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REVIEW

Effects of health care interventions on quality of life among frail elderly: a systematized review

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Introduction: Many health care interventions have been developed that aim to improve or maintain the quality of life for frail elderly. A clear overview of these health care interventions for frail elderly and their effects on quality of life is missing.

Purpose: To provide a systematic overview of the effect of health care interventions on quality of life of frail elderly.

Methods: A systematic search was conducted in Embase, Medline (OvidSP), Cochrane Central, Cinahl, PsycInfo and Web of Science, up to and including November 2017. Studies describing health care interventions for frail elderly were included if the effect of the intervention on quality of life was described. The effects of the interventions on quality of life were described in an overview of the included studies.

Results: In total 4,853 potentially relevant articles were screened for relevance, of which 19 intervention studies met the inclusion criteria. The studies were very heterogeneous in the design: measurement of frailty, health care intervention and outcome measurement differ. Health care interventions described were: multidisciplinary treatment, exercise programs, testosterone gel, nurse home visits and acupuncture. Seven of the nineteen intervention studies, describing different health care interventions, reported a statistically significant effect on subdomains of quality of life, two studies reported a statistically significant effect of the intervention on the overall quality of life score. Ten studies reported no statistically significant difference between the intervention and control groups.

Conclusion: Reported effects of health care interventions on frail elderly persons' quality of life are inconsistent, with most of the studies reporting no differences between the intervention and control groups. As the number of frail elderly persons in the population will continue to grow, it will be important to continue the search for effective health care interventions. Alignment of studies in design and outcome measurements is needed.

Keywords: frailty, quality of life, interventions, systematic review, multidisciplinary treatment, exercise programs

Introduction

The number of elderly people is expected to increase worldwide in the next decades. The number of persons aged 60 and above is expected to increase from 901 million in 2015 to 2.1 billion in 2050 and 3.2 billion in 2100. The number of persons aged 80 and above is expected to increase from 125 million in 2015 to 434 million in 2050 and 944 million in 2100.[1] Concurrently, the number of frail elderly will increase as well.

With the growing number of frail elderly, the concept of frailty has received more and more attention in recent years, and several definitions of frailty have been proposed.[2–4] Many of these definitions are based on the theory that frailty is a multifactorial concept.[2–6] These definitions are not only based on physical components,

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resulting in difficulties with activities of daily living (ADL), but also includes components referring to psychological and social functioning of older persons. One of the definitions which describe frailty as a multifactorial concept is the definition of Gobbens et al:

> Frailty is a dynamic state affecting an individual who experiences losses in one or more domains of human functioning (physical, psychological, social), which is caused by the influence of a range of variables and which increases the risk of adverse outcomes.[3]

The variables referred to in this definition are: socio-demographic factors (age, sex, marital status, ethnicity), socioeconomic factors (education, income), lifestyle, life events, environment and genetic factors.[3]

The adverse outcomes of frailty are also diverse and present on different domains. Frailty is associated with increased risk of hip fractures, disability in ADL, hospitalization, institutionalization and mortality.[2,7–9] Also, several studies have shown that frail elderly experience lower quality of life than elderly with less frailty.[10–13] Kojima et al[14] have shown in a systematic review that there is an inverse association between frailty/pre-frailty and quality of life among community-dwelling older people. Several studies also recommend conducting intervention studies to determine if quality of life in this frail population could be improved or maintained.[15,16]

Therefore, many health care interventions have been developed aiming to improve or maintain quality of life of frail elderly. These health care interventions are of a diverse nature, including all interventions with the aim to maintain or improve the health of the body and/or mind. Examples of these health care interventions are multidisciplinary interventions or physical exercise interventions. Nonetheless, a clear overview of these health care interventions for frail elderly and their effects on quality of life is missing. The objective of this review is therefore to provide a systematic overview of the effect of health care interventions on quality of life of frail elderly.

Material and methods

Study design

Systematized review according to the description of Grant et al.[17] This included a systematic research process. The presentation of the results is narrative with tabular accompaniment.[17] The review protocol was not registered.

Eligibility criteria

Type of studies: All clinical trials with a quantitative design.

Type of participants: Frail elderly identified with any frailty measurement instrument that assessed frailty on different domains.

Type of interventions: All types of health care interventions. These interventions were compared with a control intervention, either usual care or another intervention.

