measurements per hand or arm position was not controlled. Conversely, handgrip strength was lower when elbow position was not controlled or verbal encouragement were not provided.
Conclusion: In general, the protocols used to assess handgrip strength in mortality studies are incomplete and highly heterogeneous. Handgrip strength values were higher when studies controlled fewer handgrip strength measurement protocol variables. There is a need to improve the controlling of handgrip strength measurement protocols and to standardise the method to enhance the accuracy of mortality risk estimates associated with handgrip strength.
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1. Introduction

Handgrip strength is one of the most used proxies for assessing overall muscle strength. It is simple, inexpensive, and quick which makes it ideal to be applied in clinical and large-scale research settings [1–4]. Handgrip strength is considered an indicator of different health outcomes, such as disability [3,5], sarcopenia [4,6], morbidity [7–9], and mortality [10–15].

Handgrip strength has shown high levels of validity and reliability using different devices [16–19]. However, in research settings, the measurement protocol for characterising handgrip strength may vary considerably, making comparisons among studies difficult [20]. This may also result in different sizes of handgrip estimates. For example, the handgrip strength of the hand may vary according to different elbow positions [21,22].

As recommended elsewhere [20,23], critical methodological considerations when reporting handgrip strength in research studies include the position of the arm, wrist and lower extremity; the number of tests performed; the stimulus during the evaluation; and the score (relative or absolute) to be used as the outcome. However, studies often do not provide sufficient information on the protocol followed [20]. A recent scoping review focused on older adults concluded that the methodology used to measure handgrip strength varied considerably among the included studies, which could lead to different results [24]. Considering that all-cause and cause-specific mortality is a crucial public health outcome, heterogeneity of measurement may affect estimates in studies examining the associations between handgrip strength and mortality outcomes. Thus, it is necessary to analyse the available evidence to identify the heterogeneity in the protocols used in such studies. The objective of this systematic review was to analyse handgrip strength measurement protocols used in all-cause and cause-specific mortality studies. We also aimed to estimate the bias associated with handgrip strength values in relation to the use of different measurement protocols.

2. Methods

This systematic review was pre-registered in the PROSPERO International Prospective Register of Systematic Reviews (reference number CRD42022334929) and was conducted following the PRISMA 2020 guidelines [25].

2.1. Search strategy

A systematic search of PubMed/MEDLINE, Web of Science (WOS) and Scopus was conducted from inception to February 2022. The specific search strategies are shown in the Supplement (Table S1). Title/abstract and full-text screening were conducted independently by RLB and RNC, with disagreements resolved by adjudication by a third author (BdPC). The reference lists of eligible articles and topic-related reviews were also screened for additional studies. All records were analysed in Endnote X7 software (Clarivate Analytics, New York, USA).

2.2. Selection criteria

We included (1) prospective cohort studies (2) with either a single or repetitive measures of handgrip strength that (3) were written in English, and (4) used any type of objectively measurement of handgrip strength. To be included, (5) studies had to report on at least one all-cause, cancer or cardiovascular mortality outcome; and (6) had to include participants aged 18 years or over. We excluded studies for which the effect of handgrip strength could not be isolated. We also excluded studies with either hospitalised or institutionalised participants, as well as studies focusing specifically on clinical populations or health conditions. All editorials, letters, reviews, in vivo and in vitro studies were excluded.

2.3. Data extraction

Data from studies that met the inclusion criteria were independently retrieved by RLB and RNC and disagreements were resolved by consensus between all authors. From each included study, we extracted the number of participants, age, sex, follow-up time, type of dynamometer, protocol for handgrip strength, and main results of the study. Information on either handgrip dynamometer tool or measurement protocol could not be retrieved from the following published reports: Fujita et al. [13]; Kim et al. [26]; Laukkanen et al. [27]; McLean et al. [28]; Soares et al. [29]; Peterman-Rocha et al. [30]; Sasaki et al. [11]; Taniguchi et al. [31]. Thus, we contacted the corresponding authors from such publications by e-mail and invited them to provide additional data on the handgrip measurement protocol. Of such studies, only one author provided the requested information [29].

2.4. Data synthesis

Following the indications of previous protocols such as the Southampton protocol [20], and the American Society of Hand Therapists (ASHT) protocol [32], we clustered studies in relation to different measuring protocol variables including type of handgrip dynamometer, laterality of the hand tested, body position, arm position, elbow position, wrist position, hand-adjustment to dynamometer, number of repetitions per arm, maximum handgrip strength estimation, handgrip strength test duration, recovery time, and any other additional measures that could characterised the protocol used.

2.5. Risk of bias and quality of evidence

The risk of bias and quality of included studies was assessed individually by three reviewers (RLB, BdPC, and RNC) using the Newcastle Ottawa Scale [33]. Each included study was judged using a rating system in three domains of bias: selection (four points); comparability (two points); and exposure/outcome (three points). The sum of points indicates the methodological quality of each study. Thus, the score ranges from 0 to 9 points.

2.6. Statistical analyses

We conducted all the analyses using R software (version 3.5.1) [34]. To assess the association between handgrip strength values and number of controlled variables concerning handgrip strength measurement protocols, a spline regression model allowing for heterogeneity among studies as well as accounting for cohort sizes was conducted. Either mean or median handgrip strength values were considered for each individual study in relation to the number of protocol measurement variables reported. We assessed the potential nonlinear association for all the protocol measurement variables using a restricted cubic spline model with three knots at the 10th, 50th and 90th percentile of pooled handgrip strength [35]. Departure from linearity was assessed using a Wald test. We also tested additional linear and quadratic regressions observing no better fitting of the model. A subgroup analysis was performed taking into account the following categories I) Sex (male or female); II) Population (mean (SD) age $\geq$65 years or <65 years); III) Race (Asian, Caucasian or Hispanic/Latino); IV) Reported handgrip strength value (maximum value or mean value). Studies that did not detail this information were not considered for subgroup

