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A Report of Synthesis and Interpretation of RCT Data in the Systematic Review of Nutritional Supplementation for Elderly People

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Abstract

Introduction: The differences of mortality and weight change between older patients who have received the nutritional supplementation and those without receiving supplementation would be reported from seven studies which included eligibly in the systematic review.

Methods: Using Cochrane risk of bias tool to assess quality of Munk's study and Tidermark's study. Outcomes of Mortality and Weight change from these seven studies were extracted and set up in Revman. Moreover, implementing the GRADE approach to determine reliability to the results in these seven studies.

Results: overall evidence showed using nutritional supplementation was favored by participants for the outcome of 'mortality', while no supplementation taken was favored by participants for the outcome of 'weight change'.

Keywords: Elderly; Mortality; Weight change; Nutritional supplementation; Grade approach

Introduction

With global demographic transformation, the numbers and percentages of old adults over 60 years experienced increase recently. It is estimated that by the year 2025, the number of populations over 60 years will exceed 1.2 billion. Obviously, the rapid growth in the number of elderly will bring considerable demands on healthcare facilitate. Maintaining a satisfactory nutritional status of elderly has been regarded as a crucial factor for healthy ageing [1]. Avoiding weight loss, decreasing the risk of developing disease, even preventing from mortality and improving quality of life may result from the benefits of receiving nutritional supplements for elderly [2].

The differences of mortality and weight change at six months between older patients who have received the nutritional supplementation and those without receiving supplementation would be reported from seven studies which included eligibly in the systematic review. Firstly, the quality of Munk's study and Tidermark's study has been assessed by using Cochrane risk of bias tool. Afterwards, forest plots for 'mortality' and 'weight change' from these seven studies have been set up in RevMan. Apart from this, the precision and reliability of the results will be assessed in this report.

Methods

The quality of Tidermark's study and Munk's study have been assessed from seven aspects, including random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias by using Cochrane risk of bias tool (Tables 1 and 2).

	Low/unclear/high	Reason
Random sequence generation	unclear	'The patients were randomized' has been stated in this study, but there were no other details to explain how to randomize these patients. Therefore, it is unclear what method was used.
Allocation concealment	low risk	'using opaque and sealed envelopes' has been mentioned in this study. The trialists have made some attempts to conceal the treatment allocation, though these envelopes may not be consecutive.
Blinding of participants and personnel	high risk	There was no blinding clearly because the participants knew who was allocated in a protein-rich formula group, who was receiving a combined therapy and who was receiving a standard treatment.
Blinding of outcome assessment: mortality	low risk	The outcome of mortality is unlikely to be influenced by blinding of the outcome assessor due to it is a survival outcome.

Blinding of outcome assessment: weight change	low risk	'A research nurse not involved in the surgery or clinical decisions assessed all clinical variables' has been informed. Therefore, the trialists have made some attempt to blind outcome assessment.
Incomplete outcome data: mortality	unclear	This study did not provide enough information about mortality data.
Incomplete outcome data: weight change	high risk	There were 2 supplemented participants and 3 non-supplemented participants were not accounted for. The numbers dropping out were not relatively small due to the small sample size. Meanwhile, the reasons of differential attrition were not given for all missing participants.
Selective reporting	unclear	Although the study protocol has been approved by the local Ethics Committee, this study did not include the protocol as a supplementary file and the protocol could not be found online. Therefore, it is difficult to assess whether this study was reporting to all the pre-specified outcomes.
Other bias	unclear	Insufficient information about whether funding could potentially be a conflict of interest.

Table 1: Criteria for judging risk of bias for Tidermark's study.

