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IMPACT OF FOOD-BASED FORTIFICATION ON NUTRITIONAL INTAKE AND STATUS IN OLDER PEOPLE: A META-ANALYSIS - PROTOCOL

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ABSTRACT

Several studies have emphasized the crucial role of protein and energy in preventing adverse health outcomes in older adults such as sarcopenia and undernutrition. However, previous researches revealed that protein and energy intake often fall below recommended levels in older population. Given the prevalent shortfall in intake and associated health risks, interventions are needed to support older adults in meeting nutritional requirements. Food-based fortification, which involves enhancing the nutritional content of commonly consumed foods by adding essential nutrients (*i.e.* fortificants) emerges as a promising solution. Specifically, the concept of "do it yourself" (DIY) fortification presents a unique opportunity for older adults and their caregivers to tailor nutritional enhancements to individual preferences and eating habits. However, it remains underused and unknown. A recent systematic literature review identified 44 original studies (Geny et al., 2023), setting the stage for a meta-analysis on the impact of DIY fortification on nutritional intake and

status. Main eligibility criteria will include older adults aged ≥ 60 years living in various settings (at home, nursing home, hospital). Both randomized and non-randomized controlled trials will be considered. This meta-analysis aims to provide insights into the effectiveness of DIY fortification, offering a practical approach to enhance nutrition among older adults.

INTRODUCTION

Maintaining an adequate protein and energy intake in old age is an essential factor in preventing pathologies such as sarcopenia and undernutrition. *Sarcopenia* refers to the progressive loss of skeletal muscle mass that occurs with aging. Sarcopenia leads to a decline in muscle strength and function, resulting in reduced mobility and increased risk of falls and fractures (Santilli et al., 2014; Cruz-Jentoft et al., 2019). *Undernutrition* encompasses a condition marked by insufficient intake of energy and essential nutrients leading to an imbalance between the body's nutritional needs and its actual supply (Cederholm et al., 2017). While undernutrition can contribute to sarcopenia, it also extends to deficiencies affecting other organs and systems. Consequences of undernutrition extend beyond muscle health and may include weight loss, fatigue (Azzolino et al., 2020), weakened immune function and higher susceptibility to infections (Kawakami et al., 1999; Alam et al., 2019), cognitive impairment (Knopman et al., 2007; LeBlanc et al., 2017; Lee et al., 2020; Feng et al., 2022), increased risk and severity of chronic diseases (Norman et al., 2008), prolonged recovery times (Shpata et al., 2015), and increased mortality risk (Corti et al., 1994; Gentile et al., 2013; Sanchez-Rodriguez et al., 2020). For a long-term perspective, sarcopenia and undernutrition threaten both daily functioning, autonomy and health of older people (Norman et al., 2020).

Research consistently underscores the critical role of protein and energy in maintaining muscle mass and preventing these adverse health outcomes among older adults (Bauer et al., 2013; Deutz et al., 2014; Volkert et al., 2019). Despite its importance, several studies have revealed that protein and energy intake fall below recommended levels (Lesser et al., 2008). A review of protein intake in older adults in the UK shows that it falls below the recommendations for nutritionally vulnerable people. About a quarter of older women consume less than 45 g protein a day (Smith et al., 2022). A meta-analysis conducted by Ter

Borg et al. (2015) on 46 studies revealed that 10-12% of community-dwelling older adults do not meet the daily allowance for protein. In the longitudinal SENECA study, 247 Danish and Dutch people aged 70-75 were first surveyed and re-examined 4-5 years later. Results showed a significant decline in energy intake for both genders over the four years of follow-up (Schroll et al., 1997). In France, Fleury et al (2021) showed that 83% and 72% of older people receiving home-delivered meals fail to meet the daily allowance for energy and protein, respectively. The average deficit between recommended and total intakes was 872 kcal and 33 g protein.

Given the prevalent shortfall in protein and energy intake observed among the older adults and the potential adverse effects associated with it, there is a clear need for interventions to support older adults in meeting their nutritional requirements. One promising solution is the implementation of food-based fortification strategies (Morilla-Herrera et al., 2016; Olson et al., 2021). Food-based fortification involves enhancing the nutritional content of commonly consumed foods by adding essential nutrients (*i.e.* fortificants), in this case, focusing on protein and energy. This approach is designed to address nutritional deficiencies without significantly altering the volume of food to be ingested (HAS, 2007). While the food industry has introduced numerous fortified products, the concept of "do it yourself" (DIY) fortification (or home fortification - Olson et al., 2021) presents a unique opportunity for older adults and their caregivers to tailor nutritional enhancements to individual preferences and eating habits. Indeed, DIY fortification allows older individuals or their caregivers to incorporate essential nutrients into their regular meals. This flexibility is a notable advantage, for older adults who may face challenges in adopting changes to their consumption patterns. Nevertheless, the concept of DIY fortification continues to be underknown and underused among older adults, caregivers and healthcare professionals. Research on this strategy is limited and scarce, further contributing to the lack of awareness and implementation (Trabal & Farran-Codina, 2015; Morilla-Herrera et al., 2016; Douglas et al., 2017; Mills et al., 2018).

