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Review

Determinants of protein–energy malnutrition in community-dwelling older adults: A systematic review of observational studies

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ABSTRACT

Protein–energy malnutrition is associated with numerous poor health outcomes, including high health care costs, mortality rates and poor physical functioning in older adults. This systematic literature review aims to identify and provide an evidence based overview of potential determinants of protein–energy malnutrition in community-dwelling older adults.

A systematic search was conducted in PUBMED, EMBASE, CINAHL and COCHRANE from the earliest possible date through January 2013. Observational studies that examined determinants of protein–energy malnutrition were selected and a best evidence synthesis was performed to summarize the results.

In total 28 studies were included in this review from which 122 unique potential determinants were derived. Thirty-seven determinants were examined in sufficient number of studies and were included in a best evidence synthesis. The best evidence score comprised design (cross-sectional, longitudinal) and quality of the study (high, moderate) to grade the evidence level. Strong evidence for an association with protein–energy malnutrition was found for poor appetite, and moderate evidence for edentulousness, having no diabetes, hospitalization and poor self-reported health. Strong evidence for no association was found for anxiety, chewing difficulty, few friends, living alone, feeling lonely, death of spouse, high number of diseases, heart failure and coronary failure, stroke (CVA) and the use of anti-inflammatory medications.

This review shows that protein–energy malnutrition is a multifactorial problem and that different domains likely play a role in the pathway of developing protein–energy malnutrition. These results provide important knowledge for the development of targeted, multifactorial interventions that aim to prevent the development of protein–energy malnutrition in community-dwelling older adults.

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1. Introduction

Protein–energy malnutrition (PEM) is a worldwide health problem among community-dwelling older adults in developed countries (Halfens et al., 2010; Health Council of the Netherlands, 2011; Schilp et al., 2012; de Hollander et al., 2012; Lee et al., 2005; Locher et al., 2007; Margetts et al., 2003; Martyn et al., 1998; Shahar et al., 2009; Wijnhoven et al., 2010) and could be defined as a wasting condition resulting from a diet inadequate in either protein or energy (calories) or both (Mosby, 2009). The World Health Organization emphasized the need for an accepted classification and definition of protein–calorie malnutrition already in 1972 (Waterlow, 1972). However, up to now, no generally accepted definition is available (White et al., 2012). Besides the challenge to define PEM, there is no gold standard to operationalize PEM. Many different criteria are currently used to measure PEM across different health care settings and target groups. The Academy of Nutrition and Dietetics and the American Society for Parenteral and Enteral Nutrition recommended in 2012 that no single criteria is definitive for PEM, and that the identification of two or more criteria is recommended for diagnosis (White et al., 2012). The upcoming ESPEN initiative for Diagnostic Criteria for PEM and approach for international consensus is expected in 2014 (personal communication) to provide a consensus statement for the diagnosis and operationalization of PEM.

Because there is no consensus on a set of criteria to operationalize PEM, we selected four criteria to operationalize PEM and to restrict our literature search: thinness (as measured by low body weight, low body mass index (BMI), or low mid-upper arm circumference (MUAC)), unintentional weight loss, low energy intake or poor appetite. The selection of these four criteria was supported by a consensus statement of the Academy of Nutrition and Dietetics and the American Society for Parenteral and Enteral Nutrition where insufficient energy intake and weight loss were defined as key criteria of PEM (White et al., 2012), a Delphi study among 30 nutritional expert (from nine different countries) where low BMI, involuntary weight loss and poor nutritional intake were mostly frequently indicated as criteria to operationalize PEM (Meijers et al., 2010). And finally, two recent Dutch reports on malnutrition ("Results Report: National Prevalence Survey of Care Problems" and "Malnutrition in the elderly" from the Dutch Health Council) described low BMI, weight loss and decreased food intake as criteria of PEM (Halfens et al., 2010; Health Council of the Netherlands, 2011). Poor appetite was included since it is included in several validated screening tools that assess (risk of) PEM in community-dwelling older adults (Kaiser et al., 2009; Wijnhoven et al., 2012; Keller et al., 2000, 2005) and because poor appetite is shown to be an independent determinant of PEM (Dean et al., 2009; Schilp et al., 2011; Shahar et al., 2003).

Studies determining the prevalence of PEM in community-dwelling older adults are scarce and vary from 7 to 35% (Halfens et al., 2010; Schilp et al., 2012). In the Netherlands, the prevalence of PEM in older adults is estimated to be 33% in hospitals, 21% in nursing homes and 16% in home care. This is based on either a body mass index $\leq$20 kg/m^2, unintentional weight loss of 3 kg in the last month or 6 kg in the previous 6 months, or a recently decreased food intake (3 days hardly/no food intake, or 1 week a decreased food intake) in combination with a BMI between 20.1 and 23.0 kg/m^2. The percentage PEM in community-dwelling older adults without homecare was estimated at 7%, based on a BMI < 20 kg/m^2 or unintentional weight loss of 5% in the previous 6 months (Health Council of the Netherlands, 2011). Although the prevalence of PEM is lowest in the older home-living adults (with or without home care) compared to hospitals or nursing homes, the absolute number is highest in this community setting because 95% of the population aged 65 years and older live at home (Garssen and Harmsen, 2011).

PEM is associated with numerous poor health outcomes in individuals and adverse consequences for society. In several prospective studies among older community-dwelling adults, low BMI, low MUAC or unintentional weight loss were significantly associated with an increased risk of all-cause mortality (de Hollander et al., 2012; Locher et al., 2007; Wijnhoven et al., 2010), an increased risk for mobility limitations (Lee et al., 2005), and with a poor health status (Margetts et al., 2003). Two other studies show that low BMI and unintentional weight loss were associated with high use of health care resources 'among older adults' (Martyn et al., 1998) and high health care costs in hospitalized adults (aged >18) (Freijer et al., 2013). Decreased food intake and poor appetite were found to be associated with an increased mortality risk among hospitalized (Sullivan et al., 2002) and well-functioning, community-dwelling older adults (Shahar et al., 2009). However, causality of the above mentioned associations cannot be established due to the observational nature of the studies.

Previous research mainly focused on the treatment of PEM by oral nutritional supplements or dietetic counseling, but these studies showed limited effects of health outcomes. On the other hand, little attention has been paid to the prevention of PEM targeting the potential underlying determinants. Recent systematic reviews that summarized the results of (quasi) randomized controlled trials on the effect of extra protein and energy supplementation in older undernourished adults found a small statistically significant effect on weight gain but not on mortality (Health Council of the Netherlands, 2011; Chapman et al., 2009; McMurdo et al., 2009; Persson et al., 2007; Rabadi et al., 2008; Neelemaat et al., 2011; Starke et al., 2011). Despite positive short-term effects on

weight gain, long term beneficial effects of nutritional supplements may be less as these products are not well appreciated and tolerated by older adults (Milne et al., 2009; Gosney, 2003). Previous RCTs examining dietetic counseling with or without extra nutritional supplementation, in different settings (i.e. Hospitalized, post-discharged, home living) have reported no or only small effects on weight gain or quality of life and physical functioning among community-dwelling older adults (Neelemaat et al., 2011; Schilp et al., 2013; Weekes et al., 2009; Wyers et al., 2013).

Because treatment of PEM appears to be difficult, prevention of PEM may be a more (cost) effective approach. To develop effective prevention strategies, evidence-based knowledge is needed on the determinants of PEM in community-dwelling older adults. Several studies and narrative reviews describe the determinants and consequences of PEM (Margetts et al., 2003; Brownie, 2006; Kubrak and Jensen, 2007; Feldblum et al., 2007; Han et al., 2009; Johansson et al., 2009; Martin et al., 2007; Payette et al., 1995; Suominen et al., 2005; Thomas et al., 2002), but systematic reviews are lacking. Therefore, the objective of this systematic review is to provide a comprehensive overview of the evidence for potential determinants of PEM in community-dwelling older adults.

2. Methods

2.1. Overview

The selection and review procedure included a systematic search in electronic databases by a specialized librarian (IJ) and a first selection of title and abstracts based on predefined inclusion and exclusion criteria by two reviewers (RvdP and HW or LS). Titles and abstracts were blinded for publishing journal and authors. Next, the selected papers were read in full text to determine eligibility based on the same inclusion and exclusion criteria. Methodological quality criteria of the selected papers were scored. Finally, a best evidence synthesis was used to report, summarize and grade the level of evidence of all determinants.

2.2. Literature search

A systematic search was conducted in the electronic databases PUBMED, EMBASE, CINAHL and the library of Cochrane Collaboration from the earliest possible date through January 17th 2013 to identify relevant observational studies on PEM in community-dwelling older adults. The systematic search was conducted by a specialized librarian (IJ) from the library of the VU University Medical Center. The search criteria combined text words related to three main themes: “PEM”, “older persons”, and “community-dwelling”. Several publication types (i.e. congress posters, letters, and editorials) and animal studies were excluded. See Appendix 1 for the complete search including all terms and limits.

