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Review

Handgrip strength and health outcomes: Umbrella review of systematic reviews with meta-analyses of observational studies

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Abstract

Purpose: The aim of the present study was to assess both the credibility and strength of evidence arising from systematic reviews with meta-analyses of observational studies on handgrip strength and health outcomes.

Methods: An umbrella review of systematic reviews with meta-analyses of observational studies was conducted. We assessed meta-analyses of observational studies based on random-effect summary effect sizes and their *p* values, 95% prediction intervals, heterogeneity, small-study effects, and excess significance. We graded the evidence from convincing (Class I) to weak (Class IV).

Results: From 504 articles returned in a search of the literature, 8 systematic reviews were included in our review, with a total of 11 outcomes. Overall, 9 of the 11 of the outcomes reported nominally significant summary results ($p < 0.05$), with 4 associations surviving the application of the more stringent *p* value ($p < 10^{-6}$). No outcome presented convincing evidence. Three associations showed Class II evidence (i.e., highly suggestive): (1) higher handgrip values at baseline were associated with a minor reduction in mortality risk in the general population ($n = 34$ studies; sample size = 1,855,817; relative risk = 0.72; 95% confidence interval (CI): 0.67–0.78), (2) cardiovascular death risk in mixed populations ($n = 15$ studies; relative risk = 0.84; 95%CI: 0.78–0.91), and (3) incidence of disability ($n = 7$ studies; relative risk = 0.76; 95%CI: 0.66–0.87).

Conclusion: The present results show that handgrip strength is a useful indicator for general health status and specifically for early all-cause and cardiovascular mortality, as well as disability. To further inform intervention strategies, future research is now required to fully understand mechanisms linking handgrip strength scores to these health outcomes.

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Keywords: Handgrip strength; Health outcomes; Meta-analysis; Umbrella review

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1. Introduction

A decline in physical function is a natural phenomenon that is associated with aging.¹ Such a decline is a public health concern because it has been shown to be associated with increased

risk of falls,² health care use,³ level of dependency,⁴ and premature mortality.⁵ Indeed, for many independent older adults, everyday tasks, such as climbing stairs, require functioning close to maximal capacity, meaning that further decline could increase their risk of becoming dependent on a carer.⁶ One widely employed measure of physical functioning is handgrip strength. The handgrip strength test is commonly used to evaluate the integrated performance of the muscles by determining the maximal grip force that can be produced in 1 muscular contraction, which further serves as a marker for general muscle strength.⁷ Handgrip strength is a valid measure of physical function and has been widely employed in observational research and clinical settings.^{8–11} Importantly, 1 study found that dynamometer-determined handgrip strength could be a useful instrument in geriatric practice to identify the “oldest old” patients (i.e., those aged over 75 years) at risk of disability.¹²

In recent years there has been an exponential increase in the literature investigating associations between handgrip strength and health outcomes (e.g., depression,¹³ cognitive function,¹⁴ suicidal ideation,¹⁵ mobility limitations,¹⁶ falls,¹⁷ cardiovascular disease,¹⁸ diabetes,¹⁹ renal outcomes,²⁰ osteoporotic factors,²¹ multimorbidity,²² and mortality²³); consequently, there has been an increase in systematic reviews with meta-analyses. However, to date, most systematic reviews have focused on a single disease end-point, and there has not been a systematic evaluation of the relationships between handgrip strength and diverse physical and mental health outcomes. Moreover, the strength and reliability of the evidence presented in the literature is unclear.

To address the breadth of the literature of physiological measurements and outcomes, an increasing emphasis has been placed on “umbrella reviews” (i.e., the syntheses of existing systematic reviews with meta-analyses in order to capture the breadth of outcomes associated with a given exposure).

Given this situation, the aim of the present study was to carry out an umbrella review of existing systematic reviews with meta-analyses of handgrip strength and all health outcomes in order to systematically assess the quality and strength of the evidence across all health outcomes and to identify those studies with the strongest evidence.