Recently, Geny et al. (2023) conducted a systematic literature review (SLR) of all studies related to the nutritional and acceptability aspects of DIY food-based fortification in older people. This review highlighted 137 distinct fortified recipes encompassing differences in the choice of food matrix (savory and sweet), fortificants (regular food ingredients and

macronutrient isolates or concentrates), and the additional load of protein and/or energy provided by fortified food compared to standard food. Building on this SLR, the current aim is to conduct a meta-analysis to assess the impact of DIY fortification on nutritional intake and status. This meta-analysis aims to provide a more quantitative and comprehensive understanding of the effects of DIY fortification, offering valuable insights into its potential contribution to improving nutrition.

MATERIALS AND METHODS

The protocol was drafted using the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols (PRISMA-P; Shamseer et al., 2015). The PRISMA checklist is presented in **Supplemental Table 1**. The protocol was deposited on PROSPERO with the registration number CRD42021244689.

PICOS question and eligibility criteria

We use a PICO framework for the formulation of our systematic review question (Methley et al., 2014). The differences between the eligibility criteria used in the systematic literature review (Geny et al., 2023) and the eligibility criteria used in the current meta-analysis are available on the **Supplemental Table 2**. For the current meta-analysis, the PICOS (Population, Intervention, Comparator, Outcome, Study design) eligibility criteria will be as follows:

Population. Any studies focusing on adults aged ≥ 60 years and any settings (home, nursing home, in hospital) will be relevant for inclusion. Older adults of all nutritional status, cognitive status and oral ability (*e.g.* chewing, swallowing) will be eligible for inclusion. Studies carried out in the context of a specific pathological condition (*e.g.* cardio rehabilitation, renal failure, cancers, diabetes) will be excluded.

Intervention. Only interventions exclusively testing DIY fortification in energy and/or protein will be eligible. Excluded from the review are: (a) interventions combining DIY food-based fortification with another enrichment strategy (*e.g.*, Oral Nutritional Supplements (ONS)),

and (b) intervention using fortified food products developed and marketed by the food industry.

Comparator. Eligible studies must include a DIY fortification intervention compared to either a control group or a control condition with no fortification (*i.e.*, standard diet). Studies lacking a comparator will be excluded.

Outcome. Two categories of outcomes will be considered: (a) assessment of the nutritional intake (protein and energy intake), and (b) evaluation of nutritional status (body weight, screening questionnaires such as the Mini-Nutritional Assessment Questionnaire (MNA; Guigoz et al., 2002), and blood levels of albumin and pre-albumin).

Study design. Randomized and non-randomized control trials will be eligible. All duration of follow-up will be eligible.

Other. No restriction will be set for the publication date. Only publications written in English will be included because of the uncertainty surrounding the words used to refer to the concept of “DIY food-based fortification” in foreign languages. Reviews, conference abstracts, editorials and grey literature will be excluded.

Search strategy

For the systematic literature review previously carried out by our laboratory (Geny et al., 2023), a search strategy with both thesaurus and free-text terms was developed after repeated attempts and adjustments to retrieve relevant articles in the following databases: Web of Science (WOS), PubMed and Scopus (**Supplemental Table 3**). Separate title, abstract and keywords searches were conducted for older people, food-based fortification and outcomes in February 2021. A first update was performed in January 2022 (Geny et al., 2023). A second update was performed in November 2023 for the purpose of the current meta-analysis. The reference lists of the included articles and those of relevant reviews will be screened manually for potentially relevant new articles.

Selection of articles

For the systematic literature review, the results for the three separate search strings were combined to identify relevant articles. After duplicates removal, article selection consisted of two screening phases. The first selection was based on title and abstract screening, and the second selection was based on a full-text screening. Screening was performed by two independent reviewers according to the inclusion and exclusion criteria. For each screening level, a training exercise was conducted before the starting of the screening process on a random sample of 100 titles and abstracts and 10 full texts to ensure high inter-reviewer reliability. Disagreements between reviewers were resolved by consensus or by consulting a third reviewer. This process led to the inclusion of 44 original studies (Geny et al., 2023). For the current meta-analysis, an additional screening will be done by two independent reviewers (AG and CSR) according to the eligibility criteria defined for the current meta-analysis. Disagreements between reviewers will be resolved by consensus or by consulting a third reviewer (VVW). The list of excluded studies and the reasons of exclusion will be presented (**Supplemental Table 4**).