2.3. Study selection

The specialized librarian (IJ) excluded duplicate studies. Three researchers (RvdP, HW and LS) independently performed the first selection based on titles and abstracts. Consensus for exclusion was reached during consensus meetings.

Predefined inclusion criteria were used to select the studies: (1) observational studies that examined determinants of PEM as their main topic. Because there is no gold standard how to measure PEM in a general older population, we decided on forehand to include papers on either low appetite, low energy intake, weight loss, or thinness as measured by low body weight, low BMI, or low mid-upper arm circumference as indicators of PEM; (2) study participants were non-institutionalized, community-dwelling older adults (if a mixed population was described, at least 50% had to meet this criterion); (3) study participants were 65 years or older (if a mixed population was described, the mean age had to be ≥65 years (Milne et al., 2009)); (4) multivariate analyses were performed; and (5) results were published in English or Dutch as full report studies in peer reviewed scientific journals.

Exclusion criteria were: (1) trials and qualitative studies; (2) observational studies that examined associations with supplementation (i.e. protein drinks), medication, or hormones (i.e. Ghrelin); (3) studies that examined voluntary weight loss, obesity or overweight; (4) studies that assessed PEM by screening or assessment tools that include risk factors of PEM (such as Nutritional Screening Initiative (DETERMINE), Mini Nutritional Assessment (MNA), Malnutrition Universal Screening Tool (MUST), Nutritional Form for The Elderly (NUFFE) etc.); (5) studies not performed in Western countries; (6) studies examining specific patient groups (i.e. oesophageal cancer patients).

The studies that seemed eligible for inclusion were examined in full text by the same reviewers (RvdP, HW and LS) and subsequently discussed during a consensus meeting. If no consensus was met on inclusion, a third independent researcher (MV) was consulted.

2.4. Quality assessment/methodological assessment

The methodological quality assessment of the papers selected based on full text evaluation was performed by three reviewers independently (RvdP, HW or LS) using a short form including 11 in consensus selected items (Appendix 2) from a previously developed quality checklist (17 items) designed for reviews of observational studies based on the QUIPS tool (Appendix 2) (Oosterom-Calo et al., 2012). The QUIPS tool consists of an evaluation of six potential biases: (1) bias due to patient selection; (2) study attrition; (3) measurement of prognostic factors; (4) outcome measurement; (5) confounding measurement; and (6) statistical analyses (Hayden et al., 2006). The 11 items in the short form quality questionnaire describe each of the potential biases in one or more questions, these questions could be answered with yes or no and were scored separately. Thereafter, the overall quality of the study was assessed and summarized by comparing each of the 11-items in a consensus meeting (RvdP, HW or LS). Finally, the studies were classified into three quality levels: low (≤5 items sufficient), moderate (>5 and <9 items sufficient) and high (≥9 quality items sufficient). A third reviewer (MV) was consulted to reach consensus when necessary.

2.5. Data extraction

Data extraction was performed based on original data described in the manuscript and authors were approached when essential data were not provided or were inconsistent. Of the selected studies data was extracted regarding study design (cross-sectional or longitudinal), characteristics of the analytical study sample (number of participants, mean age or age range, percentage of females, study setting), publication year and data collection year, duration of follow-up for studies with a longitudinal design, country, the definition of the outcome PEM as applied in the study, multivariately analysed statistically significant determinants ($p \leq 0.05$) and statistically non-significant determinants ($p > 0.05$), statistics and effect measures with 95% confidence limits.

2.6. Best evidence synthesis

Due to heterogeneity between studies regarding study design, study population, determinants, outcome measures and statistical analyses, a quantitative approach or meta-analysis was not possible. We performed a best evidence synthesis to systematically report, summarize and grade the level of evidence for all determinants included in the review. This approach is well suited to

summarize heterogeneous studies (Slavin, 1995) and has been used in previous studies (Slavin, 1995; Xing et al., 2012; Gomes and Higginson, 2006; Lievense et al., 2002).

The best evidence synthesis was performed as follows. First, the included studies were rated according to the quality and design of the study. High quality studies with a longitudinal design were rated with 4 points, moderate quality studies with longitudinal design with 3 points, high quality cross-sectional studies with 2 points and moderate quality cross-sectional studies with 1 point. Second, we summed the scores of all studies that investigated the same determinant separately for the statistically significant and non-significant results. *For example: DETERMINANT-A was assessed in 3 studies. One study was rated with 3 points and provided a statistically non-significant association, 1 study was rated with 4 points, and 1 study with 1 point both reporting a statistically significant association for DETERMINANT-A. The total sum score of this DETERMINANT-A was 8 points (3+4+1), 3 points for a statistically non-significant association and 5 for a statistically significant association.* Third, determinants with a total sum score (summing the score of the statistically significant and non-significant results, *which was 8 points for DETERMINANT-A*) of less than 4 points and/or determinants described in a single study only were not included in the best evidence synthesis because of insufficient evidence. Fourth, for all determinants with a total sum score of 4 or more points and described in at least two studies, the total score of the statistically significant results and the total score of the statistically non-significant results were divided to reach a best evidence score (BES). *For example: the previously used DETERMINANT-A was not statistically significantly associated with PEM in study 1 (3 points) and statistically significantly associated with PEM in study 2 (1 point) and study 3 (4 points), the BES was calculated as: 5 points (significant) divided by 3 points (statistical non-significant) = BES: 1.67.* In case there were no studies with a statistically non-significant score, the BES was based on the score of the statistically significant studies. *For example: DETERMINANT-B had a sum score of 7 (significant) and 0 (non-significant), resulting in a BES of 7 points.* Fifth, cut-off values for the BES were interpreted as: $\geq$4 = strong evidence for an association; 2–4 = moderate evidence for an association; 0.5–2 = inconclusive evidence; >0–0.5 = moderate evidence for no association; and 0 = strong evidence for no association.

3. Results

3.1. Search results

The systematic literature search resulted in 17498 studies from which 6007 duplicate studies were deleted. In total the search provided 11491 studies which were screened for in- and exclusion criteria based on title and abstract and 166 were read in full-text. Two full text studies were not traceable through inter library loaning or authors and were therefore excluded from this review (Donkin et al., 1998; Miller and Daniels, 2000). The most frequent reasons for exclusion after reading full text papers were: outcome not PEM (n = 65), study design other than inclusion criteria (n = 23) and study population not community-dwelling (n = 16). Fig. 1 shows the flow diagram for the identification of the included studies.

3.2. Quality assessment

The methodological quality was determined for 32 studies. Four studies were excluded from further data extraction because of a low quality score. Of the remaining 28 studies included in this review, 13 were rated as high quality and 15 were rated as moderate quality. In high quality studies, the outcome and determinants were clearly described. In moderate quality studies often information on the measurement of the determinants (i.e. by means of a questionnaire or test) or information on study attrition was lacking.

3.3. Study characteristics

Table 1 shows the characteristics of the 28 included studies in this review. The total number of participants in the 10 longitudinal studies varied from 563 to 4512 subjects and in the 18 cross-sectional studies from 49 to 12,883 subjects. All studies were performed in a mixed sample of males and females. The follow-up period of the longitudinal studies ranged from one to 12 years. All studies were published between 1995 and 2012. Of the 28 studies, 11 were conducted in the USA, five in Canada, two in the Netherlands and two in Sweden, one each performed in Cuba, France, Japan, Brazil, UK, Israel, Russia and one multi-country study. PEM was defined as weight loss over a certain time period (11 studies), low nutritional intake (6 studies), low body weight (6 studies), poor appetite (1 study) or a combination of these outcome measures (referred to as miscellaneous, 4 studies).

3.4. Best evidence synthesis

In total, 122 independent determinants were studied in the 28 included studies. Of these, 37 were included in the best evidence syntheses based on a total sum score of at least 4 and a minimum of two studies. Table 2 shows the results of the best evidence synthesis. We found strong evidence for a positive association with PEM for: poor appetite. Moderate evidence for a positive association was found for hospitalization, no diabetes, edentulousness and self-reported health. For 13 determinants there was inconclusive evidence for an association. For 18 determinants there was moderate evidence for no association and for 11 determinants there was strong evidence for no association with PEM. These were alcohol use, anxiety, chewing difficulty, few friends, living alone, feeling lonely, death of spouse, high number of diseases, heart failure and coronary failure, stroke (CVA) and the use of anti-inflammatory medications. Table 3 shows the determinants, ordered by domain, which could not be included in the best evidence synthesis because too few studies of high quality were performed. In the paragraphs below, the findings for all 122 determinants are described, categorized into nine domains: demographic; financial; food and appetite; lifestyle; psychological; physical functioning; disease and care; oral domain and social domain.