2. Methods

This umbrella review was registered in PROSPERO: (https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=158547).

2.1. Data sources and searches

We conducted an umbrella review²⁴ by first searching several databases (MEDLINE, Scopus, and Embase) from inception until 20 November 2019. The following search terms were used: (“meta-analysis”[ptyp] OR “metaanaly*”[tiab] OR “meta-analy*”[tiab] OR “systematic review”[ptyp] OR “systematic review” [tiab]) AND “handgrip” [tiab]). In addition, we hand-searched the reference lists of eligible articles.

2.2. Study selection

In this umbrella review, we included systematic reviews and/or meta-analyses of observational studies that investigate the relationship between handgrip strength and any health outcome. Specific inclusion criteria included the following: (1) meta-analyses or systematic reviews containing sufficient data for a meta-analysis (as defined by the authors) that measured handgrip strength and ascertained health outcomes using self-report (e.g., depression questionnaires), observed (e.g., clinical diagnoses), or objective (e.g., biomarkers and mortality) criteria; (2) case control studies or cohort studies (retrospective and prospective cohorts); and (3) meta-analyses of cohort studies that investigated the association between handgrip strength with any health-related outcome (e.g., cardiovascular disease, cancer, death, obesity/overweight, mental illness, diabetes, and metabolic diseases). Studies had to report these outcomes as odds ratio, relative risk (RR), hazard ratio, or continuous data. Two authors (PS and CH) independently performed title and abstract screening in couples. Disagreements were resolved through consensus with another independent author (LS).

2.3. Data extraction

Four independent investigators (PS, LS, CH, and NV) extracted in pairs the following information for each article: first author name, year of publication, journal, the number of included studies and the total number of participants included in the studies reviewed, the inclusion criteria for the studied populations, the measures by which handgrip strength was captured, how handgrip strength was categorized, the effect sizes used in the review, the subgroupings used in the meta-analysis, the study design (case control, retrospective, and prospective), the number of cases and controls for each study, and health outcomes.

We then extracted the study-specific estimated RR for health outcomes (RR, odds ratio, hazard ratio, standardized mean difference), along with the 95% confidence interval (CI), and the number of cases for each study by subjects and controls. If 2 reviews covered the same association, we included the review with the largest number of studies.

2.4. Risk of bias assessment

Two authors (PS and CH) independently rated the methodological quality of the included systematic reviews using “A MeaSurement Tool to Assess systematic Reviews 2 (AMSTAR2)”,²⁵ which ranks the quality of a meta-analysis in one of 4 categories ranging from “critically low” to “high” according to 16 predefined items. The review is ranked as high quality if it has no or 1 noncritical weakness (the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest). The review is ranked as moderate quality if it has more than 1 noncritical weakness (the systematic review has more than 1 noncritical weakness but no critical flaws; it may provide an accurate summary of the results of the available

studies that were included in the review). The review is ranked as low quality if it has 1 critical flaw with or without noncritical weaknesses (the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest). Finally, the review is ranked as critically low quality if it has more than 1 critical flaw with or without noncritical weaknesses (the review has more than 1 critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies).²⁶ For further reading relating to the AMSTAR 2 and what constitutes a critical flaw or a critical weakness, and so on, we refer the reader to the following reference.²⁶

2.5. Statistical analysis

For each meta-analysis, we estimated the summary effect size and its 95%CI through random-effects models.²⁷ We also estimated the prediction interval and its 95%CI, which further accounts for between-study effects and estimates the certainty of the association if a new study addresses that same association.²⁸ Between-study association was estimated with the I^2 metric; values of 50% or greater are indicative of high heterogeneity, while values above 75% suggest very high heterogeneity.²⁹