Study characteristics and data extraction

The following characteristics will be extracted from all included studies by two reviewers (AG and CSR), independently, with conflicts resolved by a third reviewer (VVW):

- First author name, publication date, funding sources
- Experimental design
- Population: age, gender, setting
- Description of DIY fortification solutions: food matrices, fortificants, additional energy and/or protein load provided by fortified food
- Description of control condition
- Intervention period duration
- Outcomes and method of measuring outcomes

Outcome data will be collected for each individual comparison as the mean, standard deviation (SD) and number of participants per group. When standard error or confidence intervals are reported, the SD values will be recalculated. When the group size is reported as a range, the smallest number of participants will be used for the meta-analysis in the interest of conservative estimates. In cases where data are presented graphically, data will be extracted in pixels using a digital screen ruler. In cases of missing data, corresponding authors will be contacted to provide missing data or original data. If no author contact details are available or if no response was obtained from the authors within three weeks after repeated contact, the data will be omitted from the meta-analysis. Outcome data will be extracted from all included studies by a first author (CSR), and a second author will check that the extracted data are consistent with information reported in articles (AG). Conflicts will be resolved after discussion, and extracted figures will be again checked for consistency.

Risk of bias assessment

A risk of bias grid was developed to accommodate both randomized and non-randomized trials and to account for the specificity of a nutrition trials. This grid was adapted from the tools proposed by Cochrane (Risk-of-Bias tool for randomized trials, RoB 2: Sterne et al., 2019; Risk Of Bias In Non-randomized Studies – of Intervention tool, ROBINS-I: Sterne et al., 2016), the Critical Appraisal Skills Programme (CASP, 2021) and the American Dietetic Association Quality Criteria Checklist (ADA, 2005). A first step aimed to identify the common risks of bias that are applicable regardless of trial design (*e.g.*, classification of intervention, appropriateness of outcome measures, method to handle missing data, result reporting). A second step aimed to include criteria specific to randomization process (*e.g.*, allocation concealment) and to non-randomized studies (*e.g.*, appropriate control for confounding variables). The grid was tested on 10 articles randomly selected for the SLR (Geny et al., 2023) by two independent reviewers (CSR, VVW) and refined. The final grid includes 8 topics (**Supplemental Table 5**). Two reviewers will independently answer to all topic-related questions, each having four possible answers, “yes”, “some concerns”, “no” and “non-applicable” (Critical Appraisal Skills Program, Long et al., 2020). Conflicts in assessment will be resolved by checking the article until agreement between the two reviewers.

Data analysis

Individual effect sizes. As included studies may report post-intervention value scores (randomized controlled trial, parallel group trial) or change-from-baseline value scores (pre-post trial, crossover trial), individual size effects will be estimated by calculating Mean Difference (MD), according to Cochrane's recommendations (Higgins et al., 2023). In case of randomized controlled or parallel group trials, MD will be calculated by subtracting the fortified group post-intervention value from the control group post-intervention value. In case of pre-post or crossover trial, MD will be calculated by subtracting the fortified condition value from the control condition value. When articles contain more than one fortification condition (multi-arms trials), each comparison will be incorporated as an independent point estimate (Higgins et al., 2023). For example, in an article with one control group and two alternative fortification conditions (*e.g.*, using two different fortificants), the two alternative fortification conditions will be compared to the same control group. For each outcome, the units will be as follows: Kcal for energy intake, g for protein intake, kg for body weight, g/l for albumin and pre-albumin.

Estimation of mean effect sizes. Meta-analyses will be performed using the *metafor* package in R (Viechtbauer, 2010) if at least five studies reported on a specific outcome. A random-effects model will be chosen *a priori*, to account for between-studies differences such as design, fortified recipes and participant characteristics. In case of multiple-arm trials, the random factor "study" will be added to the model (argument *slad* in the *rma* function of the *metafor* package). Positive MDs will indicate an increase in the outcome measures after DIY fortification, whereas negative MD will indicate a decrease in the outcome measures. The significance level of the meta-analyses will be set at $p < 0.05$. Heterogeneity will be assessed using the I^2 statistic (Higgins et al., 2003). Exploratory sensitivity analyses will be conducted to evaluate results' robustness. First, subgroup analyses will be performed to check for potential issues with study design inclusion (*i.e.*, exclusion of Non-Randomized Controlled trials; exclusion of within-subject design). Second, an analysis will be performed by excluding studies of potential high risk of bias. Finally, a meta-regression will be conducted on the effect of additional energy or protein load (*i.e.*, the addition amount of energy or protein provided by a fortified food compared to a standard food) and the effect of setting (home,

nursing home, hospital...) on the mean difference (argument *mods* in the *rma* function of the *metafor* package).

Publication bias. Funnel plots will be visually inspected for non-symmetrical distribution of standard errors around size effect. Funnel plot asymmetry will be tested using Egger's regression method (Egger et al., 1997; function *regtest* of the *metafor* package). In addition, the 'trim and fill' method will be used to estimate the number of studies missing from the meta-analysis due to suppression of the most extreme results on one side of the funnel plot (function *trimfill* of the *metafor* package). This non-parametric method then augments the observed data so that the funnel plot is more symmetric, and recomputes the summary estimate based on the complete data to assess the sensitivity of the results to possible publication bias (Duval and Tweedie, 2000a, 2000b).