3.4.1. Demographic domain

For sex, inconclusive evidence for an association was found (BES: 0.79) in 17 studies. Seven studies showed female sex was associated with PEM while in one study male sex was associated with PEM (regarded as statistically non-significant when summarizing the results of female sex). For older age (BES: 0.48, 20 studies), region (BES: 0.17, three studies) and low education (BES: 0.11, seven studies) moderate evidence for no association with PEM was found. Four determinants could not be included in the best evidence synthesis: marital status; ethnicity; race and religion.

3.4.2. Financial domain

Moderate evidence showed that a low income was not associated with PEM (BES: 0.22) in four studies performed in France (n = 1), Canada (n = 2) and USA (n = 1). Two determinants could not be included in the best evidence synthesis: not enough money for food and not enough money for medication.

3.4.3. Food and appetite domain

Strong evidence for an association with PEM was found for a poor appetite in five studies (BES: 12.00). A statistically significant

Table 1
Full text data extraction.

Reference	Study type	Analytical sample				Year	Country	Outcome	Determinants	Statistics	Quality score	Study score
		N	Age (y) mean (SD)	Female %	Setting							
Rodrigues Barbosa et al., 2010	CS	1905	71.1 (8.6)	65.2	Population based household survey	PY: 2010 DCY:1999–2000	Cuba	**Low weight (M)** **BMI < 22 kg/m²** vs. Normal weight BMI ≥ 22–27 kg/m² M: Mean of 3× height and weight	***(Questionnaire)*** **Age (older)** **Smoker (current)** **Hypertension (vs. no)** **Diabetes (vs. no)** Sex (male vs. female), Education (low vs. high), Physical activity (yes)	***Odds Ratios (95% CI)*** **2.05 (1.46, 2.88)** **1.83 (1.36, 2.45)** **0.77 (0.61, 0.99)** **0.58 (0.40, 0.84)** NS *Adjusted: all variables above*	H	2
St-Arnaud-McKenzie et al., 2010	LT	1497	(67–84)*	52.3	Healthy well-functioning community-dwelling older adults	PY: 2010 DCY: 2003–2005 FU: 2y	Canada	**Weight loss (M)** **≥ 5% over 2y** vs. Weight stable < 2% weight change over 2y	***(Measure + test)*** **Physical performance** (total score: range 0–32) *Sum of biceps, quadriceps, grip strength, timed up and go, chair stand, gait speed, balance performance scores (individual 0–4 score)*	***Odds Ratios (95% CI)*** **0.79 (0.63, 0.99)** *Adjusted: sex age, BMI, depressive symptoms, energy intake, PA, smoking, #medication, #chronic illnesses, albumin concentrations*	H	4
Stephen and Janssen, 2010	LT	4512	≥65	57.1	Population based community-dwelling older adults non-institutionalized	PY: 2010 DCY: 1989–1990 FU: 7 ± 1.8y	Canada	**Weight loss (M)** **≥10% weight loss group**	***(Questionnaire)*** Physical activity Inactive vs. Active	***Hazard Ratio (95% CI)*** 0.88 (0.74–1.03) NS *Adjusted: sex, age, race, height, income, smoking, alcohol, baseline disease, incident disease, number of weight measures over 8 years*	H	4
Meijers et al., 2009	CS	12883	76.2 (12.0)	62.8	Older adults in home-care organizations	PY: 2009 DCY: 2005	Netherlands	**Miscellaneous** **BMI (M)** **<18.5 kg/m² *or*** **Weight loss (Q)** **6 kg in 6 months or 3 kg in 1 month** ***or*** **BMI (M)** **18.5–20 kg/m² and no nutritional intake (Q) for 3 days or reduced intake >10 days** vs. Well-nourished	***(Questionnaire + measure)*** **Cancer (%)** **Diabetes mellitus (%)** **Gastrointestinal Tract (%)** Sex (m/f), Age/groups, Region/ward type, Time since admission, Infection disease, Blood disease, Dementia, Coronary heart disease, Stroke (CVA), COPD, Musculoskeletal disorders, Prevalent disease	***Odds Ratios (95% CI)*** **4.19(3.32, 5.29)** **0.67(0.52, 0.87)** **1.58 (1.18, 2.11)** NS	H	2
Locher et al., 2008	CS	230	79.1 (8.6)	78.7	Home bound older adults receiving home care	PY: 2008	USA	**Low intake** **Under eating (Q)** **Caloric intake (24-h recall) – estimated energy requirement (kcal)**	***(Questionnaire)*** **Male sex (vs. female)** **Frequency of care (vs. >1time/day)** **Once daily** **1–3 time/week** **Prior hospitalization** **BMI obese class II and III (vs. underweight)**	***Odds Ratios (95% CI)*** **4.02 (1.54, 10.52)** **0.29 (0.10, 0.80)** **6.69 (1.05, 42.42)** **2.08 (1.02, 4.25)** **48.07 (8.30, 278.57)**	M	1

									Age (younger), Education (lower), African/American ethnicity, Social support, Caregiver, Religion	NS		
Sorbye et al., 2008	CS	4010	Males: 80.9 (7.5) Females: 82.8 (7.3)	74	Older adults in home care	PY: 2008	Multi country	**Weight loss (Q)** **5% weight loss in 30 days *or*** **10% in 180 days** vs. No weight loss	***(Questionnaire)*** **Intake less than one meal a day** **Reduced appetite** **Severe malnutrition** **Reduced social activity** **Hospitalization in last 90 days** **Eating less** **Constipation** **Falls** **Oral problems swallowing food** **Flare-up of chronic disease** **Pressure ulcers** **Daily pain** Male Sex (vs. female), Older Age, Living alone, Use of formal services, Hospital visit Emergency unit visit, Emergency at home, Frequency of care, Insufficient fluid/food intake, Mouth pain during eating, Dry mouth, Tube feeding, Vomiting, Diarrhea, Pain, Vision decline (last 90 days), IADL dependency >3 (0–7), ADL dependency >3 (0–8), Loneliness, Not out of house last week, Depression risk ≥1 (0–9), Cognition performance >3 (0–6), Self-Reported health (bad vs. good), Terminal prognosis <6 months, Cancer, Unstable condition, Disease/chronic problem, stroke, heart failure, dementia, Parkinson's disease, psychiatric diagnosis	***Odds Ratios (95% CI)*** **4.2 (2.8, 6.4)** **2.5 (1.9, 3.4)** **7.1 (4.2, 11.9)** **2.0 (1.6, 2.5)** **2.1 (1.6, 2.7)** **2.8 (1.8, 4.4)** **1.9 (1.3, 2.7)** **1.5 (1.2, 1.9)** **2.8 (1.8, 4.4)** **1.5 (1.1, 2.1)** **1.5 (1.2, 1.9)** **1.3 (1.0, 1.6)** NS	M	1
Lee et al., 2006	CS	2169	(70–79)*	54.6	Community-dwelling older adults	PY: 2006 DCY: 1997–1998	USA	**Impaired appetite (Q)** **(5 point Likert scale: very good, good, moderate, poor, very poor)** **Impaired:moderate, poor and very poor appetite**	***(Questionnaires)*** **Female sex** **Smoking** **Current** **Former** **Weight change (M)** **Loss**	***Odds Ratios (95% CI)*** **1.74 (1.29, 2.35)** **2.16 (1.42, 3.29)** **1.38 (1.01, 1.89)** **1.78 (1.25, 2.54)**	H	2

Table 1 (*Continued*)