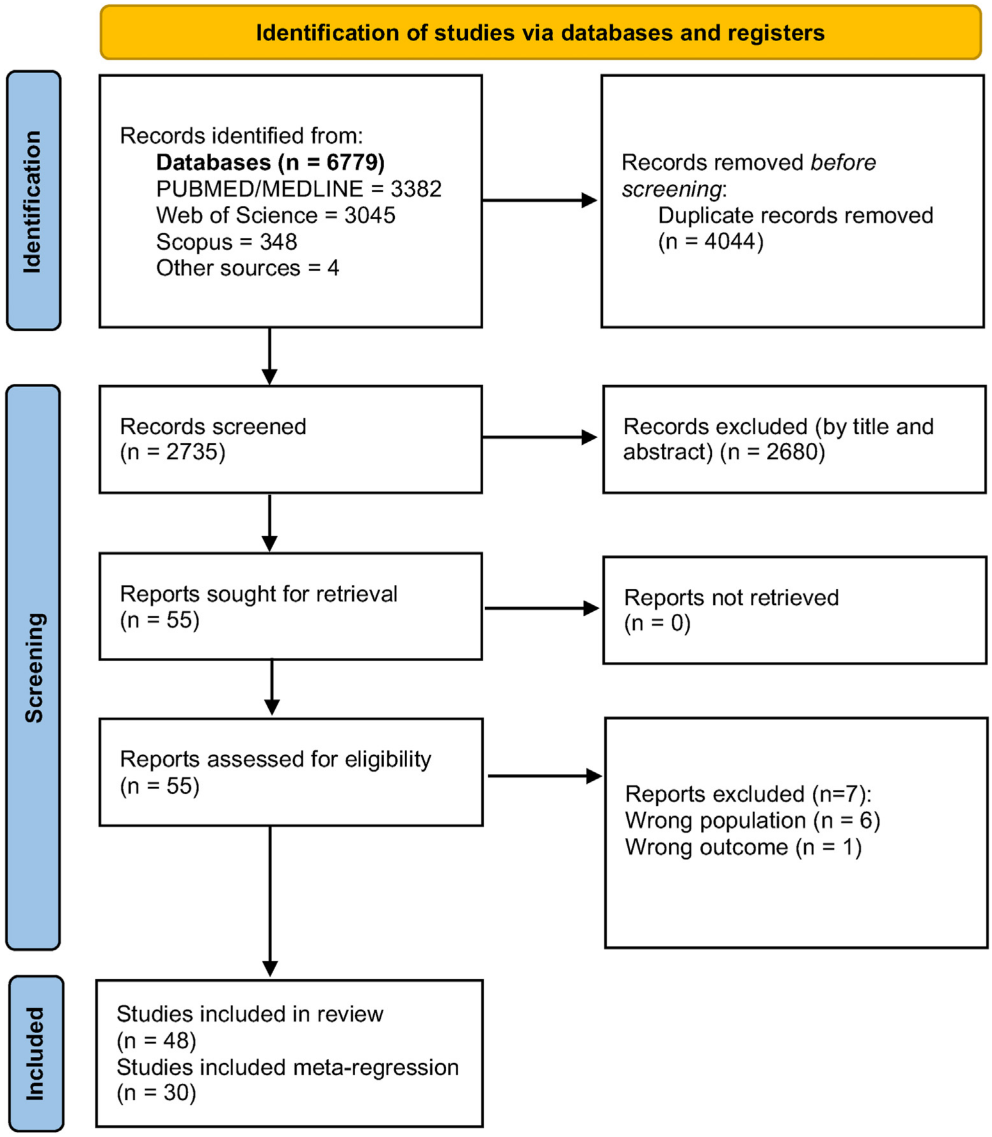

Fig. 1. Study selection process.

analysis. In a secondary analysis, for the individual protocol measurement variables, a Bayesian multilevel regression was used, where all individual variables were entered into the model. Conditional effects were the handgrip strength values according to the subgroup within a variable (i.e., 0 or 1, variable not reported or reported respectively) [36]. Estimations are reported with 95% confidence intervals.

3. Results

3.1. Study selection

A total of 2735 potential eligible studies were identified through initial electronic searches and removal of duplicates. After screening publications by title and abstract we obtained 55 potentially eligible studies for inclusion and retrieved full-text articles. Finally, full-text articles were retrieved and, after applying the inclusion criteria, 48 studies remained in the final selection for the systematic review [11,13–15,26–31,37–74]. The flowchart of the study selection process is shown in Fig. 1.

3.2. Study characteristics

The characteristics of included studies are displayed in Table 1. Studies were conducted in the United Kingdom (10 studies), the United States (7), multi-country (7), Japan (5), South Korea (4), the Netherlands (2), Norway (2), Finland (2), Germany (1), Singapore (1), Taiwan (1), China (1), Brazil (1), France (1), Israel (1), Russia (1), Italy (1). The year of publication ranged from 1995 [13,27] and 2022 [52,60]. A total of 3,135,473 participants (49.6% female) were enrolled in the included studies, and the age of participants ranged from 35 [11] to ≥85 years [46]. The sample size ranged from 436 [71] to 502,293 participants [41]. The duration of follow-up ranged from 2.3 [42] to 44 years [64].

3.3. Characteristics of the protocols

Eighty-five percent of the included studies controlled the type of dynamometer used. Twenty-eight studies measured handgrip strength in both hands (58%), 12 in the dominant hand (25%), one in the nondominant hand (2%), and seven did not control which hand

Table 1
Description of included articles.

Study, year	Country	Participants (N)	Age (years)	Covariates	Follow-up duration	Handheld dynamometer	Protocol	Main results	Newcastle–Ottawa Scale
Arvandi, 2016	Germany	1066	Mean (SD) 76 (11)	Women: 536 BMI: Yes Physical activity: Yes Chronic condition: Yes	3.0 years.	Jamar.	Dominant hand. Three trials. Maximum value. Sex-specific tertiles. ±1 kg.	Grip strength is inversely associated with mortality risk in older adults.	8/9
Andrasfay, 2020	Taiwan	887	Mean (SD) 70.1 (8.7)	Women:430 BMI: No Physical activity: No Chronic condition: No	4.0 years.	North Coast.	Both hands. Three trials. Maximum value. ±1 kg.	Conditional on the baseline measurement, a one standard deviation (SD) decline in grip strength is associated with a 61% increased risk of mortality.	6/9
Bae, 2019	South Korea	9393	Mean (SD) 61 (10.7)	Women:5235 BMI: Yes Physical activity: Yes Chronic condition: Yes	8.0 years.	Tanita, 6103.	Sit or stand-up. Arms one side of the trunk. Elbows 90° degrees. 5 s. Average maximum value of both hands. Sex specific quartiles. ±1 kg.	Robust independent relationships between weaker handgrip strength and higher all-cause mortality	9/9
Cai, 2021	Multi-country	13,231	65 and over	Women:7073 BMI: Yes Physical activity: Yes Chronic condition: Yes	4.0 years.	Smedley.	Stand or sit. Upper arms tight against the trunk. Elbows 90° degrees. 5 s squeezing. ±1 kg.	Inverse linear association of handgrip with all-cause mortality.	6/9
Celis-Morales, 2018	UK	502,293	Mean (SD) 56.5 (8.1)	Women: 260,063 BMI: Yes Physical activity: Yes Chronic condition: Yes	7.1 years.	Jamar, J00105.	Single 3-s maximal grip effort. Both arms. Seated upright. Elbow flexed at 90°. Forearm facing forward and resting on an armrest. Mean maximum strength of both hands. ±1 kg	Lower grip strength was associated with higher cardiovascular, cancer and all-cause mortality risk.	9/9
Chua, 2020	Singapur	13,789	Mean (SD) 74 (6.0)	Women: 8133 BMI: Yes Physical activity: No Chronic condition: Yes	2.3 years.	Takei, TKK5401 Grip D.	Upright. Arms let down naturally. ±0.1 kg (accuracy) Two trials for each hand. Highest value obtained from each hand. Mean of both hands.	Handgrip strength was inversely associated with risk of mortality in a dose-dependent manner.	7/9
Eekhoff, 2019	Netherlands	1505	Mean (SD) 76.0 (6.6)	Women: 778 BMI: Yes Physical activity: No Chronic condition: Yes	15.4 years.	Takei, TKK 5001.	Average grip strength of maximum handgrip of both hands. ±1 kg. Hand-size adjusted.	Handgrip strength predicted all-cause mortality.	8/9
Farmer, 2019	UK	452,931	Mean (SD) 55.9 (8.9)	Women: 247,183 BMI: Yes	6.1 years.	Jamar.		Low handgrip strength was associated with	8/9

