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Effective SLOPE: EffectS of Lifestyle interventions in Older PEople with obesity – a systematic review and network meta-analysis protocol

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Effective SLOPE: EffectS of Lifestyle interventions in Older PEople with obesity – a systematic review and network meta-analysis protocol

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Abstract

Introduction

Obesity is highly prevalent in older adults aged 65 years or older. Different lifestyle interventions (diet, exercise, behavioural) are available but benefits and harms have not been fully quantified comparing all available health promotion interventions. Special consideration must be given to functional outcomes and possible adverse effects (loss of muscle and bone mass, hypoglycaemia) of weight loss interventions in this age group. The objective of this study is to synthesize the evidence regarding the effects of different types and modalities of lifestyle interventions, or their combinations, on physical function and obesity-related outcomes such as body composition in older adults with obesity.

Methods and analyses

Six databases (Medline, Embase, Cochrane Central Register of Controlled Trials, Cinahl, Psychinfo and Web of Science) and two trial registries (Clinicaltrials.gov and the WHO International Clinical Trials Registry Platform) will be searched for randomised controlled trials of lifestyle interventions in older adults with obesity. Screening (title/abstract and full-text) and data extraction of references as well as assessment of risk of bias and rating of the certainty of evidence (Grading of Recommendations, Assessment, Development and Evaluation (GRADE) for network meta-analyses) will be performed by two reviewers independently. Frequentist random-effects network meta-analyses will be conducted to determine the pooled effects from each intervention.

Ethics and dissemination

We will submit our findings to peer-reviewed journals and present at national and international conferences as well as in scientific medical societies. Patient-targeted dissemination will involve local and national advocate groups.

PROSPERO registration number

CRD42019147286

Strengths and limitations of this study

- This will be the first NMA on lifestyle interventions in older adults with obesity
- Rather than focussing on weight loss, physical functioning will be the primary interest due to its subjective and objective relevance for older people

- Methods will be applied based on the standards of the updated version 6.0 of the Cochrane Handbook for Interventions (updated July 2019)
- Recommendations will be derived based on the results according to the GRADE approach for NMA
- Heterogeneity (clinical and statistical) will be evaluated and discussed in detail

Introduction

Obesity is defined as an abnormal and excessive accumulation of body fat,[1] while on a population-level, is defined using a body mass index (BMI) ≥30 kg/m^2. Over the past four decades, the prevalence of obesity has been increasing worldwide across all age groups.[2] The rates of obesity in older adults, the fastest growing population segment[3] have now exceeded 40%, making this a public health concern.[4] As BMI has poor sensitivity in older adults due to age-related changes in body composition and a reduction of body height,[5] waist circumference and, more directly, objectively-measured fat mass can be considered in ascertaining obesity. In the United States, central obesity measured using waist circumference has been found in ~63% of community-dwelling adults aged ≥60 years.[6] The prevalence of obesity according to a high proportion of fat mass is 64% and 77% in German women and men ≥70 years respectively.[7 8] Due to the higher mechanical load of a higher body weight, for a long time obesity has not been linked to a low proportion of muscle mass. However, in recent years, sarcopenic obesity, a syndrome combining obesity with low muscle mass and strength or physical function has gained considerable attention. Sarcopenic obesity is a largely underdiagnosed condition in clinical practice, and prevalence rates of up to 94% in older adults depending on the operationalization of this construct have been reported.[9]

In community-dwelling older adults, (sarcopenic) obesity is associated with increased mortality[10 11] as well as with reduced quality of life (QoL).[12 13] Obesity is a well-known risk factor for metabolic and cardiovascular diseases, pulmonary abnormalities and certain types of cancer in older age.[14] Furthermore, obesity is associated with the onset of osteoarthritis in older adults,[15] one of the most disabling medical conditions, severely affecting one's QoL.[16] A meta-analysis of 26 prospective studies in older adults revealed obesity as risk factor for functional decline[17] which is of utmost importance for independent living.[18 19] Older adults with sarcopenic obesity are considered a group at particular risk for functional limitations as they are suffering from two conditions determining functional disability simultaneously.[20 21] Moreover, in older people (sarcopenic) obesity is associated with an increased risk of falls[22-25] and nursing home admissions.[26] Alley and colleagues have predicted that given the increasing prevalence of obesity, a disabled older person with obesity may become the most common phenotype of frailty[27] – another syndrome in the geriatric population that is associated with decline in health and function[28 29] – posing a marked personal and societal burden. In 2015, a high BMI contributed to about 120 million disability-adjusted life years (DALY) representing

~5% of DALYs from any causes among adults worldwide.[2] A recent systematic review found that compared to healthy weight, the total annual health care costs are 30% (interquartile range: 20-34%) higher in middle-aged and older people with obesity.[30] An analysis of the World Obesity Foundation in 2017 has forecasted that costs of consequences of overweight and obesity will further increase in the future.[31]

Although other therapeutic options to treat obesity exist (e.g. bariatric surgery), lifestyle strategies should always be first-line treatment.[32-34] Lifestyle interventions mainly focus on diet, exercise, behavioural or combined strategies that vary in treatment modality (e.g. specific content), type of delivery (e.g. level of supervision) and dose. Due to higher levels of multimorbidity, frailty, sarcopenia and malnutrition risk, findings from younger people cannot be generalised to older people.[35] Moreover, harmful side effects of interventions aiming at weight loss have to be considered, such as the loss of muscle mass[36] and bone mineral density.[37] Thus, in older people at risk of adverse events functional decline, functional limitations as well as falls and fracture risk may be increased.[38] Very low caloric diets may lead/contribute to an inadequate intake of nutrients and consequently to the development of malnutrition.[39] In addition, perceived and actual barriers differ between younger and older adults in their impact on adopting lifestyle changes.[40] Despite these issues, obesity treatment in older adults is still not sufficiently addressed in existing obesity guidelines.[33 41 42]

Several systematic reviews on obesity treatment in older adults published between 2006-2019[43-53] generally agree that weight-loss interventions in older adults are safe and effective in reducing weight. Combined interventions (e. g, including dietary and exercise components) are to be favoured to preserve muscle mass, bone mineral density and to improve physical performance. However, behavioural and educational strategies, which are known to be important for the long-term weight maintenance from studies in younger adults,[54] have been addressed insufficiently in existing reviews on the management of obesity in older adults. In addition, methodological issues prevent the drawing of firm conclusions, e.g. recommendations for obesity treatment. These include too specific searches in only one database, not covering the complete time period of databases and application of language restrictions. This must be considered insufficient as it likely missed relevant evidence.[55 56] Further, a quality rating of the included RCTs was missing in the majority of these systematic reviews or when done, some used no standardised tools. The only published meta-analysis dates back to 2010,[53] and there is no meta-analysis available for functional outcomes in older

people with obesity. Considering, recently published intervention studies, e.g. Ard et al. (2018)[57] and Beavers et al. (2019),[58] it is likely that accumulated evidence enables quantitative syntheses.

These limitations of existing systematic reviews highlight an evidence gap and justify the need for a thoroughly conducted high-quality systematic review according to the updated standards described by the Cochrane Collaboration for network meta-analysis.[59 60] As older adults are particularly susceptible to negative effects of excess body mass on physical function due to the age-related decline in muscle mass and strength[14] and frequently report the priority of functional outcomes related to mobility and daily life tasks,[61] these outcomes should be investigated comprehensively.

An important question remaining is which type of lifestyle intervention or treatment modality offers optimal benefits in older adults with obesity. As there exists a large number of possible interventions, multiple pairwise meta-analyses are insufficient to provide an answer of high certainty. Therefore, we will conduct a comprehensive systematic review with network meta-analyses (NMA) of RCTs to synthesize the evidence regarding the beneficial and potentially harmful effects of different types and modalities of lifestyle interventions, or their combinations, on physical function and obesity-related outcomes such as body composition in older adults with obesity.

Methods and analysis

Reporting

We report this protocol according to the PRISMA-statement for systematic review protocols (PRISMA-P, (see Table 1)),[62] the additional guidance for NMA by Chaimani et al[63] and the guidance for systematic reviews of older adults by Shenkin et al[64] to ensure thorough reporting and implementation. The methodology is preregistered on the International Prospective Register of Systematic Reviews (PROSPERO) (registration number CRD42019147286).[65]

Eligibility criteria

We will select primary studies according to the criteria below.

Population

To focus this systematic review on older adults, we will include studies including adults with a minimum age of 60 years and a mean of ≥65 years.[66] Obesity will be defined using total fat

mass ≥35% and ≥25%[67] and waist circumference of ≥88cm and ≥102cm for women and men,[68] respectively. Because of its use clinically, we will also consider BMI, applying the standard adult cut-off of ≥30kg/m^2 since there is no consensus on age-adjusted cut-offs.[69] For all three operationalizations, the methods of measurement applied by individual studies will be used. When studies report mixed samples of older adults with overweight and obesity, we will contact the authors to request the data for the subgroup with obesity. If the provision of data is not possible, the study will be excluded. No consensus definition of sarcopenic obesity exists and various operationalisations are in use.[9] As such, the definition applied by the primary study will be used, and we shall acknowledge differences in potential sub-group or sensitivity analyses, if possible. Due to the high prevalence of multimorbidity in older people and existing obesity-related co-morbidities, participants with common comorbidities of obesity (e.g. diabetes, cardiovascular, metabolic syndrome, chronic kidney disease, osteoarthritis and geriatric syndromes (e.g. frailty and sarcopenia)) will be included. We will only include studies comprising community-dwelling older adults, due to the predictive value of obesity for nursing home admissions.[70] Studies focusing on animals, genetics or biochemistry will be excluded. References that have not been included after full-text screening will be listed in a table with the respective reason(s) for exclusion.

Interventions

We will include any type of lifestyle intervention, e.g. diet, exercise, behavioural, as well as all treatment modalities and their combinations with all types of deliveries and doses. For the dietary component, interventions such as energy restriction, balanced (healthy) diet (e.g. food pyramid), Mediterranean diet, high-protein diet, low-fat diet, moderate-carbohydrate diet, low-carbohydrate diet, low glycaemic index/glycaemic load diet, vegetarian diet, DASH-diet will be considered. Interventions providing only micronutrient supplements (e.g. Vitamin D) as well as studies using only very low energy diets (<800 kcal/day) or total diet replacement will be excluded.[71] The exercise component will be defined as any planned, structured, and repetitive movement with the objective to improve or maintain physical fitness, e.g. aerobic, resistance, balance training, according to the definition of the American College of Sports Medicine.[72] We will also consider physically supported methods, such as electrical muscle stimulation and vibration training when combined with gross movements or done in an upright position. Finally, as recommended in obesity guidelines, behavioural strategies such as motivational interviewing, goal setting, self-management, stress management, social

support, training of self-efficacy and relapse management that support lifestyle changes will be considered.

Comparators

Since NMA will be conducted, all interventions will be compared to each other. Additionally, control groups, such as usual care or health counselling, will be considered as comparators.

Outcomes

Only previously validated outcomes will be considered and need to be measured at least pre- and post-intervention.

Main Outcome

The change in **functional status** with focus on physical function was shown to be important to health and adverse outcomes[18 19] and patient-relevant[61] and will therefore be our main outcome. This includes standard measures of strength, mobility and functional performance for independence in daily living, including their modifications. Common measurements include but are not limited to one-leg stance (balance), gait speed (gait, mobility), 6-min-walk test (endurance), repeated chair stands (functional strength, lower extremity function), grip strength (strength, overall function), leg power as well as composite scores of functional tests such as the Short-Physical-Performance-Battery (SPPB)[19] or the Physical Performance Test (PPT).[73] Patient-reported outcomes of functional status (e.g. Late-Life Function and Disability Instrument (LLFDI)) and digital measurements (e.g. instrumented gait analysis) will also be considered.

Other outcomes

To evaluate changes in **weight and body composition**, we will consider measures such as total body mass, fat mass (e.g. total, central, peripheral), lean mass, muscle mass (e.g. total, appendicular, lower extremity skeletal), bone mineral density (e.g. hip, lumbar spine, whole body).

(Health-related) quality of life will be summarised when reported by standardized instruments such as 36-Item Short Form Survey (SF-36)[74] or EuroQol-5D (EQ-5D).[75] If reported in primary studies, **emotional status** (e.g. depressive symptoms, depression), **social participation** (e.g. informal social relationships, community life) and satisfaction with intervention will also be captured.

We will summarise **any reported adverse event (AE)** (e.g. hypoglycaemia, hypotension, falls, cardiovascular events, institutionalization and mortality), related to the intervention as well as an outcome measure of safety or efficacy.

Design of primary studies

We will include (quasi-) RCTs (parallel and cross-over). Due to a lower level of initial fitness, prevalent health restrictions and the time needed to respond to treatment, we will include studies with intervention durations of ≥12 weeks.[40]

We will not set any restrictions regarding language or time frame. We will involve colleagues who are fluent in the respective languages or use online translators (e. g. https://www.deepl.com/home).