RESULTS

The following results will be included in the final paper:

Figure 1. PRISMA Flowchart

The flow diagram will depict the flow of information through the different phases of the systematic review and the meta-analysis. It will map out the number of records identified, included and excluded, and the reasons for exclusions.

Table 1. Characteristics of the articles included in the meta-analysis.

This table will display the characteristics for all included studies:

- First author name, publication date
- Experimental design
- Population: age, gender, setting
- Description of DIY fortification solutions: food matrices, fortificants, additional energy and/or protein load provided by fortified food
- Description of control condition

- Intervention period duration
- Outcomes and method of measuring outcomes

Table 3. Risk of bias

This table will present the risk of bias for all included studies.

Table 3. Meta-analysis main results

This table will display result of the meta-analyses performed for each outcome. Specifically, this table will include:

- The number of datasets
- The mean effect size (MD, SD, p value)
- The heterogeneity between studies (I^2 , p value)
- The publication bias: (1) Egger's t , p value to assess funnel plot asymmetry; (2) the number of missing studies and the mean estimate based on computed complete dataset to examine the sensitivity of the mean effect sized to publication bias ('trim and fill' method)

Figure 2. Forest plot

This figure will display forest plot for each outcome. Forest plots will provide a visual summary of the effect sizes and confidence intervals of individual studies, as well as the mean effect size and its 95% confidence interval.

Figure 3. Funnel plot

This figure will display funnel plots for each outcome. Funnel plots will include observed studies (solid circles) and imputed studies (empty circles).

Table 4. Sensitivity analysis

This table will display results of subgroup analyses to check for potential issues with study design inclusion or potential high risk of bias. For each subgroup analysis, this table will include:

- The number of datasets
- The mean effect size (MD, SD, p value)
- The heterogeneity between studies (I^2 , p value)

DISCUSSION

Limitations of the Meta-analysis

A first limitation pertains to the inclusion of both randomized and non-randomized controlled trial. The systematic literature review which underpins the current meta-analysis revealed that slightly less than half of the studies assessing the impact of DIY fortification on nutritional outcomes had implemented RCTs (42% - Geny et al., 2023). One possible reason for the low number of RCTs is the complexity of implementing a fortified diet, especially in institutional or hospital settings. Indeed, it requires the active involvement and commitment of catering services to develop and produce fortified recipes. In practice, rather than a top-down approach in which researchers design a fortified food intervention under controlled conditions, the introduction of fortified foods is often initiated by catering services and/or health professionals. Researchers then collaborate to assess the consequences of this change, often in circumstances where it would be difficult to implement a randomised controlled trial. In fact, if an institution introduces a fortified food offer, the residents would find it very difficult to accept the fact that some of them would benefit from this offer while others would not, on the basis of a random draw. In addition, it can be difficult for catering services to offer a fortified diet alongside a standard diet. Although these studies present a higher risk of bias than the RCTs, it is worth including them in the meta-analysis because they test DIY fortification under real-life conditions. In addition, we can legitimately wonder whether the risk of bias linked to the preparation of recipes (repeatability of production processes, variation in the quality of final dishes) is not higher when it is initiated by a research team than when it comes from the institution's catering service.

A second limitation arises from the restriction of the search strategy to scientific literature in the English language. The challenge lies in the lack of a universally accepted terminology for expressing the concept of “fortification”. As a result, we opted for a comprehensive search

strategy employing a wide range of keywords. This approach initially yielded an extensive pool of over 10,000 articles, from which fewer than 50 articles were ultimately selected. This strategy proved successful by enabling the extraction of several pertinent articles not identified in previous systematic literature reviews that employed narrower search criteria (Trabal & Farran-Codina, 2015; Morilla-Herrera et al., 2016; Douglas et al., 2017; Mills et al., 2018). However, because of time constraints, it was not possible to pursue non-English publications or exploring the grey literature.

As a third limitation, it would have been better to have data extracted by two independent reviewers. However, upon an initial examination of studies included in the former systematic literature review, it became evident that there is considerable variability among these studies in terms of how they present data. This variability encompasses different formats (tables, text, figures), diverse estimators (e.g., mean, mean change, standard deviation, standard error, 95% confidence interval, t-value, p-value), and varied units (e.g., kJ or kcal for energy intake). Given this complexity, a more efficient and secure approach emerged: one reviewer will be responsible for extracting relevant data from each paper and conducting the necessary calculations to derive means and standard deviations for each group or condition. A second reviewer will then independently verify the process and recomputed the calculations to identify any errors. Finally, both reviewers collaboratively conducted a third check (one reviewer will read the paper, while the other will check the data file) to identify any potential typographical mistakes. As a recommendation for future primary studies, it is advisable to present data in a standardized and straightforward manner (e.g., a table that includes the mean and standard deviation for each group or condition at each measurement time).