	Low/unclear/high	**Reason**
Random sequence generation	unclear	'Patients were randomly assigned to intervention or control group by using stratified block randomization' has been mentioned in this study. However, no more details of whether the sequence generation used in the study would be truly random.
Allocation concealment	low risk	Sequential sealed and opaque envelopes with a total of nine blocks have been provided by the trialists who was not involved in the study.
Blinding of participants and personnel	high risk	Participants would know their allocations or which interventions they would receive when conducting the interviews. Therefore, there was no blinding for the participants.
Blinding of outcome assessment: mortality	low risk	A death is recorded as an outcome is unlikely to be influenced by blinding of the outcome assessor due to it is a survival data.
Blinding of outcome assessment: weight change	high risk	'Blinding of data assessors was not possible because of the way in which nutritional intake was monitored' has been reported in this study.
Incomplete outcome data: mortality	unclear	This study did not provide enough information about mortality data.
Incomplete outcome data: weight change	unclear	Although numbers of participants dropping out were relatively small, the reasons were not provided clearly in this study.
Selective reporting	unclear	Although the study protocol has been approved by the Danish Regional Committee and the Danish Data Protection Agency, this study did not include the protocol as a supplementary file and the protocol could not be found online. Therefore, it is difficult to assess whether this study was reporting to all the pre-specified outcomes.
Other bias	low risk	'The sources of funding had no influence or no conflicts of interest' has been declared by the authors in this study.

Table 2: Criteria for judging risk of bias for Munk's study.

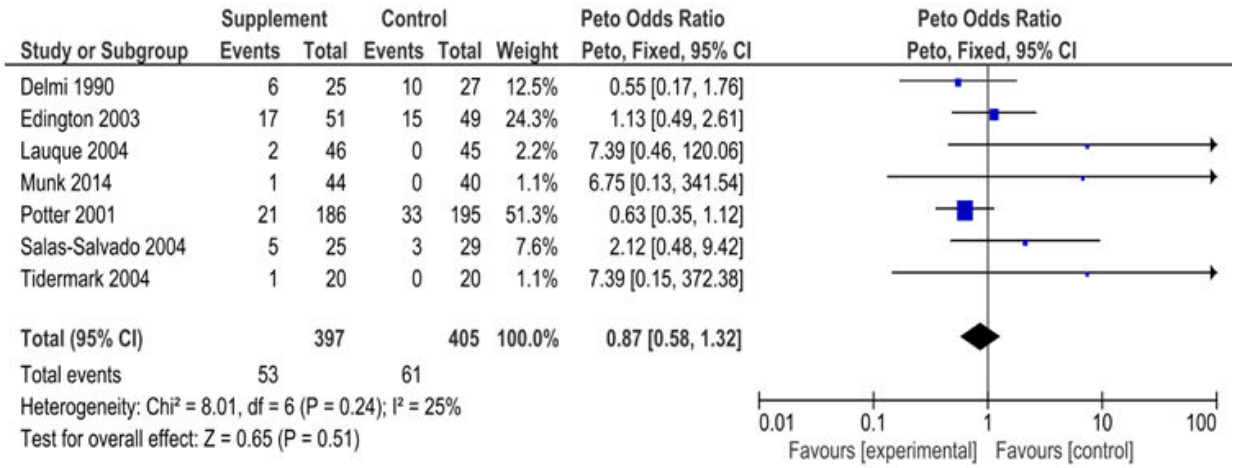
For outcome of 'mortality', Peto's odds ratio method has been used to combine all the mortality data from these seven studies. There are three reasons choosing Peto's odds ratio method. Firstly, odds ratio is that it has better mathematical properties for meta-analysis. Then, 'mortality' is always treated as a binary outcome when hazard ratios cannot be found in studies. Thirdly, Peto's odds ratio method is suitable for no events or rare events. In these seven studies, the number of died patients was relatively small. Moreover, all the seven studies have reported the same effect size would be an important reason to use the fixed effects method. The more sophisticated meta-analysis techniques would become possible if the raw datasets of mortality (IPD) could be obtained from the study authors.

For outcome of 'weight change', Weighted mean difference (WMD) method has been used to combine all the weight change data from these seven studies because the weight change data was continuous and all the studies reported the same type of outcome. In addition, the random effects method has been chosen for the weight change data because the statistical heterogeneity could be assessed by X^2 test and I^2.