Type of outcome measurement: Quality of life.

Inclusion criteria were: 1) population of frail elderly; 2) measurement of frailty described in the study; 3) study about health care interventions; 4) study described the effect of the intervention on quality of life; 5) study designed as a randomized controlled trial, quasi-randomized controlled trial, controlled clinical trial or clinical trial; and 6) study was written in English, Dutch, German, or French.

Search strategy

Studies were identified by searching the Embase, Medline (OvidSP), Cochrane Central, Cinahl, PsycInfo and Web of Science databases from their inception up to and including November 2017. Keywords used were “frail elderly” (or frail* in a combination with eg, old or aged) and “quality of life” (or related terms such as QoL or HRQL). The complete search strategy for Embase and Medline (OvidSP) is presented in Supplementary material. This search strategy was adapted for the other databases. The adapted search strategies are available on request. The reference lists of all relevant reviews and potentially relevant studies were screened for additional studies. When relevant study designs or congress abstracts were found, the databases were searched for articles describing results of these studies more completely.

Study selection

Titles and abstracts of potentially relevant studies were screened by JvR or RW based on the inclusion criteria. Both authors independently read all full text articles reporting potentially relevant studies to make the final selection, using the same inclusion criteria. Disagreement was solved by discussion and consensus by the two reviewers. In case of persistent disagreement, a third reviewer could be consulted.

Risk of bias in individual studies

Risk of bias of the included studies was assessed using the “Cochrane collaboration’s tool for assessing risk of bias”.[18] This list contains seven items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. Each item was rated as low risk of bias, high risk of bias, or unclear. The methodological quality of the selected studies was independently assessed by two authors (JvR, RW). Disagreement was resolved by discussion and consensus of the two reviewers. In case of persistent disagreement, a third reviewer could be consulted.

Data extraction and analysis

The following data were extracted from the included studies: study population (age, setting, number of participants), measurement of frailty, study characteristics (design, length of follow-up), type of intervention, control treatment and outcome: quality of life. If provided, the mean scores and SD for quality of life in the intervention and control groups were extracted. Given outcomes were extracted when mean scores and SD were not presented. One author (JvR or RW) performed the data extraction, which was checked by another author (JvR or RW). The authors of an included study were contacted if more information was required.

The outcomes of the included studies were described.

Results

Literature search

The literature search resulted in 4,853 potentially relevant articles (Figure 1). After screening titles and abstracts, 250 potentially eligible articles were identified. Most of the articles excluded at this stage did not report about an intervention study (n=2,107) or the study population was not frail (n=513). This means that frailty either was not measured at all or was measured with an instrument that only assessed ADL. After reviewing the literature lists of potentially relevant studies, two studies were added for full text screening. Thus, in total 252 full text articles were evaluated. Twenty-three were included in this review. Most of the excluded articles reported a study that did not describe the results of a health care intervention (n=92), did not measure frailty (n=48), or did not measure quality of life (n=28). The 23 included articles described the results of 19 different interventions studies. Several articles described different follow-up periods from