				Physical activity: Yes Chronic condition: Yes			Maximum handgrip strength of the dominant hand.	increased risk of all-cause mortality but not cardiovascular mortality.	
Fujita, 1995	Japan	6259	Mean (SD) Men 53.6 (9.0) Women 54.5 (8.5)	Women: 3142 BMI: No Physical activity: No Chronic condition: No	6.1 years.	Unknown.	Average of right and left hands. 1 kg	Risk of death due to all-causes observed for men with lower handgrip values, but not in women.	6/9
Gao, 2021	China	3686	65 and over	Women: 1809 BMI: Yes Physical activity: No Chronic condition: Yes	7.0 years.	Yuejian, TM WL-1000.	Standing position. Elbows at right angles. Two measures in each hand. Average of four measurements.	The decline of handgrip significantly increased all-cause mortality.	8/9
Granic, 2017	UK	845	85 and over	Women:374 BMI: Yes Physical activity: Yes Chronic condition: Yes	9.6 years.	Takei, A5401.	Two measurements for each hand. Mean of the four measurements. Sex-specific quartiles.	Higher baseline grip strength and 5-year increase in GS were protective of mortality.	7/9
Ho, 2019	UK	356,721	Mean (SD) 55.7 (8.1)	Women: 194,540 BMI: Yes Physical activity: No Chronic condition: No	5.0 years.	Jamar, J00105.	Single 3-s maximal grip effort. Both arms. Seated upright. Elbow flexed at 90°. Forearm facing forward and resting on an armrest. Mean maximum strength of both hands. ±1 kg	Higher grip strength was associated with lower risk of all-cause mortality. These associations did not meaningfully differ when grip-strength was expressed in absolute or relative terms.	8/9
Karlsen, 2017	Norway	2529	Mean (SD) 72.6 (4.8)	Women: 2529 2529 BMI: Yes Physical activity: Yes Chronic condition: Yes	15.6 years.	Martin Vigorimeter.	Seated. Hand-adjusted. 3 attempts and 1 min rest between them. Mean of the 2 highest tests.	Handgrip strength is associated with all-cause mortality in elderly women but not with cancer and cardiovascular mortality.	8/9
Kim, 2017	UK	403,199	Range 40–69	Women: 220,193 BMI: Yes Physical activity: No Chronic condition: Yes	7.0 years.	Jamar, J00105.	Once each hand. Participants choose grip position. Hand-adjustable. Seated. 90° angle of their elbow. Squeezing for 3 s.	Lower grip is a predictor of higher all-cause mortality in men and women, as well as a predictor of higher cardiovascular disease in men but not in women.	9/9
Kim, 2018	UK	70,913 (Individuals with cancer, heart attack or stroke were removed)	Mean (SD) 57.2 (8.2)	Women: 37,655 BMI: Yes Physical activity: No Chronic condition: Yes	5.7 years.	Jamar, J00105.	Calibrated each day. Once each hand. Participants choose grip position. Hand-adjustable. Seated. 90° angle of their elbow. Squeezing for 3 s.	Improving both CRF and muscle strength, as opposed to either of the two alone, may be the most effective behavioral strategy to reduce all-cause and cardiovascular mortality risk.	9/9
Kim, 2019	South Korea	5859	Mean (SD) 63.2 (8.8)	Women: 3191 BMI: Yes Physical activity: Yes Chronic condition: Yes	7.9 years.	Tanita, 6103.	Seated. Elbow flexed at 90°. Neutral forearm and wrist.	These results demonstrate that lower handgrip strength is an independent predictor	

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Table 1 (*continued*)

Study, year	Country	Participants (N)	Age (years)	Covariates	Follow-up duration	Handheld dynamometer	Protocol	Main results	Newcastle–Ottawa Scale
							Two trials for each hand. Average of four measures. Accuracy 0.125 kg	of all-cause and cardiovascular mortality.	
Kim, 2020	South Korea	2927	67 and over	Women: 1530 BMI: Yes Physical activity: No Chronic condition: No	10.0 years.	Unknown.	Twice for each hand. Maximum value among the 4 tests.	These findings suggest that handgrip strength has a significant impact on elderly mortality and does so in a negatively gradient manner.	6/9
Kim, 2022	South Korea	9229	Mean (SD) 60.7 (0.1)	Women: 5098 BMI: Yes Physical activity: Yes Chronic condition: Yes	9.4 years.	Tanita, 6103.	Standing posture. Twice for each hand. Elbow at their side and flexed at right angle. Neutral wrist position. Average of both hands' maximum strength. Relative handgrip strength calculated.	Handgrip strength is strongly associated with an increased risk mortality.	9/9
Kishimoto, 2014	Japan	2527	40 and over	Women: 1463 BMI: Yes Physical activity: Yes Chronic condition: Yes	19.0 years.	Smedley.	Two trials for each hand. Maximum value of the four. The width of the handle was adjusted such that the second phalanx was against the inner stirrup.	Higher levels of handgrip strength were significantly associated with decreased risks of all-cause and cardiovascular death but not cancer death.	8/9
Laukkanen, 1995	Finland	463	Range 75–84	Women: Unknown BMI: No Physical activity: No Chronic condition: Yes	4.0–4.8 years.	Unknown.	Dominant hand. Handgrip strength divided by BMI.	Lower handgrip strength significantly associates with all-cause mortality.	4/9
Laukkanen, 2020	Finland	861	Mean (SD) 69.0 (3.0)	Women: 454 BMI: Yes Physical activity: Yes Chronic condition: Yes	12.6–18.4 years.	Martin-Balloon-Vigorimeter.	Upright position. Arms parallel to the body. Two measures of the dominant hand. Average of the two measures. Values of handgrip strength divided by weight.	Relative handgrip strength is inversely associated with all-cause and cardiovascular mortality events.	8/9
Leong, 2015	Multi-country	139,691	Median (IQR) 50 (42–58)	Women: 81,039 BMI: Yes Physical activity: Yes Chronic condition: Yes	4.0 years.	Jamar.	Three measures from the non-dominant hand, and three measures from each hand later. Mean of the maximum value of each hand.	Measurement of grip strength is a simple, inexpensive risk-predictor for all-cause and cardiovascular death but not cancer death.	8/9