Conference abstracts will be excluded.

Search strategy

Six electronic databases (Medline, Embase, Cochrane Central, CINAHL, PsychInfo and Web of Science) for published trials and two trial registries (Clinicaltrials.gov, WHO International Clinical Trials Registry Platform) for unpublished or ongoing trials will be searched. We developed the search strategy for Medline (via Ovid) (see Table 2) using a search block for people aged ≥65 years and adapted a block for interventions from a recently published Cochrane review evaluating lifestyle interventions in paediatric patients with overweight and obesity, which was reviewed and revised by information specialists.[76] For other databases, the search strategy will be adapted according to the database-specific requirements. Additionally, we will screen reference lists of published SRs and eligible RCTs for potential consideration of further primary RCTs and will contact the advisory board which consists of clinical and scientific experts to enquire whether all relevant studies were identified.

Selection process

Identified references will be saved in Endnote and after excluding duplicates, references will be uploaded to Covidence (http://www.covidence.org). Two reviewers (GT, DS) will independently screen titles/abstracts and full-texts for eligibility according to the criteria described above. The title/abstract screening will be piloted using the first 200 references and in case of too many deviations (>10%), it will be revised. Disagreements will be solved by discussion or if no consensus can be reached by a third reviewer who will be asked based on

his/her expertise (nutrition/general (EK), exercise (WK), behaviour (NSB)). If relevant information is lacking, we will contact the corresponding author/s twice at a weekly interval.

Data extraction

Two reviewers (GT, DS) will extract data of included references independently using a piloted data extraction table. In case of no consensus, a third reviewer (based on expertise) will solve disagreements. If relevant data is missing, we will contact the corresponding author/s twice at weekly intervals.

When extracting the data, we will consider the following information:

study characteristics: e.g. author, publication year, eligibility criteria, setting, study duration, sample size, follow-up time, conflict of interest;

participants' characteristics: e.g. age, sex, ethnicity, BMI, body composition (e.g. fat mass, muscle mass, height/weight adjusted indices), comorbidities (e.g. diabetes, cardiovascular disease), geriatric syndromes (e.g. sarcopenia, frailty, cognitive impairment), functional status, lifestyle behaviour (e.g. sedentary);

intervention characteristics: type and modality, type of delivery, dose (e.g. duration, frequency, intensity), control arms, co-interventions, compliance and adherence, drop out, (serious) adverse events related to intervention;

outcomes: baseline values and follow-up values of functional status, BMI, weight, body composition (lean mass, fat mass), quality of life, emotional status, social participation and any reported AE as reported by study authors.

Assessment of risk of bias

The risk of bias will be assessed after a pilot trial (n=3) by two reviewers (GT, DS; not blinded to authors and journal of primary studies) independently using the revised Cochrane risk of bias tool (RoB 2.0) for RCTs.[77 78] According to this, sources of bias will be identified by assessing: i) the randomization process, ii) deviations from intended interventions, iii) missing outcome data, iv) measurement of the outcome and v) selection of the reported result. For each domain, available algorithms will be followed to answer the signalling questions (response options: yes, probably yes, probably no, no, or no information) and to judge the risk of bias as low, some concerns, or high. The overall risk of bias will also be rated as low (if low risk of bias in all domains), some concerns (at least one domain is rated as having some concerns but no domain is rated by a high risk of bias), or high (if at least one domain is judged

with a high risk of bias or multiple domains are rated as having some concerns which might impact the confidence in a result). We will present results in a risk of bias summary graph.

Assessment of certainty of evidence

Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach for NMA will be used to assess the certainty of evidence.[79-81] In addition to the risk of bias rating for every outcome, this includes the rating of direct and indirect evidence for inconsistency, indirectness and dissemination bias. In case of high certainty and a similar contribution of direct and indirect evidence to the network estimate, the highest rating will be used but could be further down-rated for incoherence and imprecision. In case of insufficient evidence as well as moderate, low or very low certainty, the indirect estimate will be rated by the lowest of two direct comparisons included in first-order loops and could be further down-rated for intransitivity. Dissemination bias will be investigated by searching for unpublished trials (see section search strategies). 'Summary of Findings' tables adapted for NMA results will be presented, similar to the proposal by Yepes-Nuñez at al.[82]

Statistical analyses

Measures of treatment effect

Effect sizes for continuous outcomes (e.g. weight loss, muscle strength) will be expressed as mean difference (MD) or standardised mean difference (SMD) with 95% confidence intervals (95%-CI). For dichotomous outcomes (e.g. AE), effect sizes will be expressed as risk ratios (RR) with 95%-CI.[83] In exceptional cases (i.e. if a minor number of RCTs expressed an AE continuously while the majority used dichotomous outcomes), the outcomes reported as continuous or categorical will be dichotomized.[84] If the post-intervention values with the corresponding standard deviation (SD) are not available, the changed scores with the corresponding SD will be used.[85]

Data synthesis

We will conduct random effects model network meta-analyses (NMA) based on a frequentist approach to derive pooled estimates for all outcomes.[86] We will use the R package 'netmeta'.[87] In NMA, evidence from direct comparisons and indirect comparisons is averaged to calculate a network estimate. The key requirement for conducting NMA is that the transitivity assumption - to compare two interventions via an indirect route in the network - is ensured. We assume that for our planned analyses, all interventions are jointly randomisable[63 88] and that all participants are likely to receive any kind of included

interventions. Network graphs will be generated by function *netgraph()* of netmeta.[87 89] We will assess global incoherence by decomposing the Q statistic into heterogeneity (within designs) and inconsistency (between designs) and visualise this using a net-heat plot.[90] In addition, We will report and assess inconsistency by calculating differences between direct and indirect effect estimates using descriptive z-tests (function *netsplit()*) and report the distribution of direct and indirect evidence. The treatment modalities (e.g. very low caloric diet, aerobic exercise, their combination or no intervention (e.g. health counselling, healthy eating/ exercise advise)) will build the nodes of the network providing maximizing similarity within and minimizing similarity between the nodes.[79] Additionally, we will analyse the components (e.g. of combined interventions using an additive model for multicomponent interventions.[91] Models of this type allow disentangling the effects of all single components (e.g. very low caloric diet (A), aerobic exercise (B), behavioural group counselling (C)) of a multicomponent intervention arm consisting of at least two single components (e.g. A+B, A+C, B+C or A+B+C). Since we do not believe that lifestyle interventions that are available for treatment of obesity may fulfil the additivity assumption for component NMA (CNMA) – i.e. the effect of a multicomponent intervention equals the sum of their components without any interactions – we will use the interaction CNMA model which is implemented in the function *netcomb()* of netmeta.[87 91] In the case of disconnected networks, we will reconnect the networks if possible (i.e. presence of at least one common component in the subnetworks). This feature of CNMA is also implemented in netmeta (function *discomb()*).

A secondary data analysis will be conducted using intervention types as network nodes (e.g. diet, exercise, behavioural). Results of NMA will be presented as forest plots. We will present league tables containing relative treatment effects for all direct comparisons (function *netleague()*) and a ranking of all treatments by P-scores.[92]

Sensitivity and subgroup analyses

If possible, sensitivity analyses will be conducted by only including studies rated as low risk of bias. We will try to conduct subgroup analyses for type of obesity (sarcopenic obesity vs obesity), intervention duration (</> 6 months), age (</> 75 years), sex, BMI-group (</> 35 kg/m^2) and co-morbidities.

Patient and public involvement

Before the start of this project, we have conducted and are currently analysing a qualitative study with semi-structured interviews in older persons with obesity. The aim is to obtain

further information on patients' motives, barriers, experiences and perceptions regarding therapeutic lifestyle interventions and thus, potentially identify evidence gaps. The results will be published in a separate manuscript.

In addition, we discuss patient-relevant outcomes, existing obstacles that exacerbate the process of contacting this population of patients as well as potential dissemination strategies with representatives of German patient advocate groups.

Ethics and dissemination

For NMA, there is no direct data collection from human participants and hence, no ethical approval is necessary.

We will submit our research articles to peer-reviewed journals and will present our results at national and international conferences. Involved experts will disseminate the results in scientific and medical societies. We will further disseminate our project via partner universities' websites and press releases. Patient-targeted dissemination will involve local and national advocate groups and offices for senior affairs. In addition, we will disseminate the results by distribution of materials in plain language.

Full references

1. WHO. Obesity and overweight. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight accessed 03.03.2020.
2. GBD 2015 Obesity Collaborators, Afshin A, Forouzanfar MH, et al. Health Effects of Overweight and Obesity in 195 Countries over 25 Years. *N Engl J Med* 2017;377(1):13-27. doi: 10.1056/NEJMoa1614362 [published Online First: 2017/06/12]
3. He W, Goodkind D, Kowal P. U.S. Census Bureau, International Population Reports, P95/16-1, An Aging World: 2015, U.S. Government Publishing Office, Washington, DC, 2016.
4. Hales CM, Fryar CD, Carroll MD, et al. Trends in Obesity and Severe Obesity Prevalence in US Youth and Adults by Sex and Age, 2007-2008 to 2015-2016. *JAMA* 2018;319(16):1723-25. doi: 10.1001/jama.2018.3060
5. Batsis JA, Mackenzie TA, Bartels SJ, et al. Diagnostic accuracy of body mass index to identify obesity in older adults: NHANES 1999-2004. *Int J Obes (Lond)* 2016;40(5):761-67. doi: 10.1038/ijo.2015.243 [published Online First: 2015/12/01]
6. Germain CM, Vasquez E, Batsis JA. Physical Activity, Central Adiposity, and Functional Limitations in Community-Dwelling Older Adults. *J Geriatr Phys Ther* 2016;39(2):71-76. doi: 10.1519/JPT.0000000000000051
7. Kemmler W, Teschler M, Weißenfels A, et al. Prevalence of sarcopenia and sarcopenic obesity in older German men using recognized definitions: high accordance but low overlap! *Osteoporos Int* 2017;28(6):1881-91. doi: 10.1007/s00198-017-3964-9 [published Online First: 2017/02/20]
8. Kemmler W, von Stengel S, Engelke K, et al. Prevalence of sarcopenic obesity in Germany using established definitions: Baseline data of the FORMOsA study. *Osteoporos Int*

2016;27(1):275-81. doi: 10.1007/s00198-015-3303-y [published Online First: 2015/08/29]
9. Batsis JA, Barre LK, Mackenzie TA, et al. Variation in the prevalence of sarcopenia and sarcopenic obesity in older adults associated with different research definitions: dual-energy X-ray absorptiometry data from the National Health and Nutrition Examination Survey 1999-2004. *J Am Geriatr Soc* 2013;61(6):974-80. doi: 10.1111/jgs.12260 [published Online First: 2013/05/06]
10. Atkins JL, Whincup PH, Morris RW, et al. Sarcopenic obesity and risk of cardiovascular disease and mortality: a population-based cohort study of older men. *J Am Geriatr Soc* 2014;62(2):253-60. doi: 10.1111/jgs.12652 [published Online First: 2014/01/15]
11. Global BMI Mortality Collaboration, Di Angelantonio E, Bhupathiraju S, et al. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet* 2016;388(10046):776-86. doi: 10.1016/S0140-6736(16)30175-1 [published Online First: 2016/07/13]
12. Laxy M, Teuner C, Holle R, et al. The association between BMI and health-related quality of life in the US population: sex, age and ethnicity matters. *Int J Obes (Lond)* 2018;42(3):318-26. doi: 10.1038/ijo.2017.252 [published Online First: 2017/10/10]
13. Cho Y, Shin S-Y, Shin M-J. Sarcopenic obesity is associated with lower indicators of psychological health and quality of life in Koreans. *Nutr Res* 2015;35(5):384-92. doi: 10.1016/j.nutres.2015.04.002 [published Online First: 2015/04/10]
14. Villareal DT, Apovian CM, Kushner RF, et al. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. *Obes Res* 2005;13(11):1849-63. doi: 10.1038/oby.2005.228
15. Silverwood V, Blagojevic-Bucknall M, Jinks C, et al. Current evidence on risk factors for knee osteoarthritis in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage* 2015;23(4):507-15. doi: 10.1016/j.joca.2014.11.019 [published Online First: 2014/11/29]
16. Cross M, Smith E, Hoy D, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. *Ann Rheum Dis* 2014;73(7):1323-30. doi: 10.1136/annrheumdis-2013-204763 [published Online First: 2014/02/19]
17. Schaap LA, Koster A, Visser M. Adiposity, muscle mass, and muscle strength in relation to functional decline in older persons. *Epidemiol Rev* 2013;35:51-65. doi: 10.1093/epirev/mxs006 [published Online First: 2012/12/04]
18. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci* 2000;55(4):M221-M31. doi: 10.1093/gerona/55.4.m221
19. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* 1994;49(2):M85-M94. doi: 10.1093/geronj/49.2.m85
20. Baumgartner RN, Wayne SJ, Waters DL, et al. Sarcopenic obesity predicts instrumental activities of daily living disability in the elderly. *Obes Res* 2004;12(12):1995-2004. doi: 10.1038/oby.2004.250
21. Rolland Y, Lauwers-Cances V, Cristini C, et al. Difficulties with physical function associated with obesity, sarcopenia, and sarcopenic-obesity in community-dwelling elderly women: the EPIDOS (EPIDemiologie de l'OSteoporose) Study. *Am J Clin Nutr*