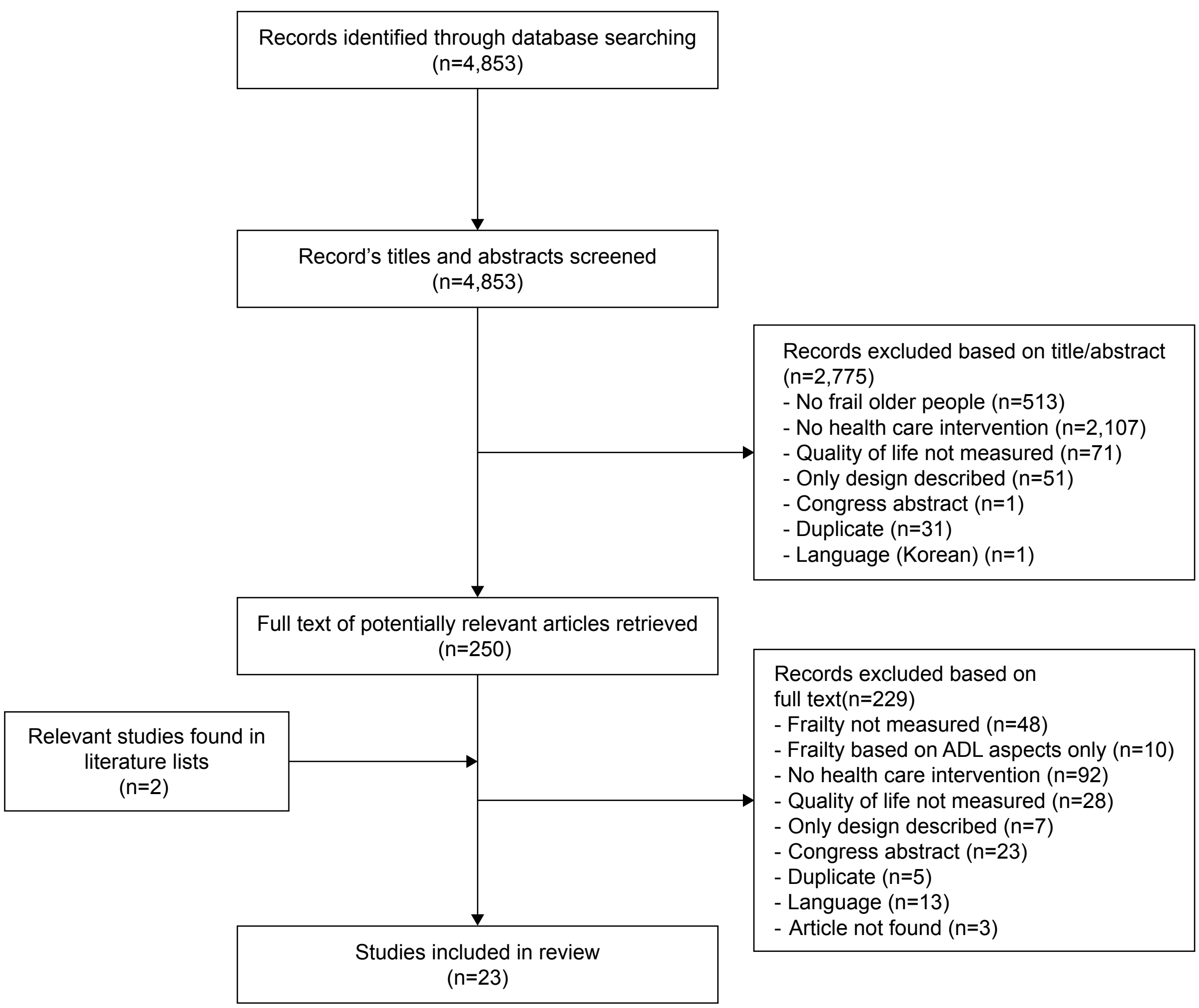

Figure 1 Study selection flowchart.
Abbreviation: ADL, activities of daily life.

the same intervention study,[19–24] and two articles described different aspects of the same intervention study.[25,26]

Methodological quality

An overview of the methodological quality of the intervention studies is presented in Figure 2.