Reference	Study type	Analytical sample				Year	Country	Outcome	Determinants	Statistics	Quality score	Study score
		N	Age (y) mean (SD)	Female %	Setting							
									Gain	**0.60 (0.43, 0.84)**		
									Poor self-reported health	**2.36 (1.72, 3.24)**		
									Depression (CES-D)	**2.52 (1.55, 4.11)**		
									Chewing pain	**1.97 (1.21, 3.20)**		
									Reported visual impairment	**1.80 (1.32, 2.45)**		
									Log TNF-α	**1.71 (1.23, 2.34)**		
									Age, Trying to lose weight, Cancer, Having anti-inflammatory medicine, Death of spouse, Race, Education (< than high school), Not enough money to buy food, Current drinker, Physical activity (kcal/week), BMI (<25 kg/m vs. >25 kg/m^2) (M), Having at least 1 chronic disease, Coronary heart disease, Diabetes, Number of medicines, Hospitalization (past 1 year), Staying in bed, Cutting down things, Difficulty preparing meals, Difficulty, shopping, Anxious, Eating alone, Living alone, Family network, Friends network, Edentulous, Denture use, Reported hearing impairment, IL-6	NS		
Feart et al., 2007	CS	1786	(68–95)* Males: 76.1 Females: 76.8	62.7	Community-dwelling older adults	PY: 2007 DCY: 1999–2000 2001–2002	France	**Low intake (Q) (kJ) (1× 24 h recall weekday)**	***(Questionnaire)***	***Unstandardized regression coefficients (95% CI)***	H	2
									Female sex	**−1970(−2184, −1754)**		
									Older age ≥ 85y	**−470 (−882, −58)**		
									Marital status			
									Single vs. married	**572 (154, 991)**		
									Divorced vs. married	**391 (3, 779)**		
									Widowed vs. married	NS		
									Education	NS		
									High income vs. lowest	**B 521 (58, 984)**		
									BMI (<21 kg/m^2) (M)	NS		
Ikebe et al., 2006	CS	807	60–64 (39.2%) 65–69 (40.5%) 70+ (20.3%)	49.4	Community-dwelling, independently living healthy older adults	PY: 2006	Japan	**Low weight (Q?) Underweight BMI <20.0 kg/m^2**	***(Questionnaire)***	***Odds Ratios (95% CI)***	M	1
									Female sex	**2.80 (1.76, 4.48)**		
									Low masticator performance (M)	**1.98 (1.14, 3.43)**		
									Age, Self-assessed general health, Number of teeth (4 cat.), Type of dentition, Low chewing/occlusal force (M)	NS		

Agostini et al., 2004	LT	885	81.0 (5.2)	72.0	Community-dwelling older adults	PY: 2004 DCY: 1991-1992	USA	**Weight loss (Q)** **≥10 pounds in 1 year follow up**	***(Recorded by nurse)*** **Medications (vs. none)** 1–2 **3–4** **≥5**	***Odds Ratios (95% CI)*** NS **1.96 (1.08, 3.54)** **2.78 (1.38, 5.60)** *Adjusted: age, sensory impairment, number of chronic disease, number* of hospitalizations, cognitive impairment, depressive symptoms	M	3
Weyant et al., 2004	LT	1053	72.7 (2.8)	50.3	Older adults	PY: 2004 DCY: 1997–1998 FU: 2y	USA	**Weight loss (M)** **body weight ≥ 5% in 2 years follow up**	***(Measure)*** **Probing depth (mm)**	***Odds Ratios (95% CI)*** **1.53 (1.32, 1.77)** *Adjusted: age, race, education, smoking, number of teeth remaining, diabetes, BMI*	H	4
Barreto et al., 2003	CS	1258	≥60	43.5	Older adults living in a town	PY: 2003 DCY: 1996	Brazil	**Low weight (M)** **BMI <20.0 kg/m²** vs. BMI 20–30 kg/m²	 Female sex (vs. male) **Older age** **Higher education** **Smoking current vs. never** Physical inactivity (y/n) **Hypertension (y/n)** **Diabetes (y/n)** **Anemia (y/n)** **T. cruzi infection (y/n)** Visit to doctor (1 vs. none) **Hospitalization >2× in the last years (vs. none)** **Poor self-related health (vs. good)**	***Odds Ratios (95% CI)*** NS **2.5 (1.5, 4.0)** **0.3 (0.1, 0.7)** **1.7 (1.1, 2.6)** NS **0.6 (0.4, 0.8)** **0.4 (0.2, 0.8)** **2.0 (1.0, 4.0)** **1.7 (1.2, 2.3)** *Adjusted: listed above* NS **2.4 (1.4, 4.2)** **1.5 (1.0, 2.4)** *Adjusted: age, sex, education + above listed*	M	1
Margetts et al., 2003	CS	1368	65–74 (37.1%) 75–84 (38.5%) 85+ (24.4%)	49.3	Free-living older adults (17% institution)	PY: 2002 DCY: 1998	UK	**Miscellaneous (M+Q)** **- BMI < 18.5 kg/m²** **or** **- BMI 18.5–20.0 kg/m² and weight loss ≥3.2 kg** **or** **- BMI >20.0 and weight loss ≥6.4 kg)** vs. low risk – BMI >20kg/m² no weight loss	***(Questionnaire)*** **Hospitalized last year (y/n)** **Institution (vs. free living)** **Longstanding illness (y/n)** **Older age** **(≥ 85years)** **Region** **Bad health (vs. good)**	***Odds Ratios (95% CI)*** **M: 1.83 (1.06, 3.16)** **M: 2.17 (1.22, 3.88)** **M: 2.34 (1.20, 4.58)** **F: 2.98 (1.58, 5.62)** **M: 2.64 (1.30, 5.33)** **M: 2.81 (1.54, 5.11)** **F: 2.82 (1.25, 6.38)** *Adjusted: age, sex, region, domicile, health status, illness, hospitalized*	M	1

Table 1 (*Continued*)

Reference	Study type	Analytical sample				Year	Country	Outcome	Determinants	Statistics	Quality score	Study score
		N	Age (y) mean (SD)	Female %	Setting							
Shahar et al., 2003	CS	377	65–74 (59.4%) >75 (40.6%)	54.4	Community-dwelling older adults	PY: 2002	Israel	**Low intake (Q)** **Total MJ (24 h recall)** vs. recommended daily allowances	***(Questionnaire)*** **Higher frequency eating alone** **Poor appetite** Gastrointestinal problems **Higher medication use** **No snacking** Older age	***Standardized regression coefficients*** **M:β 0.20, p:0.01** F: NS **M:β 0.19, p:0.01** F:**β** 0.27, p:0.001 NS **M:β 0.24, p:0.002** F:**β** 0.16, p:0.03 **M:β 0.26, p:0.01** F:NS NS	M	1
Shatenstein et al., 2001	LT	584	70–79 (27%) 80–89 (55%) 90+ (18%)	59.6	Community-dwelling older adults	PY: 2001 DCY: 1991–1992 FU: 5y	Canada	**Weight loss (M)** **Risk: ≤ 95% of initial body weight** vs. No risk: >95% of initial body weight	***(Questionnaire)*** **Loss of interest in life (y/n)** **Loss of appetite (y/n)** Age, Sex, Cognitive diagnosis (3MS score), Study region, Presence of spouse, Functional vulnerability, Difficulty feeding self, Depressive symptoms, Weight loss self-reported, Clinical impression depression, Frailty scale (7cat.), Income	***Standardized regression coefficients*** **β** 0.22 (0.12–0.42) **β** 0.56 (0.34–0.90) NS	H	4
Ritchie et al., 2000	LT	563	Males: 77.3 (4.7) Females: 78.1 (5.3)	57.9	Home living community-dwelling older adults	PY: 2000 FU: 1y	USA	**Weight loss (Q)** **≥10% of total body weight in 1 year**	***(Questionnaire)*** **Sex – female** Age ≥ 80 year Annual income **Higher baseline weight** **Edentulous (M)** More than 2 diagnoses **Dependent in ADL**	***Odds Ratios (95% CI)*** **3.77 (1.71, 8.33)** NS NS **1.02 (1.01, 1.03)** **2.03 (1.05, 3.96)** NS **2.27 (1.08, 4.78)** *Adjusted: depression, smoking, alcohol use, PA*	H	4
Marshall et al., 1999	CS	1006	74.5 (65–99)*	56	Rural community-dwelling adults	PY: 1999 DCY: 1993–1995	USA	**Weight loss (M)** **>10 lb in past 6 months**	Hispanic ethnicity (vs. other) Female sex (vs. male)	***age adjusted*** p:0.73 NS p:0.34 NS	M	1