2009;89(6):1895-900. doi: 10.3945/ajcn.2008.26950 [published Online First: 2009/04/15]
22. Himes CL, Reynolds SL. Effect of obesity on falls, injury, and disability. *J Am Geriatr Soc* 2012;60(1):124-29. doi: 10.1111/j.1532-5415.2011.03767.x [published Online First: 2011/12/08]
23. Scott D, Chandrasekara SD, Laslett LL, et al. Associations of Sarcopenic Obesity and Dynapenic Obesity with Bone Mineral Density and Incident Fractures Over 5-10 Years in Community-Dwelling Older Adults. *Calcif Tissue Int* 2016;99(1):30-42. doi: 10.1007/s00223-016-0123-9 [published Online First: 2016/03/04]
24. Follis S, Cook A, Bea JW, et al. Association Between Sarcopenic Obesity and Falls in a Multiethnic Cohort of Postmenopausal Women. *J Am Geriatr Soc* 2018;66(12):2314-20. doi: 10.1111/jgs.15613 [published Online First: 2018/10/30]
25. Scott D, Seibel M, Cumming R, et al. Sarcopenic Obesity and Its Temporal Associations With Changes in Bone Mineral Density, Incident Falls, and Fractures in Older Men: The Concord Health and Ageing in Men Project. *J Bone Miner Res* 2017;32(3):575-83. doi: 10.1002/jbmr.3016 [published Online First: 2016/11/03]
26. Zizza CA, Herring A, Stevens J, et al. Obesity affects nursing-care facility admission among whites but not blacks. *Obes Res* 2002;10(8):816-23. doi: 10.1038/oby.2002.110
27. Alley DE, Ferrucci L, Barbagallo M, et al. A research agenda: the changing relationship between body weight and health in aging. *J Gerontol A Biol Sci Med Sci* 2008;63(11):1257-59. doi: 10.1093/gerona/63.11.1257
28. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56(3):M146-M56. doi: 10.1093/gerona/56.3.m146
29. Rockwood K, Stadnyk K, MacKnight C, et al. A brief clinical instrument to classify frailty in elderly people. *Lancet* 1999;353(9148):205-06. doi: 10.1016/S0140-6736(98)04402-X
30. Kent S, Fusco F, Gray A, et al. Body mass index and healthcare costs: a systematic literature review of individual participant data studies. *Obes Rev* 2017;18(8):869-79. doi: 10.1111/obr.12560 [published Online First: 2017/05/22]
31. Calculating the costs of the consequences of obesity 2017. Available from: https://www.worldobesity.org/resources/resource-library/calculating-the-costs-of-the-consequences-of-obesity accessed 19.02.2020.
32. Alfadda AA, Al-Dhwayan MM, Alharbi AA, et al. The Saudi clinical practice guideline for the management of overweight and obesity in adults. *Saudi Med J* 2016;37(10):1151-62. doi: 10.15537/smj.2016.10.14353
33. Hauner H, Moss A, Berg A, et al. Interdisziplinäre Leitlinie der Qualität S3 zur „Prävention und Therapie der Adipositas". *Adipositas-Ursachen, Folgeerkrankungen, Therapie* 2014;8(04):179-221.
34. Kushner RF, Ryan DH. Assessment and lifestyle management of patients with obesity: clinical recommendations from systematic reviews. *JAMA* 2014;312(9):943-52. doi: 10.1001/jama.2014.10432
35. Cetin DC, Nasr G. Obesity in the elderly: more complicated than you think. *Cleve Clin J Med* 2014;81(1):51-61. doi: 10.3949/ccjm.81a.12165
36. Weinheimer EM, Sands LP, Campbell WW. A systematic review of the separate and combined effects of energy restriction and exercise on fat-free mass in middle-aged and older adults: implications for sarcopenic obesity. *Nutr Rev* 2010;68(7):375-88. doi: 10.1111/j.1753-4887.2010.00298.x
37. Soltani S, Hunter GR, Kazemi A, et al. The effects of weight loss approaches on bone mineral density in adults: a systematic review and meta-analysis of randomized

controlled trials. *Osteoporos Int* 2016;27(9):2655-71. doi: 10.1007/s00198-016-3617-4 [published Online First: 2016/05/06]

38. Mathus-Vliegen EMH, Obesity Management Task Force of the European Association for the Study of O. Prevalence, pathophysiology, health consequences and treatment options of obesity in the elderly: a guideline. *Obes Facts* 2012;5(3):460-83. doi: 10.1159/000341193 [published Online First: 2012/06/30]
39. Volkert D, Beck AM, Cederholm T, et al. ESPEN guideline on clinical nutrition and hydration in geriatrics. *Clin Nutr* 2019;38(1):10-47. doi: 10.1016/j.clnu.2018.05.024 [published Online First: 2018/06/18]
40. Brawley LR, Rejeski WJ, King AC. Promoting physical activity for older adults: the challenges for changing behavior. *Am J Prev Med* 2003;25(3 Suppl 2):172-83. doi: 10.1016/s0749-3797(03)00182-x
41. American College of Cardiology/American Heart Association Task Force on Practice Guidelines OEP. Expert Panel Report: Guidelines (2013) for the management of overweight and obesity in adults. *Obesity (Silver Spring)* 2014;22 Suppl 2:S41-S410. doi: 10.1002/oby.20660
42. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation* 2014;129(25 Suppl 2):S102-S38. doi: 10.1161/01.cir.0000437739.71477.ee [published Online First: 2013/11/12]
43. Bales CW, Buhr G. Is obesity bad for older persons? A systematic review of the pros and cons of weight reduction in later life. *J Am Med Dir Assoc* 2008;9(5):302-12. doi: 10.1016/j.jamda.2008.01.006
44. Batsis JA, Gill LE, Masutani RK, et al. Weight Loss Interventions in Older Adults with Obesity: A Systematic Review of Randomized Controlled Trials Since 2005. *J Am Geriatr Soc* 2017;65(2):257-68. doi: 10.1111/jgs.14514 [published Online First: 2016/09/19]
45. Bouaziz W, Schmitt E, Kaltenbach G, et al. Health benefits of endurance training alone or combined with diet for obese patients over 60: a review. *Int J Clin Pract* 2015;69(10):1032-49. doi: 10.1111/ijcp.12648 [published Online First: 2015/05/11]
46. Felix HC, West DS. Effectiveness of weight loss interventions for obese older adults. *Am J Health Promot* 2013;27(3):191-99. doi: 10.4278/ajhp.110617-LIT-259
47. Haywood C, Sumithran P. Treatment of obesity in older persons-A systematic review. *Obes Rev* 2019;20(4):588-98. doi: 10.1111/obr.12815 [published Online First: 2019/01/15]
48. McTigue KM, Hess R, Ziouras J. Obesity in older adults: a systematic review of the evidence for diagnosis and treatment. *Obesity (Silver Spring)* 2006;14(9):1485-97. doi: 10.1038/oby.2006.171
49. Poggiogalle E, Migliaccio S, Lenzi A, et al. Treatment of body composition changes in obese and overweight older adults: insight into the phenotype of sarcopenic obesity. *Endocrine* 2014;47(3):699-716. doi: 10.1007/s12020-014-0315-x [published Online First: 2014/06/22]
50. Porter Starr KN, McDonald SR, Bales CW. Obesity and physical frailty in older adults: a scoping review of lifestyle intervention trials. *J Am Med Dir Assoc* 2014;15(4):240-50. doi: 10.1016/j.jamda.2013.11.008 [published Online First: 2014/01/17]
51. Rejeski WJ, Marsh AP, Chmelo E, et al. Obesity, intentional weight loss and physical disability in older adults. *Obes Rev* 2010;11(9):671-85. doi: 10.1111/j.1467-789X.2009.00679.x

52. Waters DL, Ward AL, Villareal DT. Weight loss in obese adults 65years and older: a review of the controversy. *Exp Gerontol* 2013;48(10):1054-61. doi: 10.1016/j.exger.2013.02.005 [published Online First: 2013/02/10]
53. Witham MD, Avenell A. Interventions to achieve long-term weight loss in obese older people: a systematic review and meta-analysis. *Age Ageing* 2010;39(2):176-84. doi: 10.1093/ageing/afp251 [published Online First: 2010/01/18]
54. Greaves C, Poltawski L, Garside R, et al. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. *Health Psychol Rev* 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583 [published Online First: 2017/04/07]
55. Catalogue of Bias Collaboration, Brassey J, Spencer EA, Heneghan C. Langauge bias. In: Catalogue Of Bias 2017. Available from: https://catalogofbias.org/biases/language-bias/ accessed 19.02.2020.
56. Puljak L. If there is only one author or only one database was searched, a study should not be called a systematic review. *J Clin Epidemiol* 2017;91:4-5. doi: 10.1016/j.jclinepi.2017.08.002 [published Online First: 2017/08/18]
57. Ard JD, Gower B, Hunter G, et al. Effects of Calorie Restriction in Obese Older Adults: The CROSSROADS Randomized Controlled Trial. *J Gerontol A Biol Sci Med Sci* 2017;73(1):73-80. doi: 10.1093/gerona/glw237
58. Beavers KM, Nesbit BA, Kiel JR, et al. Effect of an Energy-Restricted, Nutritionally Complete, Higher Protein Meal Plan on Body Composition and Mobility in Older Adults With Obesity: A Randomized Controlled Trial. *J Gerontol A Biol Sci Med Sci* 2019;74(6):929-35. doi: 10.1093/gerona/gly146
59. Cumpston M, Li T, Page MJ, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database Syst Rev* 2019;10:ED000142-ED42. doi: 10.1002/14651858.ED000142
60. Higgins JPT TJ, Chandler J, Cumpston M, Li T, Page MJ, Welch VA. (editors). Cochrane Handbook for Systematic Reviews of Interventions. 2nd Edition: Chichester (UK): John Wiley & Sons 2019.
61. Jackson SE, Holter L, Beeken RJ. 'Just because I'm old it doesn't mean I have to be fat': a qualitative study exploring older adults' views and experiences of weight management. *BMJ Open* 2019;9(2):e025680-e80. doi: 10.1136/bmjopen-2018-025680
62. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4(1):1-1. doi: 10.1186/2046-4053-4-1
63. Chaimani A, Caldwell DM, Li T, et al. Additional considerations are required when preparing a protocol for a systematic review with multiple interventions. *J Clin Epidemiol* 2017;83:65-74. doi: 10.1016/j.jclinepi.2016.11.015 [published Online First: 2017/01/11]
64. Shenkin SD, Harrison JK, Wilkinson T, et al. Systematic reviews: guidance relevant for studies of older people. *Age Ageing* 2017;46(5):722-28. doi: 10.1093/ageing/afx105
65. Torbahn G, Schoene D, Schwingshackl L, et al. EffectiveSLOPE: EffectS of Lifestyle interventions in Obese older PEople – a systematic review and network meta-analysis. PROSPERO 2019 CRD42019147286 2019. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019147286 accessed 19.02.2020.