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare for the present manuscript. During the past 36 months, CSGA and CHU Dijon received research grants from OGUST, SAVEURS et VIE and INSTITUT NUTRITION; Claire Sulmont-Rossé received consulting fees from BEL FOOD and author fees from Correspondances en Métabolismes Hormones Diabète et Nutrition.

ETHICAL STATEMENTS

Not applicable (Systematic Literature Review and Meta-Analysis).

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AUTHOR CONTRIBUTION

Alexia Geny: conceptualization, search strategy, selection of articles, data extraction, writing – original draft; Virginie Van Wymelbeke-Delannoy: conceptualization, risk of bias assessment, writing - review & editing; Claire Sulmont-Rossé: conceptualization, selection of articles, risk of bias assessment, data extraction, statistical analysis, writing – original draft, funding acquisition.

REFERENCES

Alam, I., Almajwal, A. M., Alam, W., Alam, I., Ullah, N., Abulmeaaty, M., Razak, S., Khan, S., Pawelec, G., & Paracha, P. I. (2019). The immune-nutrition interplay in aging – facts and controversies. *Nutrition and Healthy Aging*, 5, 73-95.

American Dietetic Association. (2005). ADA Evidence Analysis Manual. Available at: chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.andeal.org/files/ADA%20Evidence%20Analysis%20Manual_ed3c%20Nov%202005.pdf. Accessed: December 2023.

Azzolino, D., Arosio, B., Marzetti, E., Calvani, R., & Cesari, M. (2020). Nutritional Status as a Mediator of Fatigue and Its Underlying Mechanisms in Older People. *Nutrients*, 12.

Bauer, J., Biolo, G., Cederholm, T., Cesari, M., Cruz-Jentoft, A. J., Morley, J. E., Phillips, S., Sieber, C., Stehle, P., Teta, D., Visvanathan, R., Volpi, E., & Boirie, Y. (2013). Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group. *Journal of the American Medical Directors Association*, 14, 542-559.

Cederholm, T., Barazzoni, R., Austin, P., Ballmer, P., Biolo, G., Bischoff, S. C., Compher, C., Correia, I., Higashiguchi, T., Holst, M., Jensen, G. L., Malone, A., Muscaritoli, M., Nyulasi, I., Pirlich, M., Rothenberg, E., Schindler, K., Schneider, S. M., De Van Der Schueren, M. a. E., Sieber, C., Valentini, L., Yu, J. C., Van Gossum, A., & Singer, P. (2017). ESPEN guidelines on definitions and terminology of clinical nutrition. *Clinical Nutrition*, 36, 49-64.

Cruz-Jentoft, A. J., Bahat, G., Bauer, J., Boirie, Y., Bruyère, O., Cederholm, T., Cooper, C., Landi, F., Rolland, Y., Sayer, A. A., Schneider, S. M., Sieber, C. C., Topinkova, E., Vandewoude, M., Visser, M., & Zamboni, M. (2019). Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*, 48, 16-31.

Deutz, N. E., Bauer, J. M., Barazzoni, R., Biolo, G., Boirie, Y., Bosy-Westphal, A., Cederholm, T., Cruz-Jentoft, A., Krznaric, Z., Nair, K. S., Singer, P., Teta, D., Tipton, K., & Calder, P. C. (2014). Protein intake and exercise for optimal muscle function with aging: recommendations from the ESPEN Expert Group. *Clinical Nutrition*, 33, 929-936.

Douglas, J. W., Lawrence, J. C., & Knowlden, A. P. (2017). The use of fortified foods to treat malnutrition among older adults: a systematic review. *QAOA*, 18, 104-119.

Duval, S., & Tweedie, R. (200b). A Nonparametric "Trim and Fill" Method of Accounting for Publication Bias in Meta-Analysis. *Journal of the American Statistical Association*, 95, 89-98.

Duval, S., & Tweedie, R. (2000a). Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics*, 56, 455-463.

Egger, M., Davey Smith, G., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *Bmj*, 315, 629-634.

Feng, L., Chu, Z., Quan, X., Zhang, Y., Yuan, W., Yao, Y., Zhao, Y., & Fu, S. (2022). Malnutrition is positively associated with cognitive decline in centenarians and oldest-old adults: A cross-sectional study. *eClinicalMedicine*, 47.

Fleury, S., Van Wymelbeke-Delannoy, V., Lesourd, B., Tronchon, P., Maître, I., & Sulmont-Rossé, C. (2021). Home-Delivered Meals: Characterization of Food Intake in Elderly Beneficiaries. *Nutrients*, 13, 2064.

Gentile, S., Lacroix, O., Durand, A. C., Cretel, E., Alazia, M., Sambuc, R., & Bonin-Guillaume, S. (2013). Malnutrition: a highly predictive risk factor of short-term mortality in elderly presenting to the emergency department. *J Nutr Health Aging*, 17, 290-294.