Ling, 2010	Netherlands	555	85 and over	Women: 361 BMI: Yes Physical activity: No Chronic condition: Yes	9.5 years.	Jamar.	Upright position. Measurement arm parallel to the body. Width adjustment. Three measures. Highest recorded measure.	Handgrip strength is a predictor of all-cause mortality in the oldest old population.	8/9
López-Bueno A, 2022	Multi-country	121,383	Mean (SD) 63.9 (10.2)	Women: 66,576 BMI: Yes Physical activity: No Chronic condition: No	7.4 years.	Smedley, S Dynamometer, TTM.	Each hand measured twice. Elbow in a 90° angle flexion. Standing or sitting. Neutral wrist position. Upper arm set in a vertical position against the trunk. Maximum value of either hand. Sex-specific tertiles.	Up to a threshold of 42 kg in men and 25 kg in women, increases in handgrip strength reduce the risk of all-cause mortality. Whereas no consistent associations were observed for cancer mortality.	8/9
López-Bueno B, 2022	Multi-country	121,116	Mean (SD) 63.7 (10.0)	Women: 66,576 BMI: Yes Physical activity: Yes Chronic condition: Yes	3.6 years.	Smedley, S Dynamometer, TTM.	Each hand measured twice. Elbow in a 90° angle flexion. Standing or sitting. Neutral wrist position. Upper arm set in a vertical position against the trunk. Maximum value of either hand.	Higher handgrip strength reduces the risk of cardiovascular and all-cause mortality.	
Mc Grath, 2020	USA	19,729	50 and over	Women: Unknown BMI: Yes Physical activity: No Chronic condition: Yes	12.0 years.	Smedley.	Fit to respondent's hand. Arm at their side at a 90° Angle. Two measures in each hand. Attempts alternating hands. Exceptions for the protocol.	A causal association between weakness and mortality may exist.	8/9
Mc Lean, 2014	Multi-country	6280	68.5 and over	Women: 1869 BMI: Yes Physical activity: No Chronic condition: No	10.0 years.	Jamar.	Unknown.	The significant association of lower handgrip strength and all-cause mortality was observed in all the subgroups except from relative to BMI handgrip strength in women.	5/9
Minneci, 2015	Italy	561	Mean (SD) 72.9 (0.3)	Women: 323 BMI: Yes Physical activity: No Chronic condition: Yes	7.0 years.	Jamar.	Dominant hand. Best of three measures. One measure per minute.	Handgrip strength did not predict all-cause mortality.	7/9
Newman, 2006	USA	2292	70 and over	Women: 1168 BMI: Yes	4.9 years.	Jamar.	Assessed in each hand. Participants with hand	Grip strength reduction increases the risk of all-cause mortality.	8/9

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Table 1 (*continued*)

Study, year	Country	Participants (N)	Age (years)	Covariates	Follow-up duration	Handheld dynamometer	Protocol	Main results	Newcastle–Ottawa Scale
				Physical activity: Yes Chronic condition: Yes			pain or recent surgery excluded.		
Nofuji, 2016	Japan	1085	Range 65–89	Women: 625 BMI: Yes Physical activity: Yes Chronic condition: Yes	10.3 years.	Smedley.	Dominant hand. Higher value from two trials. Sex-specific cut-off points.	Weak grip strength predicted all-cause and cardiovascular mortality (T1).	7/9
Oksuzyan, 2017	Multi-country	15,130	Range 55–89	Women: 7942 BMI: Yes Physical activity: No Chronic condition: Yes	6.2–7.5 years.	Smedley.	Upper arm held against the trunk. Elbow in a 90° degree flexion. Three trials for each hand. Exclusion of those with fewer than three attempts or a difference of more than 20 kgs between attempts.	Handgrip strength is a powerful predictor of all-cause mortality across countries.	8/9
Park, 2022	UK	324,486	Range 40–69	Women: 177,130 BMI: Yes Physical activity: Yes Chronic condition: Yes	4.0 years.	Jamar, J00105.	One measurement per hand. Average of the two measures.	The study supports the causal effects of poor handgrip strength on the risks of all-cause, cancer and cardiovascular mortality.	6/9
Peterman-Rocha, 2020	UK	469,830	Range 37–73	Women: 215,655 BMI: Yes Physical activity: Yes Chronic condition: Yes	6.9 years.	Unknown.	Unknown.	Low handgrip strength is associated with higher all-cause, cardiovascular, and respiratory disease.	8/9
Peterson, 2020	USA	3050	65 and over	Women: 1759 BMI: Yes Physical activity: No Chronic condition: Yes	16.0 years.	Jamar, 5030J1.	Hand adjusted. Preliminar trial. Standing position when no limitations. Two attempts. Relative to BMI.	Longitudinal declines in strength are significantly associated with all-cause mortality.	9/9
Prasitsiriphon, 2018	Multi-country	11,037	50 and over	Women: 1759 BMI: Yes Physical activity: No Chronic condition: Yes	3.0 years.	Smedley.	Standing or sitting. Elbow flexed at 90°. Neutral wrist position. 5 s maintenance. Maximum force of both hands. Sex-specific.	Grip strength is a significant indicator of all-cause and cardiovascular mortality.	7/9
Rantanen, 2000	USA	6040	Range 45–68	Women: 0 BMI: Yes Physical activity: No Chronic condition: No	30.0 years.	Smedley.	Handle adjustment up to the second phalanx was against the inner stirrup. Three trials for each hand.	Mid-life grip strength predicts long-term all-cause mortality.	7/9

							Best result was selected.		
Rantanen, 2012	USA	2239	Range 56–68	Women: 0 BMI: Yes Physical activity: Yes Chronic condition: Yes	44.0 years.	Smedley.	Sitting. Arm extended on a table. If necessary, the tester held the dynamometer. Handle adjustment up to the second phalanx was against the inner stirrup. Three trials for each hand. Best result selected.	High midlife grip strength may increase the probability of extreme longevity.	8/9
Rolland, 2006	France	7250	Mean (SD) 80.5 (3.8)	Women: 7250 BMI: Yes Physical activity: Yes Chronic condition: Yes	3.8 years.	Martin Vigorimeter.	Hand-adjusted. Upright. Arm vertical and dynamometer close to the body. Newton/m^2. Maximum of three attempts.	Handgrip strength significantly predicted all-cause mortality.	7/9
Sasaki, 2007	Japan	4912	Range 35–74	Women: 3217 BMI: Yes Physical activity: No Chronic condition: Yes	27.0 years.	Unknown.	Measured two times each hand. Standing position. Thigh level handheld. Calibrated devices. Selection of maximum measurement.	Grip strength is an accurate and consistent predictor of all causes of mortality in middle-aged and elderly persons.	9/9
Smith, 2019	UK	5240	Mean (SD) 65.9 (9.4)	Women: 2818 BMI: Yes Physical activity: No Chronic condition: No	9.7 years.	Smedley.	Dominant hand. Average of three measurements. Right angle to their body when holding the device. Sex-specific tertiles	No association between handgrip strength and mortality when controlled for inflammatory markers.	8/9
Snih, 2002	USA	2488	65 and over	Women: 1433 BMI: Yes Physical activity: No Chronic condition: Yes	5.0 years.	Jamar, 5030J1.	Hand adjustment. Dominant hand. Two attempts. Higher measurement selected.	Handgrip strength was highly predictive of all-cause mortality.	7/9
Soares, 2019	Brazil	900	65 and over	Women: 618 BMI: Yes Physical activity: No Chronic condition: Yes	8.4 years.	Unknown.	Dominant hand. Three attempts. Median cutoff points (weak: $\leq$ 34 kg men, $\leq$ 20.6 kg women).	Lower handgrip strength was associated with higher all-cause mortality risk.	7/9
Stessman, 2017	Israel	2241	70 and over	Women: 1090 BMI: Yes Physical activity: Yes Chronic condition: Yes	25.0 years.	Takei.	Three measurements from the strongest hand. Arm flexed at 90° the elbow while sitting. Highest measurement was used.	A low handgrip strength was associated with significantly higher all-cause mortality.	8/9