In addition, we calculated the evidence of small-study effects (i.e., whether small studies would have inflated effect sizes compared to larger ones). To this end, we used the regression asymmetry test developed by Egger and co-workers.³⁰ A p value of less than 0.10, with more conservative effects in larger studies than in random-effects meta-analysis, was considered as indicative of small-study effects.²¹ Finally, we applied Ioannidis's excess of significance test to evaluate whether there was an excess of studies reporting statistically significant results.³¹

2.6. Grading the evidence

We used the credibility assessment criteria, which are based on established tools for observational evidence as summarized previously.^{24,32–35} We classified evidence from meta-analyses of observational studies with nominally statistically significant summary results ($p < 0.05$) into 4 categories (Class I, II, III, and IV). Associations were considered to be convincing (Class I) if they had (1) a statistical significance of p value of less than 10^{-6} , (2) included more than 1000 cases (or more than 20,000 participants for continuous outcomes), (3) had the largest component study reporting a significant result ($p < 0.05$), (4) had a 95% prediction interval that excluded the null, (5) did not have large heterogeneity ($I^2 < 50\%$), and (6) showed no evidence of small study effects ($p > 0.10$) or of excess significance bias ($p > 0.10$). Highly suggestive (Class II) evidence was assigned to associations that (1) reported a significance of p values of less than 0.001, (2) included more than 1000 cases (or more than 20,000 participants for continuous outcomes), and (3) had the largest component study reporting a statistically significant result ($p < 0.05$). Suggestive (Class III) evidence was assigned to associations that

reported a significance of a p value of less than 0.01 with more than 1000 cases (or more than 20,000 participants for continuous outcomes). Weak (Class IV) evidence was assigned to the remaining significant associations with a p value of less than 0.05.

Due to the inherent limitations of case control studies in examining temporal associations, we had planned to provide the classification of evidence for Class I and II based on the following order: (1) meta-analyses of prospective studies and (2) meta-analyses of prospective and retrospective case control studies. However, no outcome had these characteristics.

3. Results

3.1. Literature review

Our search identified 20 potentially eligible reviews. Of the 20 reviews, eight were deemed to be eligible for our umbrella review. The 8 reviews had 11 different outcomes that were included in our umbrella review.

3.2. Meta-analyses of observational studies

The median number of studies of meta-analyses that included observational studies for each outcome was 8 (range 4–34), the median number of participants was 23,064 (range 2775–1,855,817), and the median number of cases was 1823 (Table 1).

The majority of the meta-analyses included studies on the general population or in adults older than 50 years, followed by patients with cardiovascular disease. Overall, nine of the 11 outcomes reported nominally significant summary results ($p < 0.05$), with 4 associations surviving to the application of the more stringent p value ($p < 10^{-6}$) (Table 1). Heterogeneity among studies was high in nine of the 11 of the outcomes included, with 7 having an I^2 of 75% or greater. Only 2 associations presented 95% prediction intervals excluding the null value. Evidence for excess statistical significance was present in 5 of 41 outcomes, and small-study effects were seen in 3 of 11 outcomes. Bias was present in three of the outcomes included. The largest study, in terms of participants for each outcome, was statistically significant in all the associations, except one.

Based on the above criteria, no outcome presented convincing evidence. However, 3 associations showed Class II evidence (i.e., highly suggestive): higher handgrip values at baseline, were associated with a minor reduction in mortality risk in the general population ($n = 34$ studies; sample size = 1,855,817; RR = 0.72; 95%CI: 0.67–0.78); cardiovascular death in mixed populations (e.g., diabetes, general, and other conditions) ($n = 15$ studies; RR = 0.84; 95%CI: 0.78–0.91), and incidence of disability ($n = 7$ studies; RR = 0.76; 95%CI: 0.66–0.87) (Table 1). The other outcomes were ranked as suggestive (association between higher handgrip values and chair rise performance over time) or weak (5 outcomes), with only 2 associations not statistically significant (i.e., the association between handgrip strength and incident hip fracture or cancer mortality) (Table 1).

Table 1
Health outcomes and evidence class reported in included meta-analyses of observational studies.