Geny, A., Petitjean, M., Van Wymelbeke-Delannoy, V., & Sulmont-Rossé, C. (2023). Impact of food-based fortification on nutritional outcomes and acceptability in older adults: systematic literature review. *Frontiers in nutrition*, 10.

Has. (2007). Stratégies de prise en charge en cas de dénutrition protéino-énergétique chez les personnes âgées. Available at: https://www.has-sante.fr/upload/docs/application/pdf/denuitrition_personne_agee_2007_-_recommandations.pdf. Accessed: 16 February 2022.

Higgins, J., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M., & Welch, V. (2023). *Cochrane Handbook for Systematic Reviews of Interventions version 6.4* Cochrane. Available from www.training.cochrane.org/handbook. Access on December 2023.

Kawakami, K., Kadota, J., Iida, K., Shirai, R., Abe, K., & Kohno, S. (1999). Reduced immune function and malnutrition in the elderly. *Tohoku J Exp Med*, 187, 157-171.

Knopman, D. S., Edland, S. D., Cha, R. H., Petersen, R. C., & Rocca, W. A. (2007). Incident dementia in women is preceded by weight loss by at least a decade. *Neurology*, 69, 739-746.

Leblanc, E. S., Rizzo, J. H., Pedula, K. L., Yaffe, K., Ensrud, K. E., Cauley, J., Cawthon, P. M., Cummings, S., & Hillier, T. A. (2017). Weight Trajectory over 20 Years and Likelihood of Mild Cognitive Impairment or Dementia Among Older Women. *J Am Geriatr Soc*, 65, 511-519.

Lee, C. M., Woodward, M., Batty, G. D., Beiser, A. S., Bell, S., Berr, C., Bjertness, E., Chalmers, J., Clarke, R., Dartigues, J. F., Davis-Plourde, K., Debette, S., Di Angelantonio, E., Feart, C., Frikke-Schmidt, R., Gregson, J., Haan, M. N., Hassing, L. B., Hayden, K. M., Hoeveraar-Blom, M. P., Kaprio, J., Kivimaki, M., Lappas, G., Larson, E. B., Leblanc, E. S., Lee, A., Lui, L. Y., Moll Van Charante, E. P., Ninomiya, T., Nordestgaard, L. T., Ohara, T., Ohkuma, T., Palviainen, T., Peres, K., Peters, R., Qizilbash, N., Richard, E., Rosengren, A., Seshadri, S., Shipley, M., Singh-Manoux, A., Strand, B. H., Van Gool, W. A., Vuoksimaa, E., Yaffe, K., & Huxley, R. R. (2020). Association of anthropometry and weight change with risk of dementia and its major subtypes: A meta-analysis consisting 2.8 million adults with 57 294 cases of dementia. *Obesity reviews : an official journal of the International Association for the Study of Obesity*, 21, e12989.

Lesser, S., Pauly, L., Volkert, D., & Stehle, P. (2008). Nutritional situation of the elderly in Eastern/Baltic and Central/Western Europe - The AgeingNutrition project. *Annals of Nutrition and Metabolism*, 52, 62-71.

Methley, A. M., Campbell, S., Chew-Graham, C., McNally, R., & Cheraghi-Sohi, S. (2014). PICO, PICOS and SPIDER: a comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews. *BMC Health Services Research*, 14, 579.

Mills, S. R., Wilcox, C. R., Ibrahim, K., & Roberts, H. C. (2018). Can fortified foods and snacks increase the energy and protein intake of hospitalised older patients? A systematic review. *J Hum Nutr Diet*, 31, 379-389.

Morilla-Herrera, J. C., Martin-Santos, F. J., Caro-Bautista, J., Saucedo-Figueroa, C., Garcia-Mayor, S., & Morales-Asencio, J. M. (2016). Effectiveness of food-based fortification in older people a systematic review and meta-analysis. *Journal of Nutrition Health & Aging*, 20, 178-184.

Norman, K., Haß, U., & Pirlich, M. (2021). Malnutrition in Older Adults-Recent Advances and Remaining Challenges. *Nutrients*, 13.

Norman, K., Pichard, C., Lochs, H., & Pirlich, M. (2008). Prognostic impact of disease-related malnutrition. *Clin Nutr*, 27, 5-15.

Olson, R., Gavin-Smith, B., Ferraboschi, C., & Kraemer, K. (2021). Food Fortification: The Advantages, Disadvantages and Lessons from Sight and Life Programs. *Nutrients*, 13.

Programme, C. a. S. (2021). CASP Randomised Controlled Trial checklist Available at: <chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://casp-uk.net/checklists/casp-rct-randomised-controlled-trial-checklist.pdf>. Accessed: December 2023.

Sanchez-Rodriguez, D., Locquet, M., Reginster, J. Y., Cavalier, E., Bruyère, O., & Beaudart, C. (2020). Mortality in malnourished older adults diagnosed by ESPEN and GLIM criteria in the SarcoPhAge study. *J Cachexia Sarcopenia Muscle*, 11, 1200-1211.