66. NHS England. Improving care for older people. Available from: https://www.england.nhs.uk/ourwork/clinical-policy/older-people/improving-care-for-older-people/ accessed 20.02.2020.
67. World Health Organisation. Physical Status: The use and interpreation of anthropometry. Technical Report Series 854,Geneva, 1995.
68. Han TS, van Leer EM, Seidell JC, et al. Waist circumference action levels in the identification of cardiovascular risk factors: prevalence study in a random sample. *BMJ* 1995;311(7017):1401-05. doi: 10.1136/bmj.311.7017.1401
69. Batsis JA, Zagaria AB. Addressing Obesity in Aging Patients. *Med Clin North Am* 2018;102(1):65-85. doi: 10.1016/j.mcna.2017.08.007 [published Online First: 2017/10/21]
70. Valiyeva E, Russell LB, Miller JE, et al. Lifestyle-related risk factors and risk of future nursing home admission. *Arch Intern Med* 2006;166(9):985-90. doi: 10.1001/archinte.166.9.985
71. Astbury NM, Piernas C, Hartmann-Boyce J, et al. A systematic review and meta-analysis of the effectiveness of meal replacements for weight loss. *Obes Rev* 2019;20(4):569-87. doi: 10.1111/obr.12816 [published Online First: 2019/01/24]
72. American College of Sports M, Chodzko-Zajko WJ, Proctor DN, et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc* 2009;41(7):1510-30. doi: 10.1249/MSS.0b013e3181a0c95c
73. Reuben DB, Siu AL. An objective measure of physical function of elderly outpatients. The Physical Performance Test. *J Am Geriatr Soc* 1990;38(10):1105-12. doi: 10.1111/j.1532-5415.1990.tb01373.x
74. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30(6):473-83.
75. EuroQol Group. EuroQol--a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16(3):199-208. doi: 10.1016/0168-8510(90)90421-9
76. Mead E, Brown T, Rees K, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese children from the age of 6 to 11 years. *Cochrane Database Syst Rev* 2017;6(6):CD012651-CD51. doi: 10.1002/14651858.CD012651
77. Recker RR, Davies KM, Dowd RM, et al. The effect of low-dose continuous estrogen and progesterone therapy with calcium and vitamin D on bone in elderly women. A randomized, controlled trial. *Ann Intern Med* 1999;130(11):897-904.
78. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:l4898-l98. doi: 10.1136/bmj.l4898
79. Reid IR, Ames RW, Evans MC, et al. Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: a randomized controlled trial [see comments]. *Am J Med* 1995;98(4):331-35.
80. Brignardello-Petersen R, Bonner A, Alexander PE, et al. Advances in the GRADE approach to rate the certainty in estimates from a network meta-analysis. *J Clin Epidemiol* 2018;93:36-44. doi: 10.1016/j.jclinepi.2017.10.005 [published Online First: 2017/10/17]
81. Puhan MA, Schünemann HJ, Murad MH, et al. A GRADE Working Group approach for rating the quality of treatment effect estimates from network meta-analysis. *BMJ* 2014;349:g5630-g30. doi: 10.1136/bmj.g5630
82. Yepes-Nuñez JJ, Li S-A, Guyatt G, et al. Development of the summary of findings table for network meta-analysis. *J Clin Epidemiol* 2019;115:1-13. doi: 10.1016/j.jclinepi.2019.04.018 [published Online First: 2019/05/02]

83. Deng HW, Stegman MR, Davies KM, et al. Genetic determination of variation and covariation of peak bone mass at the hip and spine. *J Clin Densitom* 1999;2(3):251-63.
84. Anzures-Cabrera J, Sarpatwari A, Higgins JP. Expressing findings from meta-analyses of continuous outcomes in terms of risks. *Stat Med* 2011;30(25):2967-85. doi: 10.1002/sim.4298 [published Online First: 2011/08/08]
85. Deeks JJ, Higgins JPT, Altman DG (editors). Chapter 10: Analysing data and undertaking meta-analyses. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane, 2019. Available from www.training.cochrane.org/handbook.
86. Rücker G. Network meta-analysis, electrical networks and graph theory. *Res Synth Methods* 2012;3(4):312-24. doi: 10.1002/jrsm.1058 [published Online First: 2012/09/25]
87. Stern Y, Tang MX, Albert MS, et al. Predicting time to nursing home care and death in individuals with Alzheimer disease. *JAMA* 1997;277(10):806-12.
88. Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: many names, many benefits, many concerns for the next generation evidence synthesis tool. *Res Synth Methods* 2012;3(2):80-97. doi: 10.1002/jrsm.1037 [published Online First: 2012/06/11]
89. Rücker G, Schwarzer G. Automated drawing of network plots in network meta-analysis. *Res Synth Methods* 2016;7(1):94-107. doi: 10.1002/jrsm.1143
90. Krahn U, Binder H, König J. A graphical tool for locating inconsistency in network meta-analyses. *BMC Med Res Methodol* 2013;13:35-35. doi: 10.1186/1471-2288-13-35
91. Rücker G, Petropoulou M, Schwarzer G. Network meta-analysis of multicomponent interventions. *Biom J* 2019:10.1002/bimj.201800167. doi: 10.1002/bimj.201800167
92. Rücker G, Schwarzer G. Ranking treatments in frequentist network meta-analysis works without resampling methods. *BMC Med Res Methodol* 2015;15:58-58. doi: 10.1186/s12874-015-0060-8

Authors' contributions

GT, DS and EK drafted the manuscript. All authors were involved in the planning and design process of this project and provided critical feedback for the manuscript. All authors approved the final version of the manuscript. EK will be the guarantor of the review.

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Competing interests' statement

GT, DS, GR, HK, WK, CCS, DTV, NSB, DV & EK declare no conflict of interest. LS is a member of the GRADE working group. JAB is funded by the National Institute on Aging and Office of Dietary Supplements of the National Institutes of Health under Award Number K23AG051681, and the R01 AG067416. The funder had no role in preparing the protocol and manuscript.

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PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page(s)
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	n.a.
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2,6
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	19
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n.a.
Support:			
Sources	5a	Indicate sources of financial or other support for the review	19
Sponsor	5b	Provide name for the review funder and/or sponsor	19
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	19
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-6
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	6
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	6-9
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	9
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Table 2

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	9
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	9-10
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	10
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	10
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	8-9
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	10-11
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	11-12
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	11-12
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	11-12
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	n.a.
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	11
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	11

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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Database(s): Ovid MEDLINE(R) ALL 1946 to March 05, 2020

Search Strategy:

#	Searches
1	obesity/
2	obesity, morbid/
3	obesity, abdominal/
4	obesity, metabolically benign/
5	overweight/
6	(adipos* or obes* or overweight* or over weight*).ti,ab,kf.
7	or/1-6 [Obesity]
8	exp behavior therapy/
9	exp counseling/
10	social support/
11	program evaluation/
12	exp exercise/
13	exp exercise therapy/
14	exp exercise movement techniques/
15	"physical education and training"/
16	exp physical fitness/
17	accidental falls/
18	postural balance/
19	motor activity/
20	gait/
21	exp muscle strength/
22	exp diet/
23	exp diet therapy/
24	patient education as topic/
25	health education/
26	exp health behavior/
27	exp health promotion/
28	life style/
29	((obesity adj3 intervention) or program or programme).ti,ab,kf.
30	(lifestyle or life style).ti,ab,kf.
31	exercis*.ti,ab,kf.
32	(physic* adj (activ* or fit*)).ti,ab,kf.
33	(walk* or swim* or aqua or cycl* or weight lift* or danc* or aerobics or balance or electric* muscle stimulation or neuromuscular electric* stimulation or electromyostimulationor ems).ti,ab,kf.
34	((physic* or strength* or resist* or circuit or weight or aerob* or cross or endurance or vibration*) adj3 train*).ti,ab,kf.
35	(behavio?ral or behavio?r modification or psychoth* or psychosocial).ti,ab,kf.
36	((group or cognit* or behav*) adj therap*).ti,ab,kf.
37	counsel?ing.ti,ab,kf.

38	educat*.ti,ab,kf.
39	(diet* or healthy nutrition or (nutrition* adj (knowledge or educat* or therap* or program* or intervention*))).ti,ab,kf.
40	(low-calori* or calori* restrict* or low-energ* or energ* restrict* or low-carbohydrate or high-carbohydrate or low-fat or high-fat or low-protein or high-protein or vegetarianor vegan or mediterranean or dash).ti,ab,kf.
41	weight loss/
42	(weight adj1 (reduc* or los* or control* or manag*)).ti,ab,kf.
43	or/8-42 [Interventions]
44	obesity/ or obesity, abdominal/ or obesity, morbid/ or overweight/ or obesity, metabolically benign/
45	(diet therapy or prevention & control or rehabilitation or therapy or psychology).fs.
46	44 and 45 [MeSH/subheading combination]
47	exp weight reduction programs/
48	or/46-47 [Obesity-specific interventions]
49	7 and 43 [Obesity AND Interventions]
50	or/48-49 [Obesity interventions complete: (Obesity AND Interventions) OR Obesity-specific interventions]
51	exp aged/
52	geriatrics/
53	frailty/
54	sarcopenia/
55	Independent Living/
56	((old* or senior or age*) adj2 (adult* or person* or subject* or individual* or people or group* or m?n or wom?n or patient* or client* or outpatient* or citizen* or "60or 65" or age*)).ti,ab,kf.
57	(elder* or eldes* or geriat* or geronto* or frail* or sarcopen* or senior* or agedly or ag?ing).ti,ab,kf.
58	community-dwell*.ti,ab,kf.
59	((commun* or indepen*) adj1 (dwell* or livi*)).ti,ab,kf.
60	(("60" or "65") adj1 year*).ti,ab,kf.
61	((advanc* or high*) adj1 age*).ti,ab,kf.
62	(super adj1 age*).ti,ab,kf.
63	(superage* or super-age* or centen* or centa* or nonagen* or octagen* or sept?agen* or supercenten* or senium*).ti,ab,kf.
64	or/51-63 [Age group]
65	randomized controlled trial.pt.
66	controlled clinical trial.pt.
67	randomi?ed.ab.
68	placebo.ab.
69	clinical trials as topic.sh.
70	randomly.ab.
71	trial.ti.

72	or/65-71
73	exp animals/ not humans.sh.
74	72 not 73 [Study filter (Cochrane Handbook v5.0.2 2008 RCT filter - sensitivity and precision maximizing version)]
75	50 and 64 [Obesity interventions complete AND Age group]
76	75 and 74 [Obesity interventions complete AND Age group AND Study filter]
77	(exp infant/ or exp child/ or adolescent/) not exp aged/ [Child/adolescent/middle aged adults-only studies]
78	76 not 77 [Remove Child/adolescent/middle aged adults-only studies]

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Effective SLOPE: EffectS of Lifestyle interventions in Older PEople with obesity – a systematic review and network meta-analysis protocol

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Title:
Effective SLOPE: EffectS of Lifestyle interventions in Older PEople with obesity – a systematic review and network meta-analysis protocol

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Abstract

Introduction

Obesity is highly prevalent in older adults aged 65 years or older. Different lifestyle interventions (diet, exercise, self-management) are available but benefits and harms have not been fully quantified comparing all available health promotion interventions. Special consideration must be given to functional outcomes and possible adverse effects (loss of muscle and bone mass, hypoglycaemia) of weight loss interventions in this age group. The objective of this study is to synthesize the evidence regarding the effects of different types and modalities of lifestyle interventions, or their combinations, on physical function and obesity-related outcomes such as body composition in older adults with obesity.

Methods and analyses

Six databases (Medline, Embase, Cochrane Central Register of Controlled Trials, Cinahl, Psychinfo and Web of Science) and two trial registries (Clinicaltrials.gov and the WHO International Clinical Trials Registry Platform) will be searched for randomised controlled trials of lifestyle interventions in older adults with obesity. Screening (title/abstract and full-text) and data extraction of references as well as assessment of risk of bias and rating of the certainty of evidence (Grading of Recommendations, Assessment, Development and Evaluation (GRADE) for network meta-analyses) will be performed by two reviewers independently. Frequentist random-effects network meta-analyses will be conducted to determine the pooled effects from each intervention.

Ethics and dissemination

We will submit our findings to peer-reviewed journals and present at national and international conferences as well as in scientific medical societies. Patient-targeted dissemination will involve local and national advocate groups.