Keller et al., 1997	CS	5073	72.7 (65–98)*	60	Community living older adults	PY: 1997 DCY: 1990	Canada	Low intake (FFQ) kJ	***(Questionnaire)***	***Unstandardized regression coefficients (95% CI)***	M	1
									Poor perceived health status (vs. good/excellent)	M: NS **F: 581 (233, 929)**		
									Dentate (y/n)	**M: −717 (−1097, −337)** **F: −290 (−576,** −4)		
									Feeling happy (y/n)	**M: −1569 (−2242, −896)** F: NS		
									Difficulty hearing (y/n)	M: NS **F: −724 (−1347, −102)**		
									Current smoking (y/n)	**M: 644 (157, 1132)** F: NS		
									Walking dependence (vs. independent)	M: NS **F:483 (55.6, 909)**		
									No longer drive (vs. drive)	**M: −602 (−1111, −93)** **F: −452 (−735, −170)**		
									IADL dependence (vs. independent)	**M: 818 (76, 1560)** F: NS		
									High Income (vs. low), Social support, Low Education level (vs. high), Nutrition/health link, Chewing difficulties, Number of chronic diseases/health problems, Number of medications, BMI, Cognition - think clearly, Age, Married	NS		
Payette et al., 1995	CS	145	78.8 (60–94)*	71	Community living older adults people	PY: 1995 DCY: 1991	Canada	Low intake (Q) (total kJ in three nonconsecutive 24-h recalls)	***(Questionnaire)***	***Unstandardized regression coefficients***	H	2
									Female sex (vs. male)	**−1.29 (SE 0.26) p: <0.01**		
									Age (y)	NS		
									Burden of disease (score)	**−0.05 (SE 0.02) p: <0.05**		
									Level of stress (high, moderate, low)	NS		
									Good appetite (often, sometimes, vs. never)	**0.39 (SE 0.15) p: <0.01**		
									Vision (good, fair, poor)	NS		
									Arthritis	NS		
									Medication use (psychotropic)	NS		
									Friends network	NS		
Rush and Welch, 1996	CS	2281	70–74 (38.5%) 7579 (28.7%) 8084 (22.0%) 85+ (10.8%)	76.1	Older rural pensioners	PY: 1996 DCY: 1992	Russia	**Weight loss (Q) ≥5 kg in previous 6 months** vs. no weight loss	***(Questionnaire)***	***Odds Ratios (95% CI)***	M	1

Table 1 (*Continued*)

Reference	Study type	Analytical sample				Year	Country	Outcome	Determinants	Statistics	Quality score	Study score
		N	Age (y) mean (SD)	Female %	Setting							
									Not enough money for food **< 3 meals a day** **Eats alone** **Difficulty to cook for self** **Difficulty to shop for self** **Illness affecting eating habits** **3+ drugs per day** **Teeth/mouth problems** **Can't afford medication** **Medication not available in pharmacy** **Low diet score (<7)** Age (y) Sex (m/f)	M: NS **F: 1.66 (1.36, 2.04)** **M: 1.95 (1.19, 3.20)** **F: 1.93 (1.47, 2.52)** M: NS **F: 1.34 (1.10, 1.63)** **M: 1.71 (1.16, 2.51)** **F:1.24 (1.01, 1.52)** **M: 1.54 (1.06, 2.24)** **F: 1.44 (1.16, 1.79)** **M: 2.17 (1.50, 3.14)** **F: 1.82 (1.49, 2.23)** **M: 2.13 (1.43, 3.19)** **F: 1.95 (1.57, 2.43)** M: NS **F: 1.33 (1.09, 1.63)** **M: 2.16 (1.43, 3.17)** **F: 1.45 (1.18, 1.79)** **M: 1.89 (1.31, 2.75)** **F: 1.49 (1.21, 1.83)** M: NS **F: 1.45 (1.14, 1.86)** *Adjusted: age and BMI* ***Standardized regression coefficients*** NS NS *Adjusted: illness affecting eating, number of drugs, not enough money to buy food*		
Dziura et al., 2004	LT	2812	Survivors: 71.0 (5.0) Non-survivors: 76.0 (7.0)	69 51	Non institutionalized older adults	PY: 2004 DCY: 1982 FU: 12y	USA	**Weight loss/change per year (Q) (pounds body weight annually)**	***(Questionnaire)*** **Physical activity × time** **Age (y) × time** Chronic condition × time **Mobility × time** Smoking × time	***Unstandardized regression coefficients (95% CI)*** **0.09 (0.02, 0.15)** **−0.07 (−0.08, −0.05)** NS **0.36 (0.09, 0.63)** NS *Adjusted: sex, race, education, height, functional disability score and housing and variables above*	H	4
Mamhidir et al., 2006	CS	508	86.2 (5.5)	72	Older adults residing in sheltered housing	PY: 2006 DCY: 2000–2002 FU: 1y	Sweden	**Miscellaneous (M)** **BMI <22 kg/m^2** **or** **Weight loss, 5%/10% over 1 year**	***(Questionnaire)*** **Impaired Cognitive performance** (CPS-scale 0–6)	***Odds Ratios (95% CI)*** **1.84 (1.27, 2.68)**	H	2

								Impaired Activities of Daily Living (ADL)	**1.79 (1.16, 2.77)**		
								Age	**1.04 (1.00, 1.08)**		
								Difficulty eating self/dependency	**2.26 (1.68, 3.04)**		
								Constipation	**2.49 (1.19, 4.96)**		
								Dementia	**2.14 (1.34, 3.41)**		
								Parkinson's Disease	**2.45 (1.01, 5.97)**		
								Depression (0-14 (DRS), Sex, Vision problems, Heart failure, Falls, Hip fracture, Stroke, Cancer, Chewing and swallowing difficulty, Mouth pain, Taste, Hunger, Intake 25% of food uneaten, Dietary supplement use, Oral health/dental status, Number of medication, Prescribed medication	NS		
Locher et al., 2005	CS	50	77.1 (8.7)	64	Homebound older adults receiving home care	PY: 2005	USA	**Low intake (Q) kcal per meal (24 h recall)**	***(Questionnaire)***	***Regression coefficients***	M	1
									Eating alone	NS		
									Living with someone vs. living alone	NS		
									Female sex vs. men	**−76.6, p:0.045**		
Martin et al., 2007	CS	130	≥65	55	Community-dwelling older adults	PY: 2007 DCY: 2003–2004	USA	**Low weight BMI <19 kg/m^2** vs. BMI ≥ 19kg/m^2	***(Questionnaire)***	***Odds Ratios (95% CI)***	M	1
									Illness that changes the kind/amount of food	**4.7 (1.6, 13.1)**		
									Weight loss ≥10 lb in past 6 months	**4.0 (1.5, 10.7)**		
									Assistance with traveling	**4.0 (1.4, 11.3)**		
									<2 meals a day	NS		
									Depression (y/n) (GDS)	NS		
									≤1 fruit/juices a day	NS		
Ritchie et al., 1997	CS	49	78 (1.1)	78	Urban homebound older adults	PY: 1997	USA	**Low weight (M) BMI <24 kg/m^2** vs. BMI ≥24 kg/m^2	***(Questionnaire)***	***Standardized regression coefficients***	M	1
									Older Age	**β 0.39 (se 0.16)**		
									Less education	NS		
									Difficulty in chewing	NS		
									Wearing of dentures	NS		
Schilp et al., 2011	LT	1120	74.1 (5.7)	51.5	Community-dwelling older adults	PY: 2011 DCY: 1992–1993 FU: 9y	Netherlands	**Miscellaneous (M) BMI <20 kg/m2 or Involuntary weight loss ≥5% in 6 months**	***(Questionnaire)*** **Poor appetite**	***Hazard Ratios (95% CI)*** **1.63 (1.02, 2.61)**	H	4

Table 1 (*Continued*)

Reference	Study type	Analytical sample				Year	Country	Outcome	Determinants	Statistics	Quality score	Study score
		N	Age (y) mean (SD)	Female %	Setting							
									Difficulties walking stairs **<75 years** ≥75 years Female, Age ≥ 75 years (vs. younger), Depressive symptoms (vs. no), Anxiety symptoms (vs. no), ≥ 2 chronic disease (vs. none), ≥ 1 Medication use (vs. no), Limitations of normal activities due to a health problem, Physical performance test, Alcohol use (vs. no), Loneliness (vs. no), Having a partner (vs. yes)	 **1.91 (1.14, 3.22)** NS NS		
Fagerstrom et al., 2011	LT	1230	76.1 (9.9) (60–96)*	57.6	Regular housing	PY: 2011 DCY: 2001-2003	Sweden	**BMI ≤23 kg/m² (M)**	 **Female sex** Older age Cognitive ability Mild impairment **Moderate or severe**	***Odds Ratios (95% CI)*** **2.31 (1.61, 3.31)** 1.02 (1.00, 1.04) NS **3.04 (1.54, 6.01)** *Adjusted: living arrangement, housing arrangement, functional ability and above mentioned*		
Alley et al., 2010	LT	2690	Men: 73.7 (2.8) 73.7 (2.9) Women: 73.5 (2.9) 73.4 (2.8)	50.8	General population	PY: 2010 RP: 1997–1998 FU: 1y	USA	**Weight loss/change per year (M)** **Total mass (kg) (DXA scan)**	**Hospitalization (vs. no hospitalization)** *(clinical visits and telephone interviews)*	***Regression coefficients (95% CI)*** **M: −0.79 (−1.04, −0.54)** **F: −0.79 (−1.07, −0.51)** *Adjusted: demographics (age, race, study site) health behaviors (smoking, walking for exercise), co morbidities (diabetes, cancer, cardiovascular disease, arthritis, chronic lung disease, depression) and baseline values of mass, fat mass, lean mass, strength or/in separate regressions*	M	3

Abbreviations: CS, cross-sectional; LT, longitudinal; Q, quality (H = high, M = moderate); Y, year; SD, standard deviation; PY, publication year; DCY, data collection year; FU, follow-up; outcome M, measure and Q, questionnaire; vs., versus; BMI, body mass index; PA, physical activity; #, number; MV, multivariate; CI, 95% confidence interval; ADL, activities of daily living; IADL, instrumental activities of daily living; COPD, chronic obstructive pulmonary disease; CVA, cerebral vascular accident; M/F, male/female; Y/N, yes/no; IL-6, interleukine-6; OHRQoL, oral health related quality of life; SE, standard error; MJ, mega joule; KJ, kilo joule; RP, recruitment period.