Santilli, V., Bernetti, A., Mangone, M., & Paoloni, M. (2014). Clinical definition of sarcopenia. *Clin Cases Miner Bone Metab*, 11, 177-180.

Schroll, K., Moreirasvarela, O., Schlettweingsell, D., Decarli, B., Degroot, L., & Vanstaveren, W. (1997). Cross-cultural variations and changes in food-group intake among elderly women in Europe: Results from the Survey in Europe on Nutrition and the Elderly a Concerted Action (SENECA). *American Journal of Clinical Nutrition*, 65, 1282-1289.

Shamseer, L., Moher, D., Clarke, M., Gherzi, D., Liberati, A., Petticrew, M., Shekelle, P., & Stewart, L. A. (2015). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *Bmj*, 350, g7647.

Shpata, V., Ohri, I., Nurka, T., & Prendushi, X. (2015). The prevalence and consequences of malnutrition risk in elderly Albanian intensive care unit patients. *Clin Interv Aging*, 10, 481-486.

Smith, R., Clegg, M., & Methven, L. Review of protein intake and suitability of foods for protein-fortification in older adults in the UK. *Critical Reviews in Food Science and Nutrition*, 1-18.

Sterne, J. A., Hernán, M. A., Reeves, B. C., Savović, J., Berkman, N. D., Viswanathan, M., Henry, D., Altman, D. G., Ansari, M. T., Boutron, I., Carpenter, J. R., Chan, A.-W., Churchill, R., Deeks, J. J., Hróbjartsson, A., Kirkham, J., Jüni, P., Loke, Y. K., Pigott, T. D., Ramsay, C. R., Regidor, D., Rothstein, H. R., Sandhu, L., Santaguida, P. L., Schünemann, H. J., Shea, B., Shrier, I., Tugwell, P., Turner, L., Valentine, J. C., Waddington, H., Waters, E., Wells, G. A., Whiting, P.

F., & Higgins, J. P. (2016). ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *Bmj*, 355, i4919.

Sterne, J. a. C., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., Cates, C. J., Cheng, H. Y., Corbett, M. S., Eldridge, S. M., Emberson, J. R., Hernán, M. A., Hopewell, S., Hróbjartsson, A., Junqueira, D. R., Jüni, P., Kirkham, J. J., Lasserson, T., Li, T., McAleenan, A., Reeves, B. C., Shepperd, S., Shrier, I., Stewart, L. A., Tilling, K., White, I. R., Whiting, P. F., & Higgins, J. P. T. (2019). RoB 2: a revised tool for assessing risk of bias in randomised trials. *Bmj*, 366, l4898.

Ter Borg, S., Verlaan, S., Mijnaerends, D. M., Schols, J. M. G. A., De Groot, L. C. P. G. M., & Luiking, Y. C. (2015). Macronutrient Intake and Inadequacies of Community-Dwelling Older Adults, a Systematic Review. *Annals of Nutrition and Metabolism*, 66, 242-255.

Trabal, J., Hervas, S., Forga, M., Leyes, P., & Farran-Codina, A. (2014). Usefulness of dietary enrichment on energy and protein intake in elderly patients at risk of malnutrition discharged to home. *Nutricion Hospitalaria*, 29, 382-387.

Viechtbauer, W. (2010). Conducting Meta-Analyses in R with the metafor Package. *Journal of Statistical Software*, 36, 1 - 48.

Volkert, D., Beck, A. M., Cederholm, T., Cruz-Jentoft, A., Goisser, S., Hooper, L., Kiesswetter, E., Maggio, M., Raynaud-Simon, A., Sieber, C. C., Sobotka, L., Van Asselt, D., Wirth, R., & Bischoff, S. C. (2019). ESPEN guideline on clinical nutrition and hydration in geriatrics. *Clin Nutr*, 38, 10-47.

SUPPLEMENTAL FILES

Supplemental Table 1. PRISMA checklist.

To be completed in the final paper.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Supplemental Table 2. Eligibility criteria of the current meta-analysis *versus* eligibility criteria of the systematic literature review (Geny et al., 2023).

	Systematic literature review Eligibility criteria	Meta-analysis Additional criteria
Population	Aged ≥ 60 years Any setting (home, institution, hospital) Any nutritional status, cognitive status and oral ability Studies not targeting a specific pathological condition	Same
Intervention	Any intervention including DIY fortification in energy and/or macronutrients	Interventions exclusively testing DIY fortification in energy and/or protein
Comparator	Any comparator No comparator	Control group or control condition with no fortification
Outcomes	Nutritional intake Nutritional status Satisfaction	Nutritional intake Nutritional status
Study design	Randomized Controlled Trial Non-randomized controlled trial Observational design	Randomized Controlled Trial Non-randomized controlled trial

Supplemental Table 3. Search strategy in Web of Science, PubMed and Scopus. (For PubMed, MeSH terms are in bold).