Author of MA ^a	Population	Outcome	Study design	Number of studies	Cases	Sample size	Effect size	Mean ES (95%CI)	<i>p</i>	<i>I</i> ²	Small study effects	Excess significance bias	Largest study significant	95%PI	Class of evidence
García-Hermoso A et al. (2018)	General population	All-cause mortality	Cohort	34	57,854	1,855,817	RR	0.72 (0.67–0.78)	2.04E-18	83.5	Yes	No	Yes	0.52–1.00	II
Chainani V et al. (2016)	Mixed	CVD mortality	Cohort/clinical trials	15	2183	29,105	RR	0.84 (0.78–0.91)	0.00001	84.3	No	No	Yes	0.67–1.07	II
Vermeulen et al. (2011)	Mixed	Disability	Cohort	7	1136	5201	RR	0.76 (0.66–0.87)	0.00009	89.9	Yes	Yes	Yes	0.5–1.16	II
Hardy R et al. (2013)	Adults aged 50 years or older	Chair rise performance	Cohort	8	NA	10,098	β	0.93 (0.65–1.21)	6.20E-11	91.0	No	NA	Yes	–0.02 to 1.88	III
Hardy R et al. (2013)	Adults aged 50 years or older	Walking speed	Cohort	8	NA	7261	β	0.89 (0.61–1.17)	5.37E-10	88.4	No	NA	Yes	–0.03 to 1.82	IV
Hardy R et al. (2013)	Adults aged 50 years or older	Inability to balance	Cohort	8	NA	11,318	OR	0.94 (0.92–0.98)	1.58E-09	76.2	No	NA	Yes	0.88–1.00	IV
Pavasini R et al. (2018)	Patients with cardiac disease	Cardiac death	Cohort/clinical trials	6	3000	23,435	OR	0.83 (0.74–0.94)	0.01	52.1	No	Yes	Yes	0.59–1.17	IV
Pavasini R et al. (2018)	Patients with cardiac disease	Hospital admission for HF	Cohort/clinical trials	4	125	23,064	OR	0.88 (0.82–0.95)	0.01	14.3	No	No	Yes	0.71–1.10	IV
Hwang SH et al. (2019)	Patients with CKD undergoing dialysis	Mortality	Cohort	10	589	2775	RR	0.92 (0.87–0.98)	0.02	70.3	Yes	No	Yes	0.85–1.19	IV
Denk K et al. (2018)	Adults aged 50 years or older	Hip fracture	Case-control	12	1462	28,579	RR	1.32 (0.97–1.79)	0.08	90.8	No	Yes	Yes	0.50–3.47	NS
García-Hermoso A et al. (2018)	Healthy youth and adults	Cancer mortality	Cohort	10	8887	1,297,163	RR	0.97 (0.92–1.07)	0.28	18.9	No	No	No	0.88–1.07	NS

Notes: Associations were considered to be convincing (Class I) if they had (1) a statistical significance of $p < 10^{-6}$, (2) included more than 1000 cases (or more than 20,000 participants for continuous outcomes), (3) had the largest component study reporting a significant result ($p < 0.05$), (4) had a 95%PI that excluded the null, (5) did not have large heterogeneity ($I^2 < 50\%$), and (6) showed no evidence of small study effects ($p > 0.10$) or of excess significance bias ($p > 0.10$). Highly suggestive (Class II) evidence was assigned to associations that (1) reported a significance of $p < 0.001$, (2) included more than 1000 cases (or more than 20,000 participants for continuous outcomes), and (3) had the largest component study reporting a statistically significant result ($p < 0.05$). Suggestive (Class III) evidence was assigned to associations that reported a significance of $p < 0.01$ with more than 1000 cases (or more than 20,000 participants for continuous outcomes). Weak (Class IV) evidence was assigned to the remaining significant associations with $p < 0.05$.

^a Please refer to the Supplementary File for reference list of included studies in the umbrella review.