PROSPERO registration number

CRD42019147286

Strengths and limitations of this study

- This will be the first NMA on lifestyle interventions in older adults with obesity
- Rather than focussing on weight loss, physical functioning will be the primary interest due to its subjective and objective relevance for older people

- Methods will be applied based on the standards of the updated version 6.0 of the Cochrane Handbook for Interventions (updated July 2019)
- Recommendations will be derived based on the results according to the GRADE approach for NMA
- Heterogeneity (clinical and statistical) will be evaluated and discussed in detail

Introduction

Obesity is defined as an abnormal and excessive accumulation of body fat,[1] while on a population-level, is defined using a body mass index (BMI) ≥30 kg/m^2. Over the past four decades, the prevalence of obesity has been increasing worldwide across all age groups.[2] The rates of obesity in older adults, the fastest growing population segment[3] have now exceeded 40%, making this a public health concern.[4] As BMI has poor sensitivity in older adults due to age-related changes in body composition and a reduction of body height,[5] waist circumference and, more directly, objectively-measured fat mass can be considered in ascertaining obesity. In the United States, central obesity measured using waist circumference has been found in ~63% of community-dwelling adults aged ≥60 years.[6] The prevalence of obesity according to a high proportion of fat mass is 64% and 77% in German women and men ≥70 years respectively.[7 8] Due to the higher mechanical load of a higher body weight, for a long time obesity has not been linked to a low proportion of muscle mass. However, in recent years, sarcopenic obesity, a syndrome combining obesity with low muscle mass and strength or physical function has gained considerable attention. Sarcopenic obesity is a largely underdiagnosed condition in clinical practice, and prevalence rates of up to 94% in older adults depending on the operationalization of this construct have been reported.[9]

In community-dwelling older adults, obesity and sarcopenic obesity are associated with increased mortality[10 11] as well as with reduced quality of life (QoL).[12 13] Contrary, several cohort studies have shown a lower risk for mortality in people with obesity and specific diseases such as type 2 diabetes, coronary artery disease or serious illnesses,[14-16] which was described as 'obesity paradox'. While research on this controversial phenomenon is still ongoing, several hypotheses are discussed, such as collider bias or effect modification.[17-19] Obesity is a well-known risk factor for metabolic and cardiovascular diseases, pulmonary abnormalities and certain types of cancer in older age.[20] Furthermore, obesity is associated with the onset of osteoarthritis in older adults,[21] one of the most disabling medical conditions, severely affecting one's QoL.[22] A meta-analysis of 26 prospective studies in older adults revealed obesity as risk factor for functional decline[23] which is of utmost importance for independent living.[24 25] Older adults with sarcopenic obesity are considered a group at particular risk for functional limitations as they are suffering from two conditions determining functional disability simultaneously.[26 27] Moreover, in older people obesity and sarcopenic obesity are associated with an increased risk of falls[28-31] and nursing home admissions.[32] Alley

and colleagues have predicted that given the increasing prevalence of obesity, a disabled older person with obesity may become the most common phenotype of frailty[33] – another syndrome in the geriatric population that is associated with decline in health and function[34 35] – posing a marked personal and societal burden. In 2015, a high BMI contributed to about 120 million disability-adjusted life years (DALY) representing ~5% of DALYs from any causes among adults worldwide.[2] A recent systematic review found that compared to healthy weight, the total annual health care costs are 30% (interquartile range: 20-34%) higher in middle-aged and older people with obesity.[36] An analysis of the World Obesity Foundation in 2017 has forecasted that costs of consequences of overweight and obesity will further increase in the future.[37]

Although other therapeutic options to treat obesity exist (e.g. bariatric surgery), lifestyle strategies should always be first-line treatment.[38-40] Lifestyle interventions mainly focus on diet, exercise, self-management or combined strategies that vary in treatment modality (e.g. specific content), type of delivery (e.g. level of supervision) and dose. Lifestyle interventions mainly focus on diet (e.g. calorie restriction,[41] high protein diet[42]), exercise (e.g. aerobic or resistance[43]), self-management interventions (e.g. relapse prevention or self-monitoring techniques[44] or combined strategies that vary in treatment modality (e.g. specific content), type of delivery (e.g. level of supervision, individual vs group sessions, in person vs technology) and dose (e.g. duration, intensity). Findings from younger people cannot be generalised to older people due to higher levels of multimorbidity, frailty, sarcopenia and malnutrition risk.[45] Moreover, harmful side effects of interventions aiming at weight loss have to be considered, such as reduced muscle mass[46] and bone mineral density. [47] Thus, in older people functional decline, functional limitations as well as the risk of adverse events, such as falls and fractures may be increased.[48] Very low caloric diets may lead to an inadequate intake of nutrients and consequently to the development of malnutrition, another geriatric syndrome associated with adverse health events.[49] In addition, perceived and actual barriers differ between younger and older adults in their impact on adopting lifestyle changes.[50] Despite these issues, obesity treatment in older adults is still not sufficiently addressed in existing obesity guidelines.[39 51 52]

Several systematic reviews on obesity treatment in older adults have been published between 2006-2019[53-63] including 126 publications of more than 60 distinct RCTs. Reviews however, did not identify the same studies for inclusion due to different search strategies, databases, search dates as well as differing definitions of obesity and applying various age cut-offs. They

generally agree that weight-loss interventions in older adults do not cause poor health outcomes (e.g. higher risk for mortality for those randomized to the weight-loss group) and significantly reduce weight). Further, more limited evidence demonstrates improvements in measures of physical performance, such as gait speed. Combined interventions (e.g., including dietary and exercise components) are to be favoured to preserve muscle mass, bone mineral density and to improve physical performance. However, self-management strategies, which are important for long-term weight maintenance from studies in younger adults,[64] have not been separately reported and discussed in existing reviews on the management of obesity in older adults. In addition, methodological issues prevent the drawing of firm conclusions, e.g. recommendations for obesity treatment. These include too specific searches in only one database, not covering the complete time period of databases and application of language restrictions. This must be considered insufficient as it likely missed relevant evidence.[65 66] Further, a quality rating of the included RCTs was missing in the majority of these systematic reviews or when done, some used no standardised tools. The only published meta-analysis dates back to 2010,[63] and there is no meta-analysis available for functional outcomes in older people with obesity. Considering, recently published intervention studies, e.g. Ard et al. (2018)[67] and Beavers et al. (2019),[68] it is likely that accumulated evidence enables quantitative syntheses.

These limitations of existing systematic reviews highlight an evidence gap and justify the need for a thoroughly conducted high-quality systematic review according to the updated standards described by the Cochrane Collaboration for network meta-analysis.[69 70] As older adults are particularly susceptible to negative effects of excess body mass on physical function due to the age-related decline in muscle mass and strength[20] and frequently report the priority of functional outcomes related to mobility and daily life tasks,[71] these outcomes should be investigated comprehensively.

An important question remaining is which type of lifestyle intervention or treatment modality offers optimal benefits in older adults with obesity. As there exists a large number of possible interventions, multiple pairwise meta-analyses are insufficient to provide an answer of high certainty. Therefore, we will conduct a comprehensive systematic review with network meta-analyses (NMA) of RCTs to synthesize the evidence regarding the beneficial and potentially harmful effects of different types and modalities of lifestyle interventions, or their

combinations, on physical function and obesity-related outcomes such as body composition in older adults with obesity and sarcopenic obesity.

Methods and analysis

Reporting

We report this protocol according to the PRISMA-statement for systematic review protocols (PRISMA-P, (see online supplementary file 1)),[72] the additional guidance for NMA by Chaimani et al[73] and the guidance for systematic reviews of older adults by Shenkin et al[74] to ensure thorough reporting and implementation. The methodology is preregistered on the International Prospective Register of Systematic Reviews (PROSPERO) (registration number CRD42019147286).[75]

Eligibility criteria

We will select primary studies according to the criteria below.

Population

To focus this systematic review on older adults, we will include studies including adults with a minimum age of 60 years and a mean of ≥65 years.[76] Participants will be classified as obese if one of the following criteria is fulfilled: percentage of total body fat mass ≥35% and ≥25%[77] or waist circumference of ≥88cm and ≥102cm for women and men,[78] or BMI, applying the standard adult cut-off of ≥30kg/m^2 since there is no consensus on age-adjusted cut-offs.[79] If proven valid, we will, however consider different cut-off values for these criteria, e.g. in Asian populations. For all three operationalizations, the methods of measurement applied by individual studies will be used. When studies report mixed samples of older adults with overweight and obesity, we will contact the authors to request the data for the subgroup with obesity. If the provision of data is not possible, the study will be excluded. No consensus definition of sarcopenic obesity exists and various operationalisations are in use.[9] As such, the definition applied by the primary study will be used, and we shall acknowledge differences in potential sub-group or sensitivity analyses, if possible. Due to the high prevalence of multimorbidity in older people and existing obesity-related co-morbidities, participants with common comorbidities of obesity (e.g. diabetes, cardiovascular, metabolic syndrome, chronic kidney disease, osteoarthritis and geriatric syndromes (e.g. frailty and sarcopenia)) will be included. We will only include studies comprising community-dwelling older adults, due to the predictive value of obesity for nursing home admissions.[80] Studies focusing on animals,

genetics or biochemistry will be excluded. References that have not been included after full-text screening will be listed in a table with the respective reason(s) for exclusion.

Interventions

We will include any type of lifestyle intervention, e.g. diet, exercise, self-management, as well as all treatment modalities and their combinations with all types of deliveries and doses. For the dietary component, interventions affecting energy balance, such as energy restriction, balanced (healthy) diet (e.g. food pyramid), Mediterranean diet, high-protein diet, low-fat diet, moderate-carbohydrate diet, low-carbohydrate diet, low glycaemic index/glycaemic load diet, vegetarian diet, DASH-diet will be considered. Interventions providing only micronutrient supplements (e.g. Vitamin D) as well as studies using only very low energy diets (<800 kcal/day) or total diet replacement will be excluded.[81] Additionally, RCTs focussing on substances such as secondary plant products (e.g. polyphenols), components of macronutrients (e.g. fatty (docosahexaenoic acid) or amino acids (e.g. leucin)) and fibres will also be excluded. The exercise component will be defined as any planned, structured, and repetitive movement with the objective to improve or maintain physical fitness, e.g. aerobic, resistance, balance training, according to the definition of the American College of Sports Medicine.[82] We will also consider physically supported methods, such as electrical muscle stimulation and vibration training when combined with gross movements or done in an upright position. Finally, as recommended in obesity guidelines[83] we will include all self-management interventions that intend to support behaviour changes (such as motivational interviewing, social support, cognitive-therapeutic intervention).[84] This is owed to the fact that many (older) people with chronic diseases (such as diabetes or obesity) have difficulties to control intended behavioural changes (such as improving eating behaviour, increasing physical activity and decreasing sedentary time).[85] In addition, self-efficacy, self-regulation skills were found important mediators for successful weight-change.[86]

Comparators

Since NMA will be conducted, all interventions will be compared to each other. Additionally, control groups, such as usual care or health counselling, will be considered as comparators.

Outcomes

Only previously validated outcomes will be considered and need to be measured at least pre- and post-intervention.

Main Outcome

The change in **functional status** with focus on physical function was shown to be important to health and adverse outcomes[24 25] and patient-relevant[71] and will therefore be our main outcome. This includes standard measures of strength, mobility and functional performance for independence in daily living, including their modifications. Common measurements include but are not limited to one-leg stance (balance), gait speed (gait, mobility), 6-min-walk test (endurance), repeated chair stands (functional strength, lower extremity function), grip strength (strength, overall function), leg power as well as composite scores of functional tests such as the Short-Physical-Performance-Battery (SPPB)[25] or the Physical Performance Test (PPT).[87] Patient-reported outcomes of functional status (e.g. Late-Life Function and Disability Instrument (LLFDI)) and digital measurements (e.g. instrumented gait analysis) will also be considered.

Other outcomes

To evaluate changes in **weight and body composition**, we will consider measures such as total body mass, fat mass (e.g. total, central, peripheral), lean mass, muscle mass (e.g. total, appendicular, lower extremity skeletal), bone mineral density (e.g. hip, lumbar spine, whole body).

(Health-related) quality of life will be summarised when reported by standardized instruments such as 36-Item Short Form Survey (SF-36)[88] or EuroQol-5D (EQ-5D).[89] If reported in primary studies, **emotional status** (e.g. depressive symptoms, depression), **social participation** (e.g. informal social relationships, community life) and satisfaction with intervention will also be captured.

Data on the occurrence of mortality, falls, fractures, hospital admission and nursing home placement as well as for other health-related event data (e.g. hypoglycaemia, hypotension), no matter if reported as outcome or adverse event, will also be considered for the current analysis.

Design of primary studies

We will include (quasi-) RCTs (parallel and cross-over). Due to a lower level of initial fitness, prevalent health restrictions and the time needed to respond to treatment, we will include studies with intervention durations of ≥12 weeks.[50]

We will not set any restrictions regarding language or time frame. We will involve colleagues who are fluent in the respective languages or use online translators (e. g. https://www.deepl.com/home).

Conference abstracts will be excluded.

Search strategy

Six electronic databases (Medline, Embase, Cochrane Central, CINAHL, PsychInfo and Web of Science) for published trials and two trial registries (Clinicaltrials.gov, WHO International Clinical Trials Registry Platform) for unpublished or ongoing trials will be searched. We developed the search strategy for Medline (via Ovid) (see online supplementary file 2) using a search block for people aged ≥65 years and adapted a block for interventions from a recently published Cochrane review evaluating lifestyle interventions in paediatric patients with overweight and obesity, which was reviewed and revised by information specialists.[90] For other databases, the search strategy will be adapted according to the database-specific requirements. Additionally, we will screen reference lists of published SRs and eligible RCTs for potential consideration of further primary RCTs and will contact the advisory board which consists of clinical and scientific experts to enquire whether all relevant studies were identified.

Selection process

Identified references will be saved in Endnote and after excluding duplicates, references will be uploaded to Covidence (http://www.covidence.org). Two reviewers (GT, DS) will independently screen titles/abstracts and full-texts for eligibility according to the criteria described above. The title/abstract screening will be piloted using the first 200 references and in case of too many deviations (>10%), it will be revised. Disagreements will be solved by discussion or if no consensus can be reached by a third reviewer who will be asked based on his/her expertise (nutrition/general (EK), exercise (WK), self-management (NSB)). If relevant information is lacking, we will contact the corresponding author/s twice at a weekly interval.