* Age range.

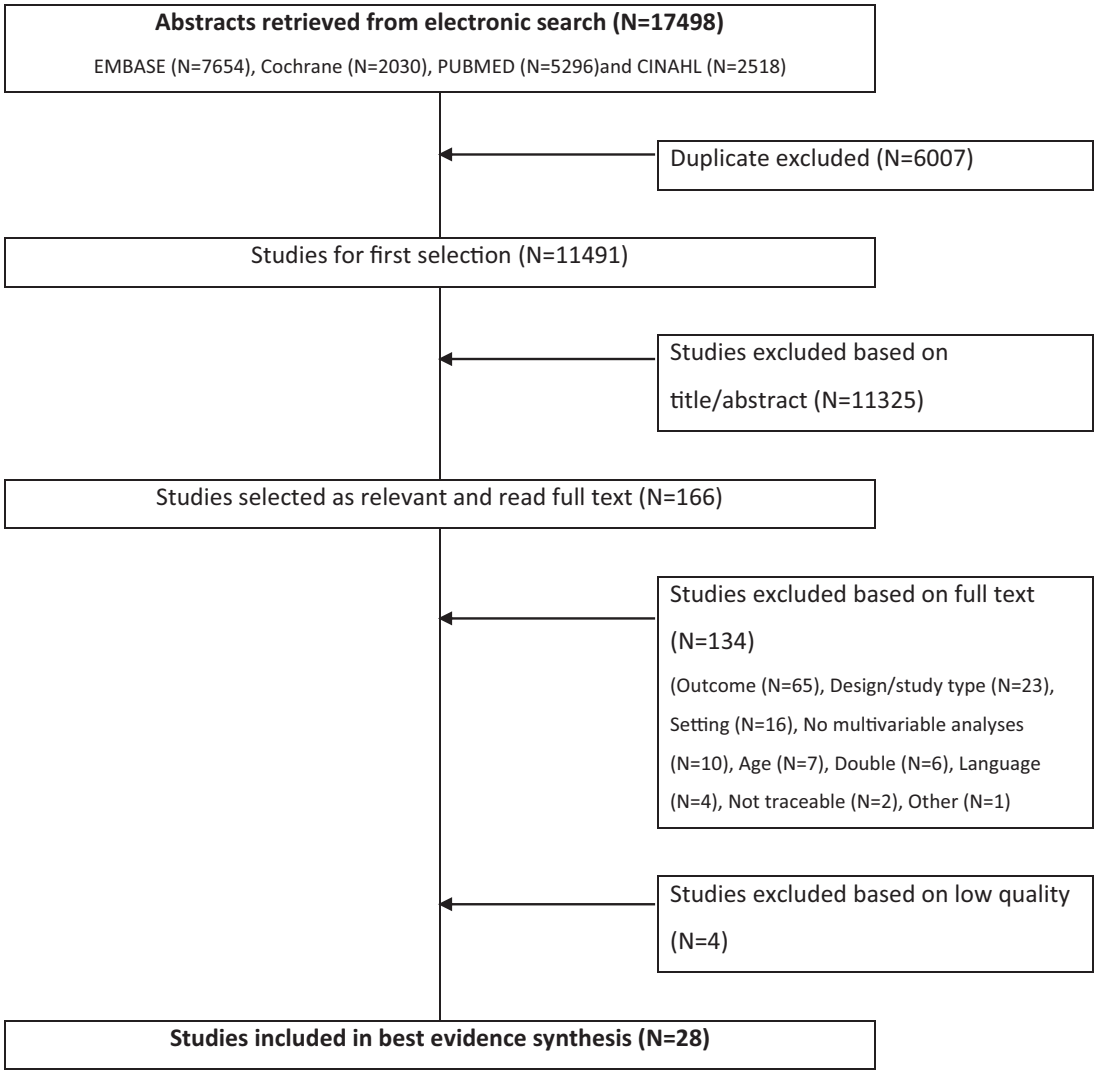

Fig. 1. Flowchart review study selection.

association was found and the outcome measure was in these five studies other than appetite (weight loss ($n = 2$), low intake ($n = 2$) and a combination of low BMI and weight loss ($n = 1$)). Determinants that could not be included in the best evidence synthesis were the number of meals consumed a day, low diet score, snacking, eating less, eating less fruit and insufficient fluid of food intake, nutritional health link, severe malnutrition, tube feeding, supplement use and hunger.

3.4.4. Lifestyle domain

Within the lifestyle domain five determinants were included in the best evidence synthesis. Low physical activity (BES: 1.60, five studies) and smoking (BES: 1.50, five studies) were inconclusive. Weight loss (BES: 0.25, two studies) and high BMI (BES: 0.20, four studies) showed moderate evidence for no association and alcohol use (BES: 0.0, two studies) provided strong evidence for no association. Insufficient evidence was found for high baseline weight, weight change and trying to lose weight.

3.4.5. Psychological domain

Four determinants were included in the evidence synthesis. Cognitive decline (BES: 0.83, five studies) and dementia (BES: 0.67, three studies) were inconclusive, moderate evidence for no association was found for depression (BES: 0.17, six studies) and strong evidence for no association for anxiety (BES: 0.0) in two studies. The determinants not included in the best evidence synthesis were loss of interest in life, feeling happy, cutting down things, psychiatric diagnosis and stress.

3.4.6. Physical functioning domain

Inconclusive evidence was found for ADL dependency (BES: 1.40, five studies), low physical functioning (BES: 1.00, two studies) and difficulty feeding (BES: 0.50, two studies). There was moderate evidence that vision decline (BES: 0.40, four studies) was not associated with PEM. The determinants with insufficient evidence within the physical domain were shown in Table 3.

3.4.7. Disease and care domain

Hospitalization (BES: 3.50, six studies), self-reported poor health (BES: 2.50, six studies) and having no diabetes (BES: 2.50, four studies) showed moderate evidence for an association with PEM. The use of high number of medications (BES: 0.56, seven studies) was inconclusive and for cancer (BES: 0.40, four studies) and having a chronic disease (BES: 0.14, four studies) there was moderate evidence for no association. For heart and coronary failure, anti-inflammatory medication, stroke and increased number of disease strong evidence was available for no association with PEM

Table 2
Best evidence synthesis determinants (Kubrak and Jensen, 2007).

Determinants	SUM # study	# sig studies	# NS studies	SUM points*	# sig points*	# NS points*	BES‡
Demographic domain							
Female sex‡	**17**	7	10	**34**	15	19	**0.79**
Older age	**20**	7	13	**40**	13	27	**0.48**
Region	**3**	1	2	**7**	1	6	**0.17**
Low education	**7**	1	6	**10**	1	9	**0.11**
Financial domain							
Low income	**4**	1	3	**11**	2	9	**0.22**
Food & appetite domain							
Poor appetite	**5**	5	0	**12**	12	0	**12.00**
Lifestyle domain							
Low physical activity	**5**	2	3	**13**	8	5	**1.60**
Smoker	**5**	4	1	**10**	6	4	**1.50**
Self-reported weight loss	**2**	1	1	**5**	1	4	**0.25**
High BMI	**4**	1	3	**6**	1	5	**0.20**
Alcohol use	**2**	0	2	**6**	0	6	**0.00**
Psychological domain							
Cognition decline	**5**	2	3	**11**	5	6	**0.83**
Dementia	**3**	1	2	**5**	2	3	**0.67**
Depression	**6**	1	5	**14**	2	12	**0.17**
Anxious	**2**	0	2	**6**	0	6	**0.00**
Physical functioning domain							
ADL dependency	**5**	3	2	**12**	7	5	**1.40**
Physical functioning	**2**	1	1	**8**	4	4	**1.00**
Difficulty feeding self	**2**	1	1	**6**	2	4	**0.50**
Vision decline	**4**	1	3	**7**	2	5	**0.40**
Disease & care domain							
Hospitalization	**6**	5	1	**9**	7	2	**3.50**
Self-reported poor health	**6**	4	2	**7**	5	2	**2.50**
No diabetes	**4**	3	1	**7**	5	2	**2.50**
High number of medications	**7**	3	4	**14**	5	9	**0.56**
Cancer	**4**	1	3	**7**	2	5	**0.40**
Disease/chronic problem	**4**	1	3	**8**	1	7	**0.14**
High number of disease	**4**	0	4	**11**	0	11	**0.00**
Heart and coronary failure	**4**	0	4	**7**	0	7	**0.00**
Anti-inflammatory medication	**3**	0	3	**6**	0	6	**0.00**
Stroke (CVA)	**3**	0	3	**5**	0	5	**0.00**
Oral functioning domain							
Edentulousness	**2**	1	1	**6**	4	2	**2.00**
Denture use	**3**	1	2	**4**	1	3	**0.33**
Chewing difficulty	**3**	0	3	**4**	0	4	**0.00**
Social functioning domain							
Eating alone	**4**	2	2	**5**	2	3	**0.67**
Few friends	**2**	0	2	**4**	0	4	**0.00**
Living alone	**3**	0	3	**4**	0	4	**0.00**
Loneliness	**2**	0	2	**5**	0	5	**0.00**
Death of spouse	**2**	0	2	**6**	0	6	**0.00**