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Table 1 (*continued*)

Study, year	Country	Participants (N)	Age (years)	Covariates	Follow-up duration	Handheld dynamometer	Protocol	Main results	Newcastle–Ottawa Scale
Strand, 2016	Norway	6850	Range 50–80	Women: 3992 BMI: Yes Physical activity: Yes Chronic condition: Yes	17.0 years.	Martin vigorimeter (bars)	Two attempts in the no-dominant hand. The highest score was recorded.	Weaker grip strength was associated with increased all-cause mortality rates, with similar effects on deaths due to cardiovascular disease, while a much weaker association was observed for cancer-related deaths.	8/9
Taniguchi, 2016	Japan	1048	Mean (SD) 71.6 (5.4)	Women: 597 BMI: Yes Physical activity: No Chronic condition: Yes	2188 days.	Unknown.	Dominant hand. Measured twice. Best result recorded.	Low handgrip strength was an independent predictor of all-cause mortality.	8/9
Turusheva, 2017	Russia	611	65 and over	Women: 436 BMI: Yes Physical activity: No Chronic condition: Yes	5.0 years.	DK-50.	Groningen Elderly Test protocol. Maximum measurement of three attempts for each hand was recorded. Highest measurement and mean values were used.	The 5th and 10th percentiles of grip strength were associated with a higher risk for 5-year all-cause mortality.	7/9
Xue, 2010	USA	436	Mean (SD) 73.6 (2.8)	Women: 436 BMI: Yes Physical activity: Yes Chronic condition: Yes	10.0 years.	Jamar, PC5030.	Three times for each hand. Sitting position. Arm pressed against the side at a right angle. Maximum measurement in the non- dominant hand.	Faster rates of decline in grip strength, independently predicted mortality after accounting for baseline levels.	7/9
Yates, 2017	UK	420,727	Median (IQR) 56.4 (38.9–73.7)	Women: 230, 670 BMI: Yes Physical activity: Yes Chronic condition: Yes	6.3 years.	Jamar, J00105.	Sitting. The measurement arm was placed against the side of the body. Bent to a 90° angle. Forearm placed on the armrest. 3-s squeezing. Both hands were measured. Mean of the measurements of the two hands.	Specific category of mean with low handgrip strength associated with cardiovascular mortality.	9/9

BMI, body mass index; SD, standard deviation; IQR, inter quartile range.

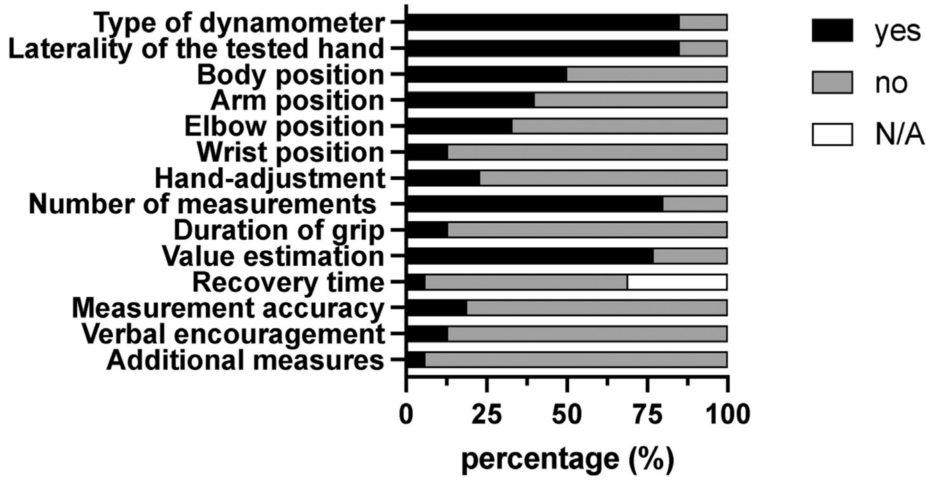

Fig. 2. Protocol information controlled in included studies (n = 48).

Table 2
Summary of the standard measurement protocol for the measurement of handgrip strength.

Protocol items	Characteristics
Type of dynamometer	Jamar dynamometer
Laterality of the tested hand	Both hands
Body position	Seated subject (use the same chair for each measurement)
Arm position	Shoulder in adduction and neutral rotation
Elbow position	Flexion to 90°, forearm in neutral position.
Wrist position	15–30° of extension and 0–15° of ulnar deviation
Hand-adjustment	Second handle position
Number of measurements	Three trials
Duration of grip	At least 3 s
Value estimation	Maximum value
Recovery time	At least 60 s
Measurement accuracy	±1 kg
Verbal encouragement	Yes

To design the summary of the handgrip strength measurement protocol, we considered the most frequent characteristic for each item in the included studies. If a variable was poorly defined in the included studies, the item was described based on previous protocols (i.e. American Society of Hand Therapists protocol or Southampton protocol).

was measured (15%). Twenty-four studies (50%) controlled body position (10 sitting, 9 standing, 5 sitting or standing). Nineteen studies reported arm position (39.6%), 16 reported elbow position (33.3%), and five (12.5%) reported wrist position. Thirty-eight (80%) of the studies controlled the number of repetitions per hand, 15 studies performed three measurements, 18 studies performed two measurements, and five studies performed only one measurement. Considering the protocols that performed more than one measurement, only 6.1% controlled recovery time. Twenty-one studies (43.8%) controlled the highest value, 16 (33.3%) reported a mean value between measurements, while 11 studies (22.9%) did not provide information on the value estimate. Thirteen percent controlled handgrip duration, 18.8% reported the measurement accuracy of the instrument, 12.5% reported whether a verbal encouragement was given during the measurement, and six percent of the included studies took additional measures for older participants or those with limitations. Figure 2 summarises the protocol information for the included studies. Table 2 summarises the standard measurement protocol for measuring handgrip strength based on the most common characteristics reported in the included studies.

3.4. Quantitative analysis

Thirty of the 48 studies were included in the meta-regression analysis, with a total of 1,836,464 participants [11,13,14,28,29,31,37–43,47,50–53,55,57–59,62,63,67,68,71–74]. Eighteen studies that measured handgrip strength in units other than kilograms and where conversion to that unit was not possible were excluded. Studies with not reported handgrip strength values and those without at least one variable related to the handgrip strength measurement protocol were also excluded. The spline regression model tested showed a trend of non-linear inverse association between handgrip strength values and the number of measurement protocol variables reported (Fig. 3). The slopes calculated for the number of variables reported (x-axis) and the location of the knots of the modelled spline were: (i) slope of the curve between 1 and 4 reported variables = −1.333; (ii) slope of the curve between 4 and 7 reported variables = 0.667; (iii) slope of the curve between 7 and 9 reported variables = −1.5 (Fig. 3).