Abbreviations: CI = confidence interval; CKD = chronic kidney disease; CVD = cardiovascular disease; ES = effect size; HF = heart failure; MA = meta-analyses; NA = not applicable; NS = not statistically significant; OR = odds ratio; PI = prediction interval; RR = relative risk.

3.3. Quality assessment

Based on scores derived from using the AMSTAR 2 tool, a total of 4 of the meta-analyses included in our review scored “critically low” and 4 scored “low” (Supplementary Table 1). Notably, most studies did not include a list of excluded studies ($n=8$) or report the source of funding for the included studies ($n=7$). Moreover, it should be noted that 1 study did not include a systematic review.

4. Discussion

In this umbrella review of 8 meta-analyses and 11 health outcomes investigating associations between handgrip strength and all health outcomes, a total of 3 outcomes (lower all-cause mortality, lower cardiovascular mortality, and lower risk of disability) were found to have highly suggestive evidence. One outcome (chair rise performance over time) was found to have suggestive evidence. Five outcomes (walking speed, inability to balance, hospital admissions, cardiac death, and mortality in those with chronic kidney disease) were found to have weak evidence. Importantly, 2 associations were found to be nonsignificant (incident hip fracture and cancer mortality). Taken together, these findings suggest that handgrip strength is a useful indicator for general health status, early all-cause mortality, cardiovascular mortality, disability, and leg power (chair rise performance).

Several mechanisms may explain the relationship between handgrip strength and early mortality. First, early life factors, such as participation in sufficient levels of physical activity, influence handgrip strength,³⁶ and childhood levels of physical activity and handgrip strength have been shown to track into adulthood.^{37,38} Importantly, maintaining adequate levels of physical activity and function over the entire life course likely yields the greatest benefit to health, owing to the reduction of any prolonged exposure from unhealthy behaviors. Next, strength is related to muscle mass and muscle mass is used as a protein reserve during cases of trauma.³⁹ Finally, other genetic contributions may be at play that result in muscle dystrophy and early mortality.⁴⁰

When considering the relationship between handgrip strength and disability and leg power, this may be explained by sarcopenia (a progressive reduction in muscle strength and mass, absolute and relative to body size, commonly occurring with aging).⁴¹ Sarcopenia is associated with a decline in physical function and an increase in disability.⁸ Next, the handgrip strength test is not just a pure measure of strength; and those with joint disorders, who will likely have increased risk of disability and lower leg power, may perform worse when carrying out this task.⁸

Umbrella reviews provide top-tier evidence and important insights, but there are a number of limitations to our review that should be considered. The meta-analyses contained studies that differed in their designs, populations, and other characteristics. However, we applied an I^2 of less than 50% as one of the criteria for Class I evidence (convincing) to assign the best evidence grade only to robust associations. Next, meta-analyses have inherent limitations:⁴² their findings depend on which

estimates are selected from each primary study and how they are applied in the meta-analysis. Finally, all the meta-analyses included in our review scored low or critically low when appraised through the use of the AMSTAR 2 tool, suggesting that future meta-analyses in this area will require more accurate reporting of methods and will also need to incorporate more robust discussions around findings.

5. Conclusion

Our results show that handgrip strength is a useful indicator for general health status, early all-cause mortality, cardiovascular mortality, disability, and leg power (chair rise performance). Future research is needed to fully understand the mechanisms linking handgrip strength scores to these health outcomes and further inform intervention strategies.

Authors' contributions

PS, CH, NV, and LS conceived the idea, wrote the protocol, extracted the data, analyzed the data, and wrote the original draft. JD, JF, RH, LY, MT, AK, PCI, GS, and LS contributed to the protocol and the drafting of the manuscript. All authors have read and approved the final version of the manuscript, and agree with the order of the presentation of the authors.

Competing interests

The authors declare that they have no competing interests.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.jshs.2020.06.009](https://doi.org/10.1016/j.jshs.2020.06.009).

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