* Score is calculated based on quality score and design: Cross-sectional/Moderate × 1 score points, Cross-sectional/High × 2 score points, Longitudinal/Moderate × 3 score points, Longitudinal/High × 4 score points.
In case there are no studies with a statistical non-significant score, the best evidence score is based on the score of the statistical significant studies.
‡Calculated as statistical significant score/statistical non significant score and cutoff values for best evidence to be interpreted as: ≥4 strong evidence for an association, 2 + 3 moderate evidence for an association, 0.5–2.0 inconclusive evidence for an association, 0–0.5 moderate evidence for no association, 0.0 strong evidence for no association.
‡One study that showed statistical significant association for male sex was regarded as non-significant in BES.

(BES: 0.00). Several solitary illnesses and diseases were studied in only few studies (Table 3).

3.4.8. Oral domain

Edentulousness (BES: 2.00) was examined in two studies and moderate evidence for an association with PEM was found. Denture use (BES: 0.33, three studies) and chewing difficulty (BES: 0.00, three studies) were not associated with PEM. Eleven determinants in the oral domain could not be included in the best evidence synthesis (Table 3).

3.4.9. Social domain

Five determinants were included in the best evidence synthesis within the social domain. None provided evidence for an association with PEM. Eating alone was found in four studies (BES: 0.67) and provided inconclusive evidence for an association. For few friends, living alone, loneliness and the death of a spouse there was no evidence for an association with PEM (BES: 0.0). Reduced social activity, family network, having a partner and social support were not included in the best evidence synthesis.

4. Discussion

This review was systematically performed including an evaluation of the methodological quality of the selected studies and the systematic procedures were documented according to the PRISMA Statements (Moher et al., 2009). Poor quality studies were excluded and only studies with multivariable adjusted risk

Table 3
Determinants ($n = 85$) excluded based on sum score and number of studies.

	SUM # study	# sig studies	# NS studies	SUM points*	# sig points*	# NS points*
Demographic domain						
Marital status	**2**	1	1	**3**	2	1
Ethnicity	**2**	0	2	**2**	0	2
Race	**1**	0	1	**2**	0	2
Religion	**1**	0	1	**1**	0	1
Financial domain						
Not enough money for medication	**1**	1	0	**1**	1	0
Not enough money for food	**2**	1	1	**3**	1	2
Food & appetite domain						
Less meals a day/number of meals	**3**	2	1	**3**	2	1
Low diet score	**1**	1	0	**1**	1	0
Severe malnutrition	**1**	1	0	**1**	1	0
Snacking	**1**	1	0	**1**	1	0
Eating less	**2**	1	1	**3**	1	2
Fruit (less intake)	**1**	0	1	**1**	0	1
Hunger	**1**	0	1	**2**	0	2
Insufficient fluid/food intake	**1**	0	1	**1**	0	1
Nutritional/health link	**1**	0	1	**1**	0	1
Supplement use	**1**	0	1	**2**	0	2
Tube feeding	**1**	0	1	**1**	0	1
Lifestyle domain						
High baseline weight	**1**	1	0	**4**	4	0
Weight change	**1**	1	0	**2**	2	0
Trying to lose weight	**1**	0	1	**2**	0	2
Psychological domain						
Loss of interest in life	**1**	1	0	**4**	4	0
Feeling happy	**1**	1	0	**1**	1	0
Cutting down things	**1**	0	1	**2**	0	2
Psychiatric diagnosis	**1**	0	1	**1**	0	1
Stress	**1**	0	1	**2**	0	2
Physical functioning domain						
Walking stairs difficulty	**1**	1	0	**4**	4	0
Mobility	**1**	1	0	**4**	4	0
Drive	**1**	1	0	**1**	1	0
Falls	**1**	1	0	**1**	1	0
IADL dependency	**2**	1	1	**2**	1	1
Institutionalized	**1**	1	0	**1**	1	0
Traveling with assistance	**1**	1	0	**1**	1	0
Difficulty preparing meals	**2**	1	1	**3**	1	2
Difficulty shopping	**2**	1	1	**3**	1	2
Hearing impairment	**2**	1	1	**3**	1	2
Frailty	**1**	0	1	**4**	0	4
Functional vulnerability	**1**	0	1	**4**	0	4
Not out of house last week	**1**	0	1	**1**	0	1
Staying in bed	**1**	0	1	**2**	0	2
Disease & care domain						
Constipation	**2**	2	0	**3**	3	0
Hypertension	**2**	2	0	**3**	3	0
Disease affecting eating habits	**2**	2	0	**2**	2	0
Burden of disease	**1**	1	0	**2**	2	0
Gastrointestinal tract	**2**	1	1	**3**	2	1
Log TNF-α	**1**	1	0	**2**	2	0
Parkinson's disease	**2**	1	1	**3**	2	1
Anemia	**1**	1	0	**1**	1	0
Flair up chronic diseases	**1**	1	0	**1**	1	0
Frequency of care	**2**	1	1	**2**	1	1
Medications not available	**1**	1	0	**1**	1	0
Daily pain	**1**	1	0	**1**	1	0
Pressure ulcers	**1**	1	0	**1**	1	0
Infection	**2**	1	1	**3**	1	2
Arthritis	**1**	0	1	**2**	0	2
Blood diseases	**1**	0	1	**2**	0	2
Caregiver	**1**	0	1	**1**	0	1
COPD	**1**	0	1	**2**	0	2
Diarrhea	**1**	0	1	**1**	0	1
Doctor visit	**1**	0	1	**1**	0	1
Emergency at home	**1**	0	1	**1**	0	1
Emergency unit visit	**1**	0	1	**1**	0	1
Hip fracture	**1**	0	1	**2**	0	2
Hospital visits	**1**	0	1	**1**	0	1
Infection markers (IL-6/TNFα)	**1**	0	1	**2**	0	2
Musculoskeletal disorders	**1**	0	1	**2**	0	2

Table 3 (*Continued*)

	SUM # study	# sig studies	# NS studies	SUM points*	# sig points*	# NS points*
Terminal prognosis <6mnd	**1**	0	1	**1**	0	1
Time since admission	**1**	0	1	**2**	0	2
Unstable condition	**1**	0	1	**1**	0	1
Use of formal service	**1**	0	1	**1**	0	1
Vomiting	**1**	0	1	**1**	0	1
Oral functioning domain						
Probing depth (extent of sites)	**1**	1	0	**4**	4	0
Chewing pain	**1**	1	0	**2**	2	0
Low masticator performance	**1**	1	0	**1**	1	0
Low occlusal force	**1**	1	0	**1**	1	0
Oral problems swallowing	**1**	1	0	**1**	1	0
Teeth/Mouth problems	**1**	1	0	**1**	1	0
Dental Type (edentulous vs. normal)	**2**	0	2	**3**	0	3
Dry mouth	**1**	0	1	**1**	0	1
Mouth pain during eating	**2**	0	2	**3**	0	3
Taste complaints about the food	**1**	0	1	**2**	0	2
Number of teeth	**1**	0	1	**1**	0	1
Social functioning domain						
Reduced social activity	**1**	1	0	**1**	1	0
Family network	**1**	0	1	**2**	0	2
Partner (having partner)	**1**	0	1	**4**	0	4
Social support	**2**	0	2	**2**	0	2

* Score is calculated based on quality score and design: Cross-sectional/Moderate × 1 score points, Cross-sectional/High × 2 score points, Longitudinal/Moderate × 3 score points, Longitudinal/High × 4 score points.

estimates were included. We found moderate to strong evidence that a poor appetite, hospitalization, poor self-reported health, no diabetes, and edentulousness are associated with PEM in community-dwelling older adults. Strong evidence for no association was found for anxiety, chewing difficulty, few friends, living alone, feeling lonely, death of spouse, high number of diseases, heart failure and coronary failure, stroke (CVA) and the use of anti-inflammatory medications. There were 85 potential determinants which could not be included in the best evidence synthesis because too few studies of high quality were performed.