Stratified analyses by subgroups showed an overlap between 95% confidence intervals and the inverse association between handgrip strength values and the number of measurement protocol variables reported remained present in the following categories: female sex, older adults, non-older adults, Asians, Caucasians, Hispanics/Latinos and the value reported as mean or maximum handgrip strength (Fig. 4).

The Bayesian multilevel regression for the binary results of each variable of the handgrip strength measurement protocol is summarised in Fig. 5 and estimates are displayed in Table S2. These results indicate that the best predictor of higher values of handgrip strength was the number of measurements per arm, with handgrip strength being higher when this variable was not controlled. On the other hand, lack of information on “arm position” is also associated with higher values of handgrip strength, while no control on elbow position and verbal encouragement is associated with lower values of strength (Fig. 5, Table S2). There was no clear trend for the other variables included in the analysis.

3.5. Risk of bias assessment

Of the 48 included studies, 38 studies (79.2%) met the criteria of the Newcastle Ottawa Scale assessment scale to be considered of good methodological quality. The overall mean score was 7.5 out of a maximum of 9 (Table S3).

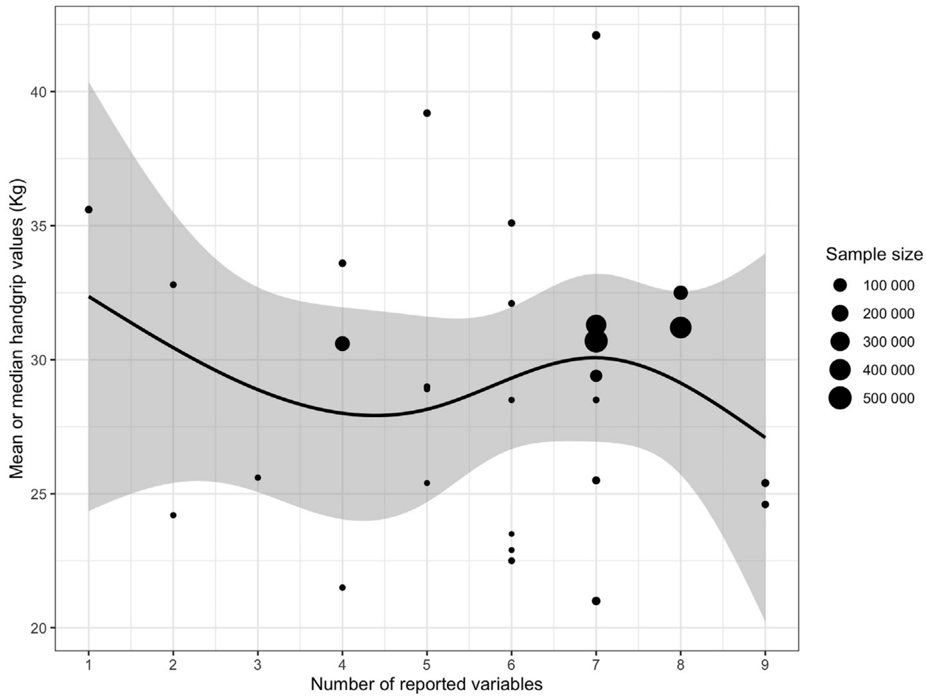

Fig. 3. Association of the number of variables controlled in the handgrip measurement protocols and handgrip strength values. The solid curve indicates the non-linear trend for the association between the number of variables controlled in the protocol and the mean or median handgrip values (kg) and its corresponding 95% confidence interval based on a restricted cubic spline model with three knots at the 10th, 50th and 90th percentile of the pooled handgrip strength. The area of each data point is proportional to the sample size of each study.

4. Discussion

This is the first systematic review aimed to analyse the handgrip strength measurement protocols used in studies assessing the associations of handgrip strength with all-cause and cause-specific mortality. The handgrip strength measurement protocols varied considerably across studies and were heterogeneous. For example, the number of repetitions, laterality of the tested hand, and the estimation of the handgrip strength value (i.e., mean or peak value) varied widely between the protocols identified. In addition, most of the included studies did not control key aspects of the protocol, such as body position, arm position, elbow position, hand-adjustment to the dynamometer, handgrip duration, and recovery time between repetitions. In general, the studies with the highest quality score on the Newcastle–Ottawa scale (9 points) controlled more protocol variables. In contrast, most of the studies with lower quality scores (≤6 points) scored zero on the item “Ascertainment of exposure” (i.e., these studies did not fully or partly control the measurement protocol of handgrip strength).

According to the results of our meta-regression analysis, when studies provided more information on the variables of the handgrip strength measurement protocol, handgrip strength values tend to be lower (Fig. 3). This non-linear trend could be explained by a likely more thorough control of the measurement process. Conversely, studies that are less rigorous in their reporting may have less control over the measurement of handgrip strength, for example, not controlling for aspects such as upper limb position. Thus, less rigorous studies may result in measurement biases that tend to overestimate handgrip strength values. Although the measurement protocol could affect the handgrip strength values, other important factors may also result in different sizes of handgrip estimates. For example, gender, age, race, or whether the handgrip strength is reported at the mean or maximum value. Our subgroup analysis accounted for these factors and identified a similar trend for most categories, with overlapping 95% confidence intervals (Fig. 4). Thus, the results therefore suggest that the inverse association between handgrip strength values and the number of measurement protocol variables reported may be independent of variables such as age, race and handgrip strength estimation (i.e., maximum or average value). However, analyses stratified by subgroups should be interpreted with caution, as they included fewer studies and are therefore more unstable.

Differences in handgrip strength measurement protocol could affect the reproducibility of measurements, comparability across populations and the accuracy of estimates linked to health outcomes. Our results are comparable to those from previous literature reviews. For example, Robert et al. [20]in a review published more than a decade ago also reported that research often did not provide sufficient information on the handgrip measurement protocol used. Although several recommendations have been published in recent years [20,23], most studies still provide incomplete information. In addition, a scoping review by Mehmet et al. [24] identified variations with respect to the participant position and length of rest periods in the measurement of handgrip strength in older adults and fragile people. Sousa et al. [75] in a systematic review of studies related to sarcopenia and frailty, also found a high heterogeneity among the handgrip protocols used. In addition, most of the included studies did not describe a complete measurement procedure. Dufner et al. [76], who systematically synthesised national temporal trends in handgrip strength for more than 2.5 million adults in 14 countries, also found differences in measurement protocols, such as dynamometer type, number of trials, scoring method, optimal hand-adjustment and elbow position.