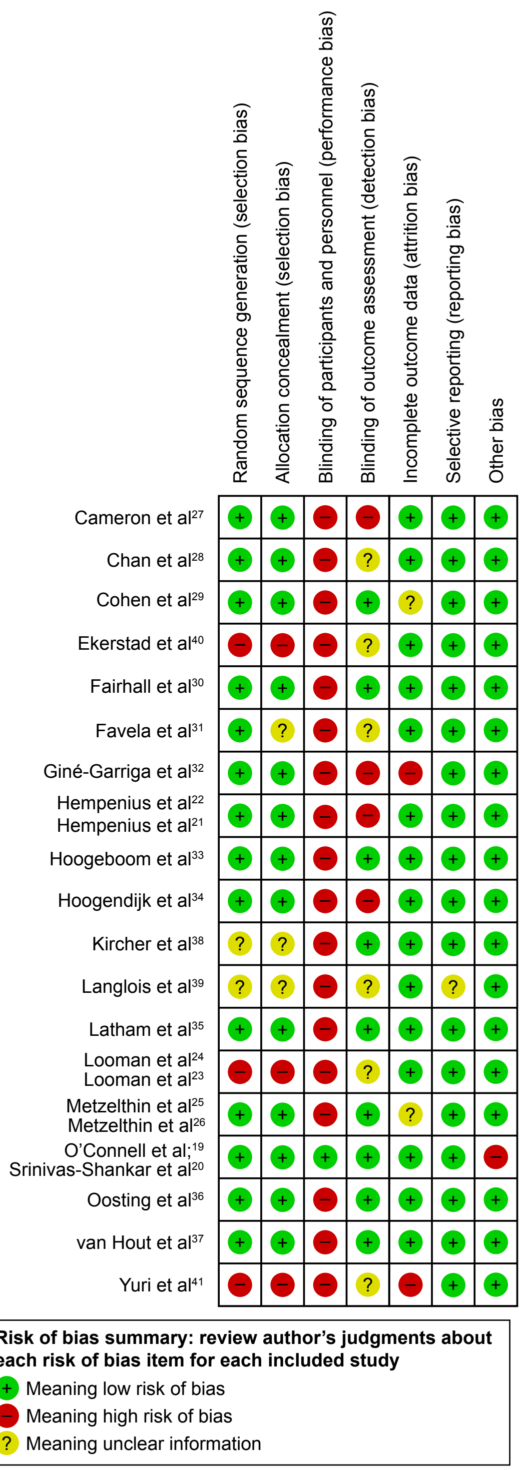

Figure 2 Methodological quality of the included studies, using the Cochrane collaboration's tool for assessing risk of bias.

Fourteen of the nineteen included intervention studies used an adequate method for random sequence generation.[19–22,25–37] Two of the nineteen studies provided insufficient information about the sequence generation process to permit judgment of low or high risk.[38,39] The only study in which participants, personnel as well as the outcome assessor, were blinded from knowledge of which intervention a participant received was the one described in the articles of O'Connell et al[19] and Srinivas-Shankar et al.[20] In this study, the use of a placebo testosterone gel served as control intervention. Eight other studies did blind the outcome assessor.[25,26,29,30,33,35–38] In the study of Cameron et al,[27] outcome assessors were blinded, but many participants disclosed their treatment status to the outcome assessor. The risk of incomplete outcome data was unclear in two studies due to lack of information.[25,26,29] The risk of incomplete outcome data was high in the study of Giné-Garriga et al[32] and the study of Yuri et al[41] due to the high percentage and imbalance of loss to follow up, both in the control group and in the intervention group, and the lack of a sensitivity analysis. Other bias was high in the study of O'Connell et al[19] and Srinivas-Shankar et al[20] because they were sponsored by the pharmaceutical industry. Figure 3 shows the risk of bias summery, presenting the review authors' judgments about each risk of bias item presented as percentages across all included studies. This indicates that across the studies there is a high risk of performance bias because many studies did not blind the participants and/or the personnel.

Characteristics of the included studies

An overview of the characteristics and outcomes of the included studies is presented in Table 1. Populations and settings, frailty measurement instruments, quality of life measurements instruments and the types of intervention analyzed varied.

Population and settings

All studies had a minimum age limit, ranging from 60 to 75 years. Study participants were recruited from general practices,[19,20,23–26,32,34,37] hospitals,[21,22,33,36,38,40] rehabilitation centers,[27,30,35] veterans affairs medical centers,[29] neighborhood elderly centers,[28] health insurance database supplied by the Mexican Social Security Institute,[31] a certain city,[41] or unknown.[39]

Frailty measurements

Different measurement instruments were used by the included studies to identify frail people. Validated instruments included the criteria of Fried which was used to identify frail people in two of the included studies,[19,20] the Groningen Frailty Indicator (GFI) was used in six of the

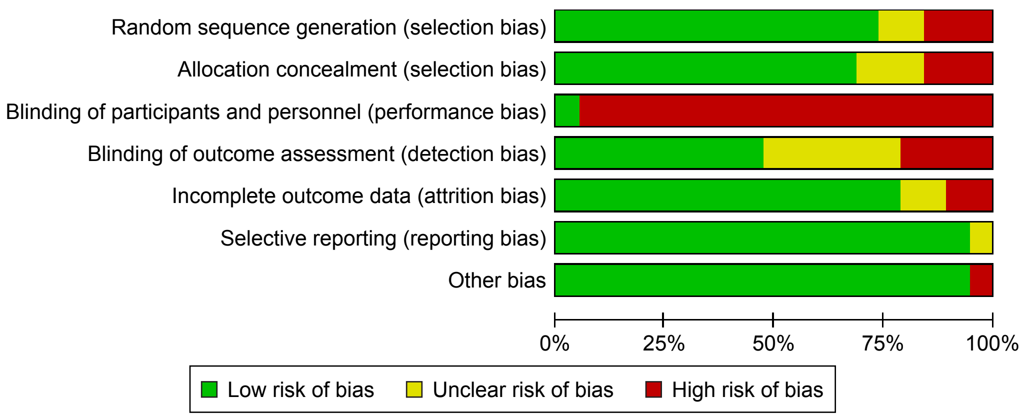

Figure 3 Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.