Poor appetite was the single determinant for which strong evidence for an association with PEM was found. Based on previous prospective work, we assumed that poor appetite would be an important determinant of a low energy intake and subsequent weight loss (Schilp et al., 2011). Poor appetite is an intermediate determinant for PEM, likely causally related, therefore we also included appetite as part of our outcome PEM. Poor appetite in older adults is reflected in low energy intakes, and could develop weight loss and a low weight over time that could result in future PEM (Donini et al., 2003). We found one study that examined the determinants of a poor appetite. In this study the authors showed that the determinants of poor appetite are divers and include depression and chewing pain (Lee et al., 2006). This finding is in line with other studies that showed physiological aspects (i.e. reduced smell, reduced taste and prolonged feeling of satiety), psychological aspects (i.e. depression or dementia), social aspects (i.e. poverty or isolation) and medical aspects (edentulous, pain) (Kmiec et al., 2013; Hays and Roberts, 2006). Older adults with a poor appetite are an important target population for future prevention strategies aiming to prevent PEM and specific focus should be signaling poor appetite in this target population.

There was strong evidence for no association between a high number of chronic diseases and PEM. Numerous specific diseases and disorders for example Chronic Obstructive Pulmonary Disease (COPD) and diarrhea were also examined as potential determinants, but did not provide a high enough best evidence score (because not enough studies, or studies with poor quality) to draw conclusions. Besides, we were unable to combine these specific diseases into several overarching disease groups as they were often studied in the same study. As a result many specific diseases could not be included in the best evidence synthesis. We therefore cannot exclude that specific, individual diseases may be important determinants of PEM.

There was moderate evidence for an association between having no diabetes and PEM. This is most likely explained by the fact that people with diabetes are more likely to be obese which is often caused by excessive weight gain (Han et al., 2011; Houston et al., 2009; Overweight, 2000). The association between hospitalization and PEM can be explained by multiple pathways. One is that illness or acute stress caused by surgery during hospitalization increases energy demands. Other likely explanations are physical discomfort (pain, nausea), compromising food intake, and poor quality of food or food services during hospitalization. In a prospective study among 306 older hospitalized patients, Chen et al. found that poor cognitive status, poor oral health, number of medication, poor functional status and depressive symptoms were determinants of poor nutritional health (defined by 18-item MNA, <17 points) during and shortly after hospitalisation (Chen et al., 2009). In addition, based on a narrative review of the available literature it was concluded that hospitalization could contribute to nutritional deficiencies in older adults, which was party explained by the medication prescriptions during hospitalization (Brownie, 2006). More studies are needed to identify and target determinants of PEM during hospitalisation.

Several studies in the oral domain concluded that adequate oral health care is essential for healthy aging (Bots-van't Spijker et al., 2006; Liu et al., 2010). We only found moderate evidence for a positive association between edentulousness and PEM. Edentulousness may result in difficulty chewing, diminished intake of specific foods and PEM. The specific oral health measures were included in few studies in our review using both subjective and various objective measurements techniques to measure oral health problems. In general, there are mayor discrepancies between self-reported oral health and clinically determined oral health status and specific denture problems (Liu et al., 2010). Because of these discrepancies, it was difficult to draw evidence based conclusions of groups or specific determinants like denture problems, masticatory problems and teeth problems. More high quality studies with standardized measurements on these potential determinants in the oral domain are necessary to draw conclusions about their impact on PEM.

As this is the first systematic review, we can only compare our results with previous narrative reviews on determinants of PEM in community-dwelling older adults. The narrative reviews were

performed in different settings, one in a general older population and one among acute care patients. Both reviews concluded that PEM is a multi-factorial problem and that the determinants could be classified into different domains (i.e. social, physiological, and financial) (Brownie, 2006; Kubrak and Jensen, 2007). This is in line with our findings, but the narrative reviews have several methodological limitations. The setting of the included studies was not specified clearly and the selection of studies included in these reviews was not performed using a systematic approach.

Currently, no gold standard is available to define PEM (Health Council of the Netherlands, 2011). PEM is often defined as unintentional weight loss or low weight (Health Council of the Netherlands, 2011). Because there is no gold standard how to measure PEM in a general older population, we decided on forehand to include a low appetite, low energy intake, weight loss, or thinness as measured by low body weight, low BMI, or low mid-upper arm circumference as indicators of PEM. We included weight loss and not unintentional weight loss as an eligible outcome measure because intentionality of weight loss is often not reported and more importantly not discernable. It could be argued that a poor appetite reflects the risk of PEM and not its presence. However, anorexia of aging is a highly prevalent problem in old age (Schilp et al., 2011; Lee et al., 2006; Mudge et al., 2011; Sullivan et al., 2004), and doubles the risk of PEM (Schilp et al., 2011). Determinants of a poor appetite therefore likely resemble determinants of PEM. We excluded screening tools for PEM as outcome measures (Phillips et al., 2010), because these instruments include potential determinants of PEM like physical functioning, chronic disease and depression, which would overestimate the role of these potential determinants.

Due to heterogeneity in the measurements and definitions of both the determinants and outcomes within the included studies, we could not summarize and weigh the existing evidence using a meta-analysis approach. For example low body weight was defined as either a BMI <22 kg/m^2, <18.5 kg/m^2, or <20 kg/m^2, and weight loss was defined as >5% over 30 days, >10% over study follow-up or >5% in two years (Ikebe et al., 2006; Meijers et al., 2009; Rodrigues Barbosa et al., 2010; Sorbye et al., 2008; St-Arnaud-McKenzie et al., 2010; Stephen and Janssen, 2010; Weyant et al., 2004). Therefore, we used a best evidence synthesis to describe, grade and summarise the included heterogeneous studies in a systematically matter. We recognize that by using this approach, the heterogeneity in determinants and outcome measures remains a limitation which cannot be avoided.

Other limitations that could have biased our results, because we merely included observational studies based on secondary data analyses, were selection bias, publication bias and incomplete adjustments for confounding in some studies. Selection bias could have occurred because not all relevant studies were indexed in the search databases, and therefore we could have missed information on potential determinants. Also, we cannot exclude that studies showing non-significant findings were more likely not to be published (publication bias), which could have resulted in stronger associations for potential determinants. In addition, adjustment for confounders (or other potential determinants of PEM) varied largely between studies. For example Rush et al. studied the determinants for weight loss and adjusted for age and BMI in multivariate analyses, while St-Arnaud-McKenzie et al. studied the association between physical performance and weight loss and adjusted for more than 10 variables including age and BMI (St-Arnaud-McKenzie et al., 2010; Rush and Welch, 1996). This could have resulted in an overestimation or underestimation of statistically significant associations reported in the included studies.

Based on professionals experience and expertise, as well as narrative reviews, we expected several determinants to be associated with PEM, including low income, depression and loneliness (Brownie, 2006; Kubrak and Jensen, 2007). However, in our systematic review we found strong or moderate evidence that these potential determinants were not associated with PEM. For some criteria sufficient evidence from high quality studies was available that indicated no association with PEM (i.e. living alone, chewing difficulties and alcohol use). These examples show that there is a tendency to 'know' the determinants for PEM, while the evidence based on the available literature does not confirm all expected associations.

In conclusion, this review shows that PEM is a multi-factorial problem and that different domains likely play a role in the pathway of developing PEM. There are many potential determinants of PEM, but for most determinants evidence is still insufficient or lacking. Of the identified evidence based determinants in this review, several are potentially modifiable determinants (i.e. poor appetite, edentulousness) which provide opportunities for new prevention strategies in the home situation. The preventive strategies should target these underlying determinants in a multidisciplinary way, rather than treating PEM with nutritional supplements or dietetic advices solely. Research should focus on the identification and confirmation of potentially modifiable determinants of PEM among community-dwelling older adults to provide guidance in developing future preventive strategies.

Author contributions

RvdP conducted the literature searches, screened all the references on title and abstract, full text on relevant studies, conducted a quality assessment and a data-extraction of the included studies and wrote the manuscript. HW and LS both screened part of the references on title and abstract, full text on relevant studies, conducted a quality assessment and contributed to the overall manuscript and the final draft. MV provided conceptualization of the study, was consulted when no consensus between the two reviewers (RvdP and HW or LS) could be obtained and contributed to the overall manuscript and the final draft. CT edited the manuscript and provided methodological expertise in the conceptualization of the study.

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