Data extraction

Two reviewers (GT, DS) will extract data of included references independently using a piloted data extraction table. In case of no consensus, a third reviewer (based on expertise) will solve disagreements. If relevant data is missing, we will contact the corresponding author/s twice at weekly intervals.

When extracting the data, we will consider the following information:

study characteristics: e.g. author, publication year, eligibility criteria, setting, study duration, sample size, follow-up time, conflict of interest;

participants' characteristics: e.g. age, sex, ethnicity, BMI, body composition (e.g. fat mass, muscle mass, height/weight adjusted indices), comorbidities (e.g. diabetes, cardiovascular disease), geriatric syndromes (e.g. sarcopenia, frailty, cognitive impairment), functional status, lifestyle behaviour (e.g. sedentary);

intervention characteristics: type and modality, type of delivery, dose (e.g. duration, frequency, intensity), control arms, co-interventions, compliance and adherence, drop out, (serious) adverse events related to intervention;

outcomes: baseline values and follow-up values of functional status, BMI, weight, body composition (lean mass, fat mass), quality of life, emotional status, social participation and any reported poor health outcome as reported by study authors.

Assessment of risk of bias

The risk of bias will be assessed after a pilot trial (n=3) by two reviewers (GT, DS; not blinded to authors and journal of primary studies) independently using the revised Cochrane risk of bias tool (RoB 2.0) for RCTs.[91 92] According to this, sources of bias will be identified by assessing: i) the randomization process, ii) deviations from intended interventions, iii) missing outcome data, iv) measurement of the outcome and v) selection of the reported result. For each domain, available algorithms will be followed to answer the signalling questions (response options: yes, probably yes, probably no, no, or no information) and to judge the risk of bias as low, some concerns, or high. The overall risk of bias will also be rated as low (if low risk of bias in all domains), some concerns (at least one domain is rated as having some concerns but no domain is rated by a high risk of bias), or high (if at least one domain is judged with a high risk of bias or multiple domains are rated as having some concerns which might impact the confidence in a result). We will present results in a risk of bias summary graph.

Assessment of certainty of evidence

Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach for NMA will be used to assess the certainty of evidence.[93-95] In addition to the risk of bias rating for every outcome, this includes the rating of direct and indirect evidence for inconsistency, indirectness and dissemination bias. In case of high certainty and a similar contribution of direct and indirect evidence to the network estimate, the highest rating will be used but could be further down-rated for incoherence and imprecision. In case of insufficient evidence as well as moderate, low or very low certainty, the indirect estimate will be rated by the lowest of two direct comparisons included in first-order loops and could be

further down-rated for intransitivity. Dissemination bias will be investigated by searching for unpublished trials (see section search strategies). 'Summary of Findings' tables adapted for NMA results will be presented, similar to the proposal by Yepes-Nuñez at al.[96]

Statistical analyses

Measures of treatment effect

Effect sizes for continuous outcomes (e.g. weight loss, muscle strength) will be expressed as mean difference (MD) or standardised mean difference (SMD) with 95% confidence intervals (95%-CI). For dichotomous outcomes (e.g. negative health outcome such as death), effect sizes will be expressed as risk ratios (RR) with 95%-CI.[97] In exceptional cases (i.e. if a minor number of RCTs expressed an negative health outcome continuously while the majority used dichotomous outcomes), the outcomes reported as continuous or categorical will be dichotomized.[98] If the post-intervention values with the corresponding standard deviation (SD) are not available, the changed scores with the corresponding SD will be used.[99]

Data synthesis

We will conduct random effects model network meta-analyses (NMA) based on a frequentist approach to derive pooled estimates for all outcomes.[100] We will use the R package 'netmeta'.[101] In NMA, evidence from direct comparisons and indirect comparisons is averaged to calculate a network estimate. The key requirement for conducting NMA is that the transitivity assumption - to compare two interventions via an indirect route in the network - is ensured. We assume that for our planned analyses, all interventions are jointly randomisable[73] [102] and that all participants are likely to receive any kind of included interventions. Network graphs will be generated by function *netgraph()* of netmeta.[101] [103] We will assess global incoherence by decomposing the Q statistic into heterogeneity (within designs) and inconsistency (between designs) and visualise this using a net-heat plot.[104] In addition, We will report and assess inconsistency by calculating differences between direct and indirect effect estimates using descriptive z-tests (function *netsplit()*) and report the distribution of direct and indirect evidence. The treatment modalities (e.g. very low caloric diet, aerobic exercise, their combination or no intervention (e.g. health counselling, healthy eating/ exercise advise)) will build the nodes of the network providing maximizing similarity within and minimizing similarity between the nodes.[93] To further identify important determinants of efficacy and safety, nodes will be further defined, e.g. according to the duration, intensity, mode of delivery of interventions.[105] Based on data availability, these

nodes will be defined after data extraction. Additionally, we will analyse the components (e.g. of combined interventions using an additive model for multicomponent interventions.[106] Models of this type allow disentangling the effects of all single components (e.g. very low caloric diet (A), aerobic exercise (B), behavioural group counselling (C)) of a multicomponent intervention arm consisting of at least two single components (e.g. A+B, A+C, B+C or A+B+C). Since we do not believe that lifestyle interventions that are available for treatment of obesity may fulfil the additivity assumption for component NMA (CNMA) – i.e. the effect of a multicomponent intervention equals the sum of their components without any interactions – we will use the interaction CNMA model which is implemented in the function *netcomb()* of netmeta.[101 106] In the case of disconnected networks, we will reconnect the networks if possible (i.e. presence of at least one common component in the subnetworks). This feature of CNMA is also implemented in netmeta (function *discomb()*).

A secondary data analysis will be conducted using intervention types as network nodes (e.g. diet, exercise, self-management). Results of NMA will be presented as forest plots. We will present league tables containing relative treatment effects for all direct comparisons (function *netleague()*) and a ranking of all treatments by P-scores.[107]

Sensitivity and subgroup analyses

If possible, sensitivity analyses will be conducted by only including studies rated as low risk of bias. We will try to conduct subgroup analyses for type of obesity (sarcopenic obesity vs obesity), intervention duration (</> 6 months), age (</> 75 years), sex, BMI-group (</> 35 kg/m^2) and co-morbidities, such as diabetes or metabolic syndrome and frailty status. Patients' characteristics for subgroup analysis were selected based on the assumption that lifestyle interventions might work differently in people who differ in aspects like vulnerability, resilience and body composition.

Patient and public involvement

Before the start of this NMA, we have conducted and are currently analysing a qualitative study with semi-structured interviews in older persons with obesity. The aim is to obtain further information on patients' motives, barriers, experiences and perceptions regarding therapeutic lifestyle interventions and thus, potentially identify evidence gaps. The results will be published in a separate manuscript.

In addition, we discuss patient-relevant outcomes, existing obstacles that exacerbate the process of contacting this population of patients as well as potential dissemination strategies with representatives of German patient advocate groups.

Ethics and dissemination

For NMA, there is no direct data collection from human participants and hence, no ethical approval is necessary.

We will submit our research articles to peer-reviewed journals and will present our results at national and international conferences. Involved experts will disseminate the results in scientific and medical societies. We will further disseminate our project via partner universities' websites and press releases. Patient-targeted dissemination will involve local and national advocate groups and offices for senior affairs. In addition, we will disseminate the results by distribution of materials in plain language.

Full references

1. WHO. Obesity and overweight. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight accessed 08.08.2020.
2. Collaborators GBDO, Afshin A, Forouzanfar MH, et al. Health Effects of Overweight and Obesity in 195 Countries over 25 Years. *N Engl J Med* 2017;377(1):13-27. doi: 10.1056/NEJMoa1614362 [published Online First: 2017/06/12]
3. He W, Goodkind D, Kowal P. U.S. Census Bureau, International Population Reports, P95/16-1, An Aging World: 2015, U.S. Government Publishing Office, Washington, DC, 2016.
4. Hales CM, Fryar CD, Carroll MD, et al. Trends in Obesity and Severe Obesity Prevalence in US Youth and Adults by Sex and Age, 2007-2008 to 2015-2016. *JAMA* 2018;319(16):1723-25. doi: 10.1001/jama.2018.3060
5. Batsis JA, Mackenzie TA, Bartels SJ, et al. Diagnostic accuracy of body mass index to identify obesity in older adults: NHANES 1999-2004. *Int J Obes (Lond)* 2016;40(5):761-67. doi: 10.1038/ijo.2015.243 [published Online First: 2015/12/01]
6. Germain CM, Vasquez E, Batsis JA. Physical Activity, Central Adiposity, and Functional Limitations in Community-Dwelling Older Adults. *J Geriatr Phys Ther* 2016;39(2):71-76. doi: 10.1519/JPT.0000000000000051
7. Kemmler W, Teschler M, Weißenfels A, et al. Prevalence of sarcopenia and sarcopenic obesity in older German men using recognized definitions: high accordance but low overlap! *Osteoporos Int* 2017;28(6):1881-91. doi: 10.1007/s00198-017-3964-9 [published Online First: 2017/02/20]
8. Kemmler W, von Stengel S, Engelke K, et al. Prevalence of sarcopenic obesity in Germany using established definitions: Baseline data of the FORMOsA study. *Osteoporos Int* 2016;27(1):275-81. doi: 10.1007/s00198-015-3303-y [published Online First: 2015/08/29]
9. Batsis JA, Barre LK, Mackenzie TA, et al. Variation in the prevalence of sarcopenia and sarcopenic obesity in older adults associated with different research definitions: dual-

energy X-ray absorptiometry data from the National Health and Nutrition Examination Survey 1999-2004. *J Am Geriatr Soc* 2013;61(6):974-80. doi: 10.1111/jgs.12260 [published Online First: 2013/05/06]

10. Atkins JL, Whincup PH, Morris RW, et al. Sarcopenic obesity and risk of cardiovascular disease and mortality: a population-based cohort study of older men. *J Am Geriatr Soc* 2014;62(2):253-60. doi: 10.1111/jgs.12652 [published Online First: 2014/01/15]
11. Global BMIMC, Di Angelantonio E, Bhupathiraju S, et al. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet* 2016;388(10046):776-86. doi: 10.1016/S0140-6736(16)30175-1 [published Online First: 2016/07/13]
12. Laxy M, Teuner C, Holle R, et al. The association between BMI and health-related quality of life in the US population: sex, age and ethnicity matters. *Int J Obes (Lond)* 2018;42(3):318-26. doi: 10.1038/ijo.2017.252 [published Online First: 2017/10/10]
13. Cho Y, Shin S-Y, Shin M-J. Sarcopenic obesity is associated with lower indicators of psychological health and quality of life in Koreans. *Nutr Res* 2015;35(5):384-92. doi: 10.1016/j.nutres.2015.04.002 [published Online First: 2015/04/10]
14. Greenberg JA. The obesity paradox in the US population. *Am J Clin Nutr* 2013;97(6):1195-200. doi: 10.3945/ajcn.112.045815 [published Online First: 2013/05/03]
15. Romero-Corral A, Montori VM, Somers VK, et al. Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. *Lancet* 2006;368(9536):666-78. doi: 10.1016/s0140-6736(06)69251-9 [published Online First: 2006/08/22]
16. Whelton SP, McAuley PA, Dardari Z, et al. Association of BMI, Fitness, and Mortality in Patients With Diabetes: Evaluating the Obesity Paradox in the Henry Ford Exercise Testing Project (FIT Project) Cohort. *Diabetes Care* 2020;43(3):677-82. doi: 10.2337/dc19-1673 [published Online First: 2020/01/18]
17. Badrick E, Sperrin M, Buchan IE, et al. Obesity paradox and mortality in adults with and without incident type 2 diabetes: a matched population-level cohort study. *BMJ Open Diabetes Res Care* 2017;5(1):e000369. doi: 10.1136/bmjdrc-2016-000369 [published Online First: 2017/03/23]
18. Banack HR, Kaufman JS. The "obesity paradox" explained. *Epidemiology* 2013;24(3):461-2. doi: 10.1097/EDE.0b013e31828c776c [published Online First: 2013/04/04]
19. Preston SH, Stokes A. Obesity paradox: conditioning on disease enhances biases in estimating the mortality risks of obesity. *Epidemiology* 2014;25(3):454-61. doi: 10.1097/ede.0000000000000075 [published Online First: 2014/03/13]
20. Villareal DT, Apovian CM, Kushner RF, et al. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. *Obes Res* 2005;13(11):1849-63. doi: 10.1038/oby.2005.228
21. Silverwood V, Blagojevic-Bucknall M, Jinks C, et al. Current evidence on risk factors for knee osteoarthritis in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage* 2015;23(4):507-15. doi: 10.1016/j.joca.2014.11.019 [published Online First: 2014/11/29]
22. Cross M, Smith E, Hoy D, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. *Ann Rheum Dis* 2014;73(7):1323-30. doi: 10.1136/annrheumdis-2013-204763 [published Online First: 2014/02/19]
23. Schaap LA, Koster A, Visser M. Adiposity, muscle mass, and muscle strength in relation to functional decline in older persons. *Epidemiol Rev* 2013;35:51-65. doi: 10.1093/epirev/mxs006 [published Online First: 2012/12/04]

24. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci* 2000;55(4):M221-M31. doi: 10.1093/gerona/55.4.m221
25. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* 1994;49(2):M85-M94. doi: 10.1093/geronj/49.2.m85
26. Baumgartner RN, Wayne SJ, Waters DL, et al. Sarcopenic obesity predicts instrumental activities of daily living disability in the elderly. *Obes Res* 2004;12(12):1995-2004. doi: 10.1038/oby.2004.250
27. Rolland Y, Lauwers-Cances V, Cristini C, et al. Difficulties with physical function associated with obesity, sarcopenia, and sarcopenic-obesity in community-dwelling elderly women: the EPIDOS (EPIDemiologie de l'OSteoporose) Study. *Am J Clin Nutr* 2009;89(6):1895-900. doi: 10.3945/ajcn.2008.26950 [published Online First: 2009/04/15]
28. Himes CL, Reynolds SL. Effect of obesity on falls, injury, and disability. *J Am Geriatr Soc* 2012;60(1):124-29. doi: 10.1111/j.1532-5415.2011.03767.x [published Online First: 2011/12/08]
29. Scott D, Chandrasekara SD, Laslett LL, et al. Associations of Sarcopenic Obesity and Dynapenic Obesity with Bone Mineral Density and Incident Fractures Over 5-10 Years in Community-Dwelling Older Adults. *Calcif Tissue Int* 2016;99(1):30-42. doi: 10.1007/s00223-016-0123-9 [published Online First: 2016/03/04]
30. Follis S, Cook A, Bea JW, et al. Association Between Sarcopenic Obesity and Falls in a Multiethnic Cohort of Postmenopausal Women. *J Am Geriatr Soc* 2018;66(12):2314-20. doi: 10.1111/jgs.15613 [published Online First: 2018/10/30]
31. Scott D, Seibel M, Cumming R, et al. Sarcopenic Obesity and Its Temporal Associations With Changes in Bone Mineral Density, Incident Falls, and Fractures in Older Men: The Concord Health and Ageing in Men Project. *J Bone Miner Res* 2017;32(3):575-83. doi: 10.1002/jbmr.3016 [published Online First: 2016/11/03]
32. Zizza CA, Herring A, Stevens J, et al. Obesity affects nursing-care facility admission among whites but not blacks. *Obes Res* 2002;10(8):816-23. doi: 10.1038/oby.2002.110
33. Alley DE, Ferrucci L, Barbagallo M, et al. A research agenda: the changing relationship between body weight and health in aging. *J Gerontol A Biol Sci Med Sci* 2008;63(11):1257-59. doi: 10.1093/gerona/63.11.1257
34. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56(3):M146-M56. doi: 10.1093/gerona/56.3.m146
35. Rockwood K, Stadnyk K, MacKnight C, et al. A brief clinical instrument to classify frailty in elderly people. *Lancet* 1999;353(9148):205-06. doi: 10.1016/S0140-6736(98)04402-X
36. Kent S, Fusco F, Gray A, et al. Body mass index and healthcare costs: a systematic literature review of individual participant data studies. *Obes Rev* 2017;18(8):869-79. doi: 10.1111/obr.12560 [published Online First: 2017/05/22]
37. Calculating the costs of the consequences of obesity 2017. Available from: https://www.worldobesity.org/resources/resource-library/calculating-the-costs-of-the-consequences-of-obesity accessed 08.08.2020.
38. Alfadda AA, Al-Dhwayan MM, Alharbi AA, et al. The Saudi clinical practice guideline for the management of overweight and obesity in adults. *Saudi Med J* 2016;37(10):1151-62. doi: 10.15537/smj.2016.10.14353

39. Hauner H, Moss A, Berg A, et al. Interdisziplinäre Leitlinie der Qualität S3 zur „Prävention und Therapie der Adipositas". *Adipositas-Ursachen, Folgeerkrankungen, Therapie* 2014;8(04):179-221.
40. Kushner RF, Ryan DH. Assessment and lifestyle management of patients with obesity: clinical recommendations from systematic reviews. *JAMA* 2014;312(9):943-52. doi: 10.1001/jama.2014.10432
41. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. *N Engl J Med* 2011;364(13):1218-29. doi: 10.1056/NEJMoa1008234 [published Online First: 2011/04/01]
42. Porter Starr KN, Pieper CF, Orenduff MC, et al. Improved Function With Enhanced Protein Intake per Meal: A Pilot Study of Weight Reduction in Frail, Obese Older Adults. *J Gerontol A Biol Sci Med Sci* 2016;71(10):1369-75. doi: 10.1093/gerona/glv210 [published Online First: 2016/01/21]
43. Villareal DT, Aguirre L, Gurney AB, et al. Aerobic or Resistance Exercise, or Both, in Dieting Obese Older Adults. *N Engl J Med* 2017;376(20):1943-55. doi: 10.1056/NEJMoa1616338 [published Online First: 2017/05/18]
44. Miller GD, Nicklas BJ, Davis C, et al. Intensive weight loss program improves physical function in older obese adults with knee osteoarthritis. *Obesity (Silver Spring)* 2006;14(7):1219-30. doi: 10.1038/oby.2006.139 [published Online First: 2006/08/11]
45. Cetin DC, Nasr G. Obesity in the elderly: more complicated than you think. *Cleve Clin J Med* 2014;81(1):51-61. doi: 10.3949/ccjm.81a.12165
46. Weinheimer EM, Sands LP, Campbell WW. A systematic review of the separate and combined effects of energy restriction and exercise on fat-free mass in middle-aged and older adults: implications for sarcopenic obesity. *Nutr Rev* 2010;68(7):375-88. doi: 10.1111/j.1753-4887.2010.00298.x
47. Soltani S, Hunter GR, Kazemi A, et al. The effects of weight loss approaches on bone mineral density in adults: a systematic review and meta-analysis of randomized controlled trials. *Osteoporos Int* 2016;27(9):2655-71. doi: 10.1007/s00198-016-3617-4 [published Online First: 2016/05/06]
48. Mathus-Vliegen EMH, Obesity Management Task Force of the European Association for the Study of O. Prevalence, pathophysiology, health consequences and treatment options of obesity in the elderly: a guideline. *Obes Facts* 2012;5(3):460-83. doi: 10.1159/000341193 [published Online First: 2012/06/30]
49. Volkert D, Beck AM, Cederholm T, et al. ESPEN guideline on clinical nutrition and hydration in geriatrics. *Clin Nutr* 2019;38(1):10-47. doi: 10.1016/j.clnu.2018.05.024 [published Online First: 2018/06/18]
50. Brawley LR, Rejeski WJ, King AC. Promoting physical activity for older adults: the challenges for changing behavior. *Am J Prev Med* 2003;25(3 Suppl 2):172-83. doi: 10.1016/s0749-3797(03)00182-x
51. American College of Cardiology/American Heart Association Task Force on Practice Guidelines OEP. Expert Panel Report: Guidelines (2013) for the management of overweight and obesity in adults. *Obesity (Silver Spring)* 2014;22 Suppl 2:S41-S410. doi: 10.1002/oby.20660
52. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation* 2014;129(25 Suppl 2):S102-S38. doi: 10.1161/01.cir.0000437739.71477.ee [published Online First: 2013/11/12]

53. Bales CW, Buhr G. Is obesity bad for older persons? A systematic review of the pros and cons of weight reduction in later life. *J Am Med Dir Assoc* 2008;9(5):302-12. doi: 10.1016/j.jamda.2008.01.006
54. Batsis JA, Gill LE, Masutani RK, et al. Weight Loss Interventions in Older Adults with Obesity: A Systematic Review of Randomized Controlled Trials Since 2005. *J Am Geriatr Soc* 2017;65(2):257-68. doi: 10.1111/jgs.14514 [published Online First: 2016/09/19]
55. Bouaziz W, Schmitt E, Kaltenbach G, et al. Health benefits of endurance training alone or combined with diet for obese patients over 60: a review. *Int J Clin Pract* 2015;69(10):1032-49. doi: 10.1111/ijcp.12648 [published Online First: 2015/05/11]
56. Felix HC, West DS. Effectiveness of weight loss interventions for obese older adults. *Am J Health Promot* 2013;27(3):191-99. doi: 10.4278/ajhp.110617-LIT-259
57. Haywood C, Sumithran P. Treatment of obesity in older persons-A systematic review. *Obes Rev* 2019;20(4):588-98. doi: 10.1111/obr.12815 [published Online First: 2019/01/15]
58. McTigue KM, Hess R, Ziouras J. Obesity in older adults: a systematic review of the evidence for diagnosis and treatment. *Obesity (Silver Spring)* 2006;14(9):1485-97. doi: 10.1038/oby.2006.171
59. Poggiogalle E, Migliaccio S, Lenzi A, et al. Treatment of body composition changes in obese and overweight older adults: insight into the phenotype of sarcopenic obesity. *Endocrine* 2014;47(3):699-716. doi: 10.1007/s12020-014-0315-x [published Online First: 2014/06/22]
60. Porter Starr KN, McDonald SR, Bales CW. Obesity and physical frailty in older adults: a scoping review of lifestyle intervention trials. *J Am Med Dir Assoc* 2014;15(4):240-50. doi: 10.1016/j.jamda.2013.11.008 [published Online First: 2014/01/17]
61. Rejeski WJ, Marsh AP, Chmelo E, et al. Obesity, intentional weight loss and physical disability in older adults. *Obes Rev* 2010;11(9):671-85. doi: 10.1111/j.1467-789X.2009.00679.x
62. Waters DL, Ward AL, Villareal DT. Weight loss in obese adults 65years and older: a review of the controversy. *Exp Gerontol* 2013;48(10):1054-61. doi: 10.1016/j.exger.2013.02.005 [published Online First: 2013/02/10]
63. Witham MD, Avenell A. Interventions to achieve long-term weight loss in obese older people: a systematic review and meta-analysis. *Age Ageing* 2010;39(2):176-84. doi: 10.1093/ageing/afp251 [published Online First: 2010/01/18]
64. Greaves C, Poltawski L, Garside R, et al. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. *Health Psychol Rev* 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583 [published Online First: 2017/04/07]
65. Catalogue of Bias Collaboration, Brassey J, Spencer EA, Heneghan C. Langauge bias. In: Catalogue Of Bias 2017. Available from: https://catalogofbias.org/biases/language-bias/ accessed 08.08.2020.
66. Puljak L. If there is only one author or only one database was searched, a study should not be called a systematic review. *J Clin Epidemiol* 2017;91:4-5. doi: 10.1016/j.jclinepi.2017.08.002 [published Online First: 2017/08/18]
67. Ard JD, Gower B, Hunter G, et al. Effects of Calorie Restriction in Obese Older Adults: The CROSSROADS Randomized Controlled Trial. *J Gerontol A Biol Sci Med Sci* 2017;73(1):73-80. doi: 10.1093/gerona/glw237
68. Beavers KM, Nesbit BA, Kiel JR, et al. Effect of an Energy-Restricted, Nutritionally Complete, Higher Protein Meal Plan on Body Composition and Mobility in Older Adults

With Obesity: A Randomized Controlled Trial. *J Gerontol A Biol Sci Med Sci* 2019;74(6):929-35. doi: 10.1093/gerona/gly146