included studies.[21–26] Other validated measurement instruments which were used by the included studies were the Tilburg Frailty Indicator (TFI),[28] the Canadian Study of Health and Aging Clinical Frailty Scale,[33] the criteria proposed by Lachs et al,[38] the Frail Elderly Support research group screening instrument,[40] the PRISMA-7,[34] the Kihon checklist,[41] and the frailty index "Identification of Seniors At Risk (ISAR)".[36] The authors of other studies used newly developed frailty measurements[29,31,35,37] or combined existing frailty measurements with their own selection criteria.[32,39]

Quality of life instruments

The different instruments used to determine quality of life were: EuroQol (EQ)-5D,[23,25–27,30,34] EQ-6D,[24] Short Form (SF)-36.[21,22,29,31,35,37] SF-12,[32,34] RAND-36,[24] Aging Males' Symptom scale,[19,20] Hip Osteoarthritis Outcome Score,[33,36] Quality of Life Philadelphia Geriatric Center Morale Scale (PGCMS),[38] the Quality of Life Systemic Inventory questionnaire,[39] the WHO Quality of Life-BREF (WHOQOL-BREF),[28] the Health Utilities Index-3 (HUI-3),[40] the Investigating Choice Experiments for CAPability measure for Older people (ICECAP)[24] and a 5-point Likert scale.[41]

Type of interventions

Nine studies examined the effect of interventions based on a multidisciplinary treatment program with geriatric evaluation vs usual care.[21–27,29,30,34,38,40] Five studies examined the effect of exercise programs vs usual care,[32,33,35,36,39] one study a combination of vitamin D and exercise vs a placebo tablet and social home visits[35] and one study a preventive care program which included physical exercise classes, oral care and nutrition education.[41] Other interventions described were testosterone gel vs placebo,[19,20] acupuncture intervention vs waiting list[28] and nurse home visits with or without alert buttons vs usual care.[31,37]

Effect of health care intervention on quality of life among frail elderly

Findings on the effect of the health care intervention on quality of life are also presented in Table 1. Based on the similarity of the intervention and the number of studies describing the intervention, the results of the included studies will be described in three subgroups: multidisciplinary treatment, exercise programs and other intervention.

Multidisciplinary treatment program with geriatric evaluation

Five of the nine studies which examined the effect of a multidisciplinary treatment program with geriatric evaluation reported no statistically significant differences concerning quality of life between the intervention and control groups.[25–27,30,34,38] Hempenius et al[21] reported no significant differences between groups at three months after discharge and no significant differences between groups for most SF-36 subscales at discharge, except for the SF-36 subscale bodily pain (OR 0.49, 95% CI: 0.29–0.82).[22] Looman et al[23] reported a statistically significant difference between groups in the attachment dimension of the ICECAP after 3 and 12 months follow-up: frail elderly in the control group perceived receiving lesser amounts of love and friendship than desired, whereas the intervention group was stable on this dimension.[23,24] Cohen et al[29] reported statistically significant differences between groups in different dimensions of the SF-36 by comparing the mean change in scores at different time points, for example at baseline and discharge, of the intervention and control groups. In their study, inpatient geriatric care had a positive effect on the following domains at discharge: physical function (mean change in score of the intervention group: −1.5, mean change in score of the control group: −5.4, P=0.006), bodily pain (P=0.001), energy (P=0.01), and general health (P=0.006). The effect on the