Regarding the Body and upper extremity position, several studies have reported that there are no significant differences when comparing the standing and sitting positions in handgrip strength

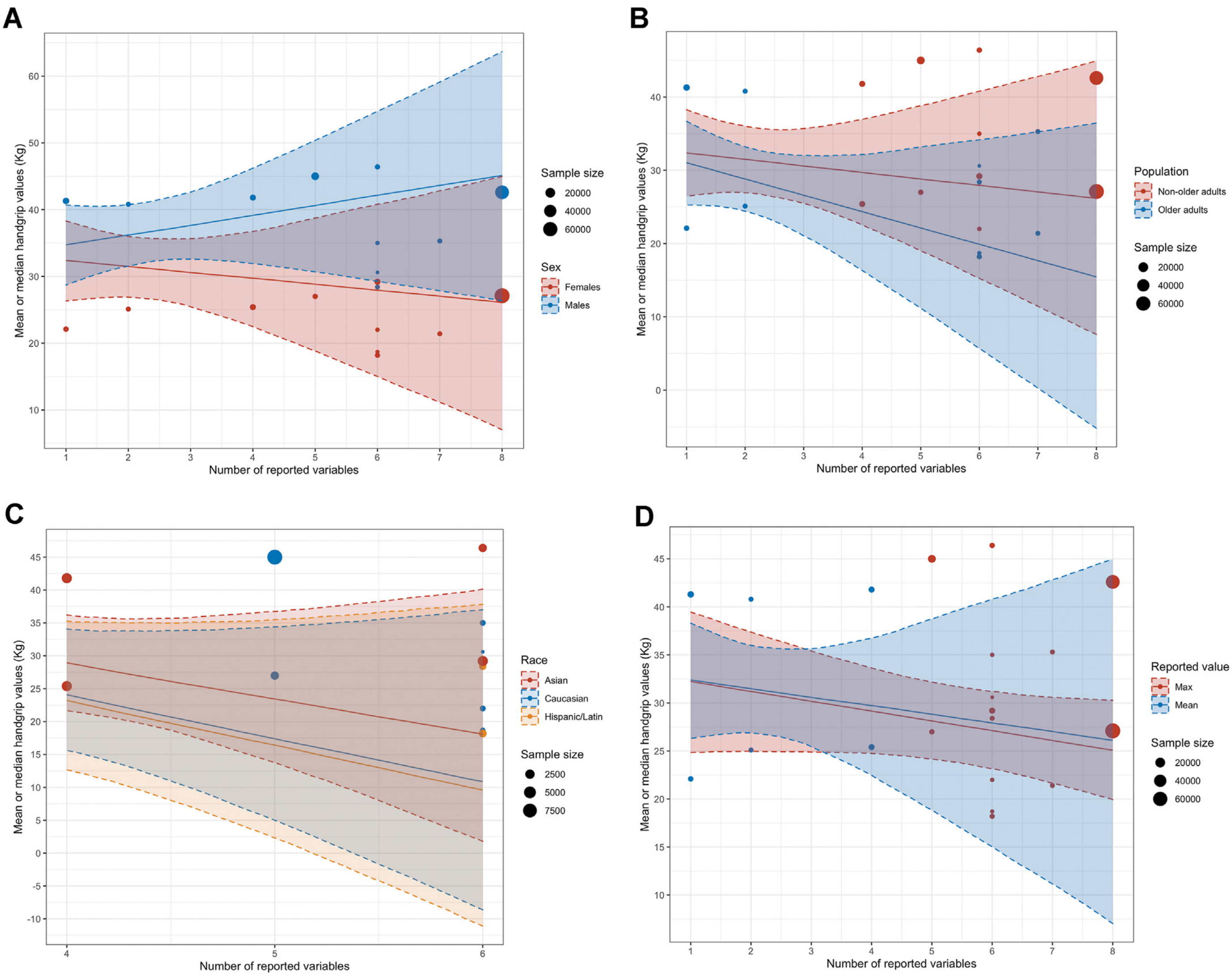

Fig. 4. Association of the number of controlled variables in the protocols and handgrip strength values stratified by sex (A), age (B), race (C), and reported value (D). The curve indicates the trend of the association for each category and its corresponding 95% confidence interval. The area of each data point is proportional to the sample size of each study.

values [77,78], which could be an advantage when assessing people with impaired balance or limited mobility. Regarding the position of the upper extremity, previous protocols, such as those of the ASHT [23], have recommended the position of the elbow flexed to 90° with adduction and neutral rotation of the shoulder. However, in the studies included in our review, only 33% reported on the position of the elbow. Spline regression for the binary outcomes indicate that reporting elbow position in the measurement protocols would be associated with higher values of handgrip strength (Fig. 5). This could be explained by the fact that all studies reporting elbow position performed the force measurement at right angles (i.e., flexed at 90°), which has been shown to be a position in which higher handgrip force could be produced [21,79,80]. On the other hand, previous studies have reported that the use of the verbal encouragement would also increase maximum handgrip strength compared to not including the verbal encouragement in the measurement [81], which is congruent with the trend observed in our Bayesian multilevel regression for this variable (i.e., greater handgrip strength when protocols report this variable).

Concerning the hand-adjustment to the dynamometer, the ASHT protocols suggest calibrating the dynamometer in the second position of the handle [23], while the Southampton protocol recommends that the instrument should feel comfortable in the hand, modifying the position of the handle if necessary [20]. The contrast between these recommendations could cause confusion. However, the literature supports the use of ASHT recommendations (i.e., measurements performed in a single standard handgrip position, handle position 2, are sufficiently accurate to assess handgrip strength for all individuals [82]. In our review we found that only 23% of the included studies reported this information, which had no association with handgrip strength values (Fig. 5).

Regarding the laterality of the tested hand, previous reviews point out to the controversy about whether there is a consistent difference in handgrip strength between when dominant and non-dominant hand is used [83], so it is not possible to draw definitive conclusions about the influence of the hand dominance on mortality risks outcomes. On the other hand, the Southampton protocol recommends the measurement of both hands [20], which was