Concept	Key-words
Old people	" aged " OR "elderly" OR "older" OR "senior" OR "aging" OR "ageing"
AND	
Food-based fortification	" food, fortified " OR "enriched food" OR "enriched foods" OR "food enrichment" OR "diet enrichment" OR "enriched diet" OR "enriched diets" OR "food fortification" OR "supplemented food" OR "supplemented diet" OR "supplemented diets" OR "food supplementation" OR "diet supplementation" OR "additional food" OR "additional foods" OR "added food" OR "fortified drink" OR "fortified beverage" OR "enriched drink" OR "enriched beverage" OR "enriched beverages" OR "dense food" OR "dense foods" OR "dense diet" OR "dense diets" OR " food, formulated " OR "formulated food" OR "fortified foods" OR "dietary enrichment"
AND	
Outcomes	<p>Nutritional intake: "eating" OR "food intake" OR "dietary intake" OR "feed intake" OR "food consumption" OR "diet pattern" OR "dietary pattern" OR "nutritional intake" OR "protein intake" OR "energy intake" OR "nutritional requirement" OR "nutritional requirements" OR "dietary protein" OR "dietary proteins" OR "feeding" OR "feeding behavior"</p> <p>OR</p> <p>Nutritional status: "nutritional status" OR "body weight" OR "weight" OR "Body Mass Index" OR "BMI" OR "muscle mass" OR "malnutrition" OR "undernutrition" OR "undernourished" OR "malnourished" OR "appetite" OR "sarcopenia" OR "frail elderly" OR "frailty" OR "frail" OR "elder nutritional physiological phenomena"</p>

Supplemental Table 4. List of studies included in the Systematic Literature Review but excluded in the current meta-analysis and reason of exclusion.

To be added in the final paper.

Supplemental Table 5. Risk of bias grid.

Critical appraisal - risk of bias

Authors, year:

Design:

Answer Yes / some concerns / no / NA (non applicable)

Domain 1	Selection of participants into the study	Answer	Comments
1.1	Inclusion/exclusion criteria are specified with sufficient detail		
1.2	Inclusion/exclusion criteria are applied equally to all study groups		NA in case of within-subject design (e.g., cross-over)
1.3	Selection of participants was based on characteristics observed/measured before the start of intervention		
1.4	Start and follow-up almost intervention coincide for all participants		NB. In nutrition trials, large differences in start intervention time is associated with a risk of bias due to season effect

Domain 2	Allocation of participants into different groups	Answer	Comments
2.1	Participants were randomly allocated into different groups		Yes if allocation used a random concealed sequence; some concerns if the allocation was randomized but the paper does not specify the process of allocation; NA if within-subject design
2.2	Baseline characteristics were similar between the different groups		NA if within-subject design (e.g., pre-post intervention, cross-over trial)
2.3	Concurrent control group was used (e.g. no historical control)		NA if within-subject design

Domain 3	Classification of intervention	Answer	Comments
3.1	The DIY fortified foods are described with sufficient details to be reproduced		Yes if the author describe the food matrix, the nature of the fortificant and the additional nutrient load provided by the DIY fortified food; some concerns if at least one information is missing; 'no' if no information is providing
3.2	Apart from DIY fortification, each group/condition received the same level of care / the same co-intervention(s)		A co-intervention could be nutritional counselling in addition to DIY fortified food

Domain 5	Confounding factors	Answer	Comments
5.1	There is no potential for confounding of the intervention in the study		Yes if randomized or parallel group with no significant difference on possible confounding factors at baseline between the groups or if the outcome is not subjected to confounding factors
5.2	In within-subject design, the order of conditions was counterbalanced between the subjects		No if pre-post design; NA if between-subject design
5.3	The authors used an appropriate analysis method that controlled for all the important confounding factors		NA if answer is Yes on 5.1; take into consideration whether authors account for the potential impact of confounding factors on outcome and for possible change in confounding factors during intervention
5.4	The confounding factors were measured using a valid or standard method/instrument		NA if answer is Yes on 5.1

Domain 6	Missing data	Answer	Comments
6.1	The number and reasons for withdrawals are described for each group (e.g. flow chart)		
6.2	Outcome data are available for all, or nearly all, participants		
6.3	Data analysis used an intent-to-treat approach		Yes if participants were analysed in the study according to their assigned group (and not received intervention) and if all enrolled participants accounted for data analysis; some concerns if 'intent-to-treat' is specified but without detail on imputation of missing data; No if per-protocol

Domain 7	Outcome measurement	Answer	Comments
7.1	The outcome data assessors were blind to the groups / conditions		
7.2	The outcomes were measured using a valid or standard method/instrument		
7.3	The outcomes were measured consistently across participants and groups		Also consider training of outcome data collectors

Domain 8	Result reporting	Answer	Comments
8.1	The groups were concealed in data analysis		
8.2	The results were reported for each outcome in each study group at each follow-up interval		