69. Cumpston M, Li T, Page MJ, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database Syst Rev* 2019;10:ED000142-ED42. doi: 10.1002/14651858.ED000142
70. Higgins JPT TJ, Chandler J, Cumpston M, Li T, Page MJ, Welch VA. (editors). Cochrane Handbook for Systematic Reviews of Interventions. 2nd Edition: Chichester (UK): John Wiley & Sons 2019.
71. Jackson SE, Holter L, Beeken RJ. 'Just because I'm old it doesn't mean I have to be fat': a qualitative study exploring older adults' views and experiences of weight management. *BMJ Open* 2019;9(2):e025680-e80. doi: 10.1136/bmjopen-2018-025680
72. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4(1):1-1. doi: 10.1186/2046-4053-4-1
73. Chaimani A, Caldwell DM, Li T, et al. Additional considerations are required when preparing a protocol for a systematic review with multiple interventions. *J Clin Epidemiol* 2017;83:65-74. doi: 10.1016/j.jclinepi.2016.11.015 [published Online First: 2017/01/11]
74. Shenkin SD, Harrison JK, Wilkinson T, et al. Systematic reviews: guidance relevant for studies of older people. *Age Ageing* 2017;46(5):722-28. doi: 10.1093/ageing/afx105
75. Torbahn G, Schoene D, Schwingshackl L, et al. EffectiveSLOPE: EffectS of Lifestyle interventions in Obese older PEople – a systematic review and network meta-analysis. PROSPERO 2019 CRD42019147286 2019. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019147286 accessed 08.08.2020.
76. NHS England. Improving care for older people. Available from: https://www.england.nhs.uk/ourwork/clinical-policy/older-people/improving-care-for-older-people/ accessed 08.08.2020.
77. World Health Organisation. Physical Status: The use and interpreation of anthropometry. Technical Report Series 854,Geneva, 1995.
78. Han TS, van Leer EM, Seidell JC, et al. Waist circumference action levels in the identification of cardiovascular risk factors: prevalence study in a random sample. *BMJ* 1995;311(7017):1401-05. doi: 10.1136/bmj.311.7017.1401
79. Batsis JA, Zagaria AB. Addressing Obesity in Aging Patients. *Med Clin North Am* 2018;102(1):65-85. doi: 10.1016/j.mcna.2017.08.007 [published Online First: 2017/10/21]
80. Valiyeva E, Russell LB, Miller JE, et al. Lifestyle-related risk factors and risk of future nursing home admission. *Arch Intern Med* 2006;166(9):985-90. doi: 10.1001/archinte.166.9.985
81. Astbury NM, Piernas C, Hartmann-Boyce J, et al. A systematic review and meta-analysis of the effectiveness of meal replacements for weight loss. *Obes Rev* 2019;20(4):569-87. doi: 10.1111/obr.12816 [published Online First: 2019/01/24]
82. American College of Sports M, Chodzko-Zajko WJ, Proctor DN, et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc* 2009;41(7):1510-30. doi: 10.1249/MSS.0b013e3181a0c95c
83. National Health and Medical Research Council (2013) Clinical practice guidelines for the management of overweight and obesity in adults, adolescents and children in Australia. Melbourne: National Health and Medical Research Council. Available from:

https://www.nhmrc.gov.au/about-us/publications/clinical-practice-guidelines-management-overweight-and-obesity#block-views-block-file-attachments-content-block-1 accessed 08.08.2020.

84. Wong SKW, Smith HE, Chua JJS, et al. Effectiveness of self-management interventions in young adults with type 1 and 2 diabetes: a systematic review and meta-analysis. *Diabet Med* 2020;37(2):229-41. doi: 10.1111/dme.14190 [published Online First: 2019/11/27]
85. Stutzer A, Meier AN. Limited Self-control, Obesity, and the Loss of Happiness. *Health Econ* 2016;25(11):1409-24. doi: 10.1002/hec.3227 [published Online First: 2015/09/01]
86. Teixeira PJ, Carraça EV, Marques MM, et al. Successful behavior change in obesity interventions in adults: a systematic review of self-regulation mediators. *BMC Med* 2015;13:84. doi: 10.1186/s12916-015-0323-6 [published Online First: 2015/04/25]
87. Reuben DB, Siu AL. An objective measure of physical function of elderly outpatients. The Physical Performance Test. *J Am Geriatr Soc* 1990;38(10):1105-12. doi: 10.1111/j.1532-5415.1990.tb01373.x
88. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30(6):473-83.
89. EuroQol Group. EuroQol--a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16(3):199-208. doi: 10.1016/0168-8510(90)90421-9
90. Mead E, Brown T, Rees K, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese children from the age of 6 to 11 years. *Cochrane Database Syst Rev* 2017;6(6):CD012651-CD51. doi: 10.1002/14651858.CD012651
91. Recker RR, Davies KM, Dowd RM, et al. The effect of low-dose continuous estrogen and progesterone therapy with calcium and vitamin D on bone in elderly women. A randomized, controlled trial. *Ann Intern Med* 1999;130(11):897-904.
92. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:l4898-l98. doi: 10.1136/bmj.l4898
93. Reid IR, Ames RW, Evans MC, et al. Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: a randomized controlled trial [see comments]. *Am J Med* 1995;98(4):331-35.
94. Brignardello-Petersen R, Bonner A, Alexander PE, et al. Advances in the GRADE approach to rate the certainty in estimates from a network meta-analysis. *J Clin Epidemiol* 2018;93:36-44. doi: 10.1016/j.jclinepi.2017.10.005 [published Online First: 2017/10/17]
95. Puhan MA, Schünemann HJ, Murad MH, et al. A GRADE Working Group approach for rating the quality of treatment effect estimates from network meta-analysis. *BMJ* 2014;349:g5630-g30. doi: 10.1136/bmj.g5630
96. Yepes-Nuñez JJ, Li S-A, Guyatt G, et al. Development of the summary of findings table for network meta-analysis. *J Clin Epidemiol* 2019;115:1-13. doi: 10.1016/j.jclinepi.2019.04.018 [published Online First: 2019/05/02]
97. Deng HW, Stegman MR, Davies KM, et al. Genetic determination of variation and covariation of peak bone mass at the hip and spine. *J Clin Densitom* 1999;2(3):251-63.
98. Anzures-Cabrera J, Sarpatwari A, Higgins JP. Expressing findings from meta-analyses of continuous outcomes in terms of risks. *Stat Med* 2011;30(25):2967-85. doi: 10.1002/sim.4298 [published Online First: 2011/08/08]
99. Deeks JJ, Higgins JPT, Altman DG (editors). Chapter 10: Analysing data and undertaking meta-analyses. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.0

(updated July 2019). Cochrane, 2019. Available from www.training.cochrane.org/handbook.
100. Rücker G. Network meta-analysis, electrical networks and graph theory. *Res Synth Methods* 2012;3(4):312-24. doi: 10.1002/jrsm.1058 [published Online First: 2012/09/25]
101. Stern Y, Tang MX, Albert MS, et al. Predicting time to nursing home care and death in individuals with Alzheimer disease. *JAMA* 1997;277(10):806-12.
102. Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: many names, many benefits, many concerns for the next generation evidence synthesis tool. *Res Synth Methods* 2012;3(2):80-97. doi: 10.1002/jrsm.1037 [published Online First: 2012/06/11]
103. Rücker G, Schwarzer G. Automated drawing of network plots in network meta-analysis. *Res Synth Methods* 2016;7(1):94-107. doi: 10.1002/jrsm.1143
104. Krahn U, Binder H, König J. A graphical tool for locating inconsistency in network meta-analyses. *BMC Med Res Methodol* 2013;13:35-35. doi: 10.1186/1471-2288-13-35
105. Pillay J, Armstrong MJ, Butalia S, et al. Behavioral Programs for Type 2 Diabetes Mellitus: A Systematic Review and Network Meta-analysis. *Ann Intern Med* 2015;163(11):848-60. doi: 10.7326/m15-1400 [published Online First: 2015/09/29]
106. Rücker G, Petropoulou M, Schwarzer G. Network meta-analysis of multicomponent interventions. *Biom J* 2019:10.1002/bimj.201800167. doi: 10.1002/bimj.201800167
107. Rücker G, Schwarzer G. Ranking treatments in frequentist network meta-analysis works without resampling methods. *BMC Med Res Methodol* 2015;15:58-58. doi: 10.1186/s12874-015-0060-8

Authors' contributions

GT, DS and EK planned and designed this project, drafted the manuscript and approved the final version. LS, GR, HK, WK, CCS, JAB, DTV, NSB, and DV were involved in the planning and design process of this project, provided critical feedback for the manuscript and approved the final version. EK will be the guarantor of the review.

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Competing interests' statement

GT, DS, GR, HK, WK, CCS, DTV, NSB, DV & EK declare no conflict of interest. LS is a member of the GRADE working group. JAB is funded by the National Institute on Aging and Office of Dietary Supplements of the National Institutes of Health under Award Number K23AG051681, and the R01 AG067416. The funder had no role in preparing the protocol and manuscript.

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PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page(s)
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	n.a.
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2,7
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	21
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n.a.
Support:			
Sources	5a	Indicate sources of financial or other support for the review	21
Sponsor	5b	Provide name for the review funder and/or sponsor	21
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	21
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-6
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	6-7
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	7-10
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	10
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be	Supplementary

		repeated	file 2
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	10
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	10
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	10
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	10-11
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	8-9
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	11
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	12-13
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	12-13
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	12-13
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	n.a.
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	12
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	11-12

***It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

Database(s): Ovid MEDLINE(R) ALL

#	Searches
1	obesity/
2	obesity, morbid/
3	obesity, abdominal/
4	obesity, metabolically benign/
5	overweight/
6	(adipos* or obes* or overweight* or over weight*).ti,ab,kf.
7	or/1-6 [Obesity]
8	exp behavior therapy/
9	exp counseling/
10	social support/
11	program evaluation/
12	exp exercise/
13	exp exercise therapy/
14	exp "physical education and training"/
15	exp exercise movement techniques/
16	exp physical fitness/
17	accidental falls/
18	postural balance/
19	motor activity/
20	gait/
21	exp muscle strength/
22	exp diet/
23	exp diet therapy/
24	fasting/
25	food preferences/
26	patient education as topic/
27	health education/
28	exp health behavior/
29	exp health promotion/
30	life style/
31	((obesity adj3 intervention) or program or programme).ti,ab,kf.
32	(lifestyle or life style).ti,ab,kf.
33	exercis*.ti,ab,kf.
34	(physic* adj (activ* or fit*)).ti,ab,kf.

35	(walk* or swim* or aqua or cycl* or weight lift* or danc* or aerobics or balance or electric* muscle stimulation or neuromuscular electric* stimulation or electromyostimulation or ems).ti,ab,kf.
36	((physic* or strength* or resist* or circuit or weight or aerob* or cross or endurance or vibration*) adj3 train*).ti,ab,kf.
37	(behavio?ral or behavio?r modification* or psychoth* or psychosocial).ti,ab,kf.
38	((group or cognit* or behav*) adj therap*).ti,ab,kf.
39	counsel?ing.ti,ab,kf.
40	educat*.ti,ab,kf.
41	(diet* or healthy nutrition or (nutrition* adj (knowledge or educat* or therap* or program* or intervention*))).ti,ab,kf.
42	(low-calori* or calori* restrict* or low-energ* or energ* restrict* or low-carbohydrate or high-carbohydrate or low-fat or high-fat or low-protein or high-protein or vegetarian or vegan or mediterranean or dash).ti,ab,kf.
43	weight loss/
44	(weight adj1 (reduc* or los* or control* or manag*)).ti,ab,kf.
45	or/8-44 [Interventions]
46	obesity/ or obesity, abdominal/ or obesity, morbid/ or overweight/ or obesity, metabolically benign/
47	(diet therapy or prevention & control or rehabilitation or therapy or psychology).fs.
48	46 and 47 [MeSH/subheading combination]
49	exp weight reduction programs/
50	or/48-49 [Obesity-specific interventions]
51	7 and 45 [Obesity AND Interventions]
52	or/50-51 [Obesity interventions complete: (Obesity AND Interventions) OR Obesity-specific interventions]
53	exp aged/
54	geriatrics/
55	frailty/
56	sarcopenia/
57	Independent Living/
58	((old* or senior or age*) adj2 (adult* or person* or subject* or individual* or people or group* or m?n or wom?n or patient* or client* or outpatient* or citizen* or "60" or "65" or age*)).ti,ab,kf.
59	(elder* or eldes* or geriat* or geronto* or frail* or sarcopen* or senior* or agedly or ag?ing).ti,ab,kf.
60	community-dwell*.ti,ab,kf.
61	((commun* or indepen*) adj1 (dwell* or livi*)).ti,ab,kf.
62	(("60" or "65") adj1 year*).ti,ab,kf.
63	((advanc* or high*) adj1 age*).ti,ab,kf.

64	(super adj1 age*).ti,ab,kf.
65	(superage* or super-age* or centen* or centa* or nonagen* or octagen* or sept?agen* or supercenten* or senium*).ti,ab,kf.
66	or/53-65 [Age group]
67	randomized controlled trial.pt.
68	controlled clinical trial.pt.
69	randomi?ed.ab.
70	placebo.ab.
71	clinical trials as topic.sh.
72	randomly.ab.
73	trial.ti.
74	or/67-73
75	exp animals/ not humans.sh.
76	74 not 75 [Study filter (Cochrane Handbook v5.0.2 2008 RCT filter - sensitivity and precision maximizing version)]
77	52 and 66 [Obesity interventions complete AND Age group]
78	77 and 76 [Obesity interventions complete AND Age group AND Study filter]
79	(exp infant/ or exp child/ or adolescent/ or young adult/ or middle aged/) not exp aged/ [Child/adolescent/middle aged adults-only studies]
80	78 not 79 [Remove Child/adolescent/middle aged adults-only studies]