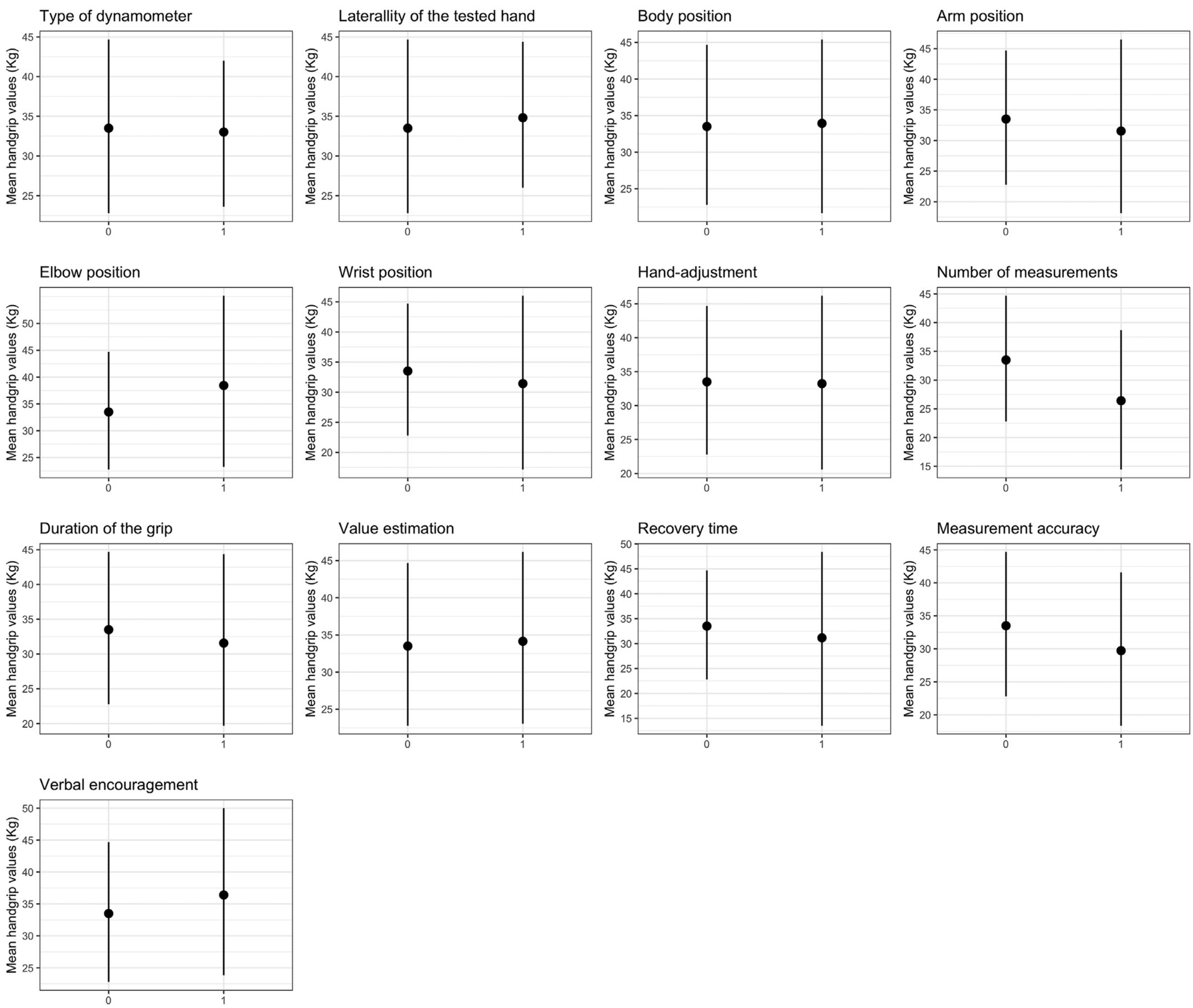

Fig. 5. Multilevel Bayesian regression for the association between individual protocol variables and handgrip strength values (kg). Value 0 indicates that the variable was not reported and value 1 indicates that the variable was reported. Estimates are presented with 95% confidence intervals.

reinforced by the review of the field by Mehmet et al. [24]. McGrath et al. [84] reported that asymmetry of handgrip strength was an indicator of increased mortality risk in aging Americans. Therefore, assessments of both hands would allow a complementary analysis to increase the prognostic value of the handgrip strength for mortality outcomes [84]. Most of the studies included in the meta-regression reported the laterality of the tested hand, which had no association with handgrip strength values (Fig. 5).

In relation to the estimation of the handgrip strength value, the literature is controversial. For example, the ASHT recommends using the mean of three trials [23]. Mathiowetz et al. [85] indicated that using the mean of three replicates offers a more accurate measure than considering the highest value. In contrast, the Southampton protocol recommends the use of the maximum handgrip score from six trials for the analysis (three trials on each side) [20], while Coldham et al. [86] suggests that a maximal trial is as reliable and less painful than the highest score of the trials or the mean of the three trials. The lack of information on this variable in the protocols did not show a clear trend in varying handgrip strength values (Fig. 5).

Most of the included studies used two or more consecutive handgrip strength tests. The Southampton and ASHT protocols recommend three measurements [20,23]. However, the resting time (at least 15 s) was only specified by the ASHT [23]. Other authors have proposed a longer recovery time (e.g., 60 s of rest) considering a possible increase in muscle fatigue between measurements [87]. Our meta-regression results indicate that incomplete reporting of the number of measurements per hand is associated with higher values of handgrip strength (Fig. 5). Failure to report the number of repetitions could imply that fewer measurements per hand were performed than recommended (i.e., less than three repetitions per hand) [20,23]. Therefore, the value of handgrip strength could be overestimated, as the influence of fatigue could be lower.

4.1. Strengths and limitations

This systematic review included data from more than 3 million adults across a wide age range and from more than 40 countries, including Europe, the Americas, Asia, and Africa. The outcome of the included studies, all-cause and cause-specific mortality, is of high relevance for public health. To our knowledge, our study is the first to examine handgrip strength measurement protocols in studies on all-cause and specific mortality outcomes.

The results of the present study should be considered in the light of several limitations. Even though we conducted systematic searches in three relevant databases, it is still possible that there are studies not included in this review. However, retrievals of studies using provided references in the included selection may have compensated for this limitation. Similarly, studies using languages other than English were not included in the final selection, but additional post-hoc searches for languages such as Spanish did not increase the number of articles found. Also, since quality of studies is usually linked to a more detailed reporting of the handgrip strength measurement protocols, it is unlikely that grey literature (i.e., studies not indexed in the examined databases) provides protocol information in more detail than the selected studies. Importantly, we assume that the information reported in the studies regarding protocols is reliable, although both reporting and publication bias should not be discarded. Finally, information on handgrip measurements protocols could not be retrieved from seven studies.

4.2. Implication of the results and future perspectives

Studies with the highest quality controlled more variables in the handgrip strength measurement protocols. In addition, most of the included studies did not control key elements such as body and upper limb position, hand-adjustment to dynamometer, duration of the testing session, and recovery time between repetitions. Studies that are less rigorous with respect to the controlled variables in the measurement protocol may result in measurement biases that tend to overestimate handgrip strength values. These shortcomings could affect the interpretation of the results and their application to both clinical and research settings (e.g., failure to identify patients requiring rehabilitation, affecting the precision of mortality-related estimates). Therefore, there is a need to improve the control of handgrip measurement protocols and to standardise the method used to evaluate handgrip strength to enhance the comparability between studies and the accuracy of mortality-related estimates. Our review presents a summary of the standard protocol for measuring handgrip strength in mortality studies that can serve as a guide for future research.

5. Conclusion

In general, the protocols used to assess handgrip strength in mortality studies are incomplete and highly heterogeneous. Handgrip strength values were higher when studies controlled fewer handgrip strength measurement protocol variables.

Statement of authorship

BdPC and RLB conceived and designed the study. RNC and RLB conducted the search. RNC, BdPC and RLB performed study selection, risk of bias assessment and data extraction. RNC, BdPC, DGG and RLB analysed and interpreted the data. RNC, BdPC and RLB drafted the manuscript with input from DGG, JC, CCM, and JFLG. All authors have read and approved the final version.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2022.09.006.

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