Results

There were two studies favoring supplement group and five study favoring control group, in accordance with the mortality results. However, the pooled effect size was 0.87 with 0.58-1.32 95% CI which indicated to favor supplement group (Figure 1). The reason may relate to Potter's study had a big sample size with higher weighting. The pooled Peto's odds ratio of 0.87 illustrated the elderly patients with supplementation had 0.87 times the risk of death compared with those without supplementation. However, the 95% CI (0.58-1.32) indicated

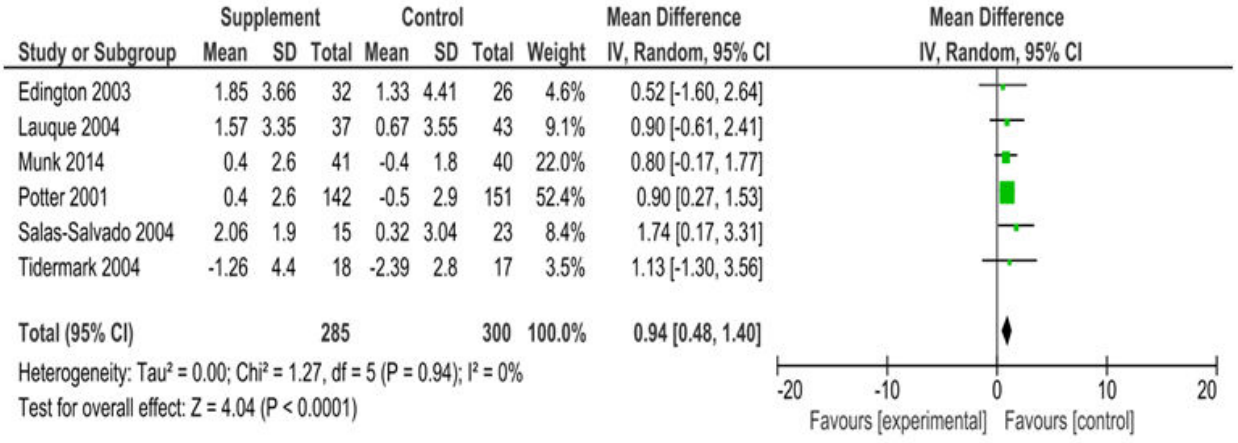
there was no difference of mortality between the supplement group and the non-supplement group because the 95% confidence interval included 1.



Note: Data for Mortality from Delmi et al. [3], Edington et al. [4], Lauque .2004 [5], Munk et al. [6], Potter et al. [7], Salas-Salvado et al. [8] and Tidermark et al. [9].

Figure 1: Funnel plot for Mortality data.

All these studies favored the control group with respect to weight change data and the overall effect size was 0.94 with 0.48-1.40 95% CI which indicated to favor non-supplement as well (Figure 2). Overall, there was a significant difference in the weight change at six months between supplement group and non-supplement group because 95% CI (0.48-1.40) of pooled effect size did not involve 0.



Note: Data for Weight Change from Edington et al. [4], Lauque et al. [5], Munk et al. [6], Potter et al. [7], Salas-Salvado et al. [8]and Tidermark et al.[9].

Figure 2: Funnel plot for Weight Change data.

Discussion

Apart from this, the reliability of the results from the seven studies would be assessed by using GRADE approach. At first, all the studies reported they have randomized their target participants, but most of them have not provided more specified information to ascertain whether the patients were truly random. The majority researchers made attempts to use sealed envelopes or central allocation to

randomize in order to avoiding inadequate concealment of allocation prior to assignment in the studies. However, lack of blinding participants and outcome assessment was a common issue among the seven studies. Moreover, only one study reported five participants were excluded due to failure intention-to-treat analysis adherence. Numbers participants dropped out were relatively small in few studies. At the same time, clear reasons were not given to explain missing data in most of the seven studies. According to I2, the weight change data showed no heterogeneity (I2=0%) in the trial. Nevertheless, it is important to explore heterogeneity for the mortality data as the result of I2 is 25% and Q/df>1. In addition, the publication bias could not be identified due to less than 10 studies included. Both results of 'mortality' and 'weight change' had the relative narrow confidence intervals which indicated moderate-to-high precision. Furthermore, the target population group (adults) in Munk's study was different from other studies (elderly people).

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