Table 1 An overview of the included studies, characteristics and outcomes

Reference	Study population	Design	Definition of frailty	Intervention	Control group	Results
Cameron et al, 2013[27]	Frail adults aged ≥70 years who completed their treatment within the division of Rehabilitation and Aged Care Services in Australia, not living in a residential aged care facility (n=241)	Randomized controlled trial	CHS criteria for frailty (≥3 of the following: weak grip, slow gait, exhaustion, low energy expenditure, and weight loss)	Interdisciplinary treatment program targeting the identified characteristics of frailty for a 12-month period	Usual care	**3 months:** EQ-5D VAS: Mean ± SD deviation Intervention (n=108): 60.6±20.1 Control (n=117): 60.3±16.9, *P*=0.99 **12 months (after treatment):** EQ-5D VAS: Mean ± SD deviation Intervention (n=107): 57.5±20.8 Control (n=108): 57.7±19.7, *P*=0.91
Chan et al, 2017[28]	Frail elderly, aged ≥65 years, openly recruited from neighborhood elderly centers in Hong Kong (n=101)	Multicenter, randomized controlled trial	Tilburg Frailty Indicator ≥5	12-week acupressure intervention four times a week during 15 minutes. Given twice by a caregiver dyad and twice by a registered Chinese medicine practitioner	Waiting list	**End of treatment (after 12 weeks):** Intervention group (n=50), control group (n=51) measurement: Mean int. group, mean control group, *P*-value WHOQOL-BREF Overall QoL: 3.70, 3.45, *P*=0.105 General health: 3.23, 3.10, *P*=0.140 Physical domain: 63.49, 56.52, *P*=0.001 Psychological domain: 67.91, 64.89, *P*=0.043 Social domain: 64.45, 63.70, *P*=0.013 Environment domain: 71.61, 68.13, *P*=0.006
Cohen et al, 2002[29]	Frail patients, aged ≥65 years and hospitalized at a Veterans Affairs medical center in the USA (n=409 included in trial)	Randomized controlled trial	Patients who met ≥ two of the following criteria were considered to be frail: inability to perform one or more ADL, a stroke ≤ three months, history of falls, difficulty walking, malnutrition, dementia, depression, ≥ one unplanned admissions in the previous three months, prolonged bed rest, or incontinence	Care in an inpatient geriatric unit followed by care at an outpatient geriatric clinic. The interventions involved teams that provided geriatric assessment and management	Usual inpatient care followed by usual outpatient care	**Inpatient geriatric care** **At discharge:** Positive effect on following domains of SF-36: MeanΔint. group, meanΔcontrol group[a], *P*-value • physical functioning: −1.5, −5.4, *P*=0.006 • bodily pain: 15.3, 9.2, *P*=0.001 • energy: 0.8, −2.6, *P*=0.01 • general health: −0.02, −3.4, *P*=0.006 **At one year:** Positive effect on following domains of SF-36: MeanΔint. group, meanΔcontrol group[a], *P*-value • Bodily pain: 24.9, 20.0, *P*=0.01 **Outpatient geriatric care** **At one year:** Positive effect on following domains of SF-36: MeanΔint. group, meanΔcontrol group[a], *P*-value • energy: 0.8, −2.5, *P*=0.009 • mental health: −0.6, −1.2, *P*=0.001 • general health: −0.5, −2.9, *P*=0.01

						At one year: Positive effect on following domain of SF-36: MeanΔint. group, meanΔcontrol group[b], *P*-value • mental health: 5.7, 1.5, *P*=0.004 Ninety-nine percent of all planned follow-up interviews were conducted successfully by telephone according to the author
Ekerstad et al, 2017[40]	Frail elderly, aged $\geq$75 year, in need of acute in-hospital treatment in Sweden (n=408)	Randomized controlled, one center, trial	Two or more criteria from the Frail Elderly Support research group screening instrument	Structured, systematic interdisciplinary comprehensive geriatric assessment-based care at an acute elderly care unit	Usual care	**3 months after discharge:** Intervention group (n=179), control group (n=166) measurement: Mean int. group, mean control group, *P*-value HUI-3-vision: 0.873, 0.862, *P*=0.664 HUI-3-Hearing: 0.818, 0.817, *P*=0.976 HUI-3-Speech: 0.995, 0.985, *P*=0.036 HUI-3-Ambulation: 0.584, 0.458, *P*=0.001 HUI-3-Dexterity: 0.856, 0.804, *P*=0.122 HUI-3-Emotion: 0.896, 0.896, *P*=0.963 HUI-3-Cognition: 0.933, 0.834, *P*<0.001 HUI-3-Pain: 0.766, 0.594, *P*<0.001
Fairhall et al, 2015[30]	Frail community-dwelling people who were discharged from a rehabilitation division of a Health Service in Sydney, aged $\geq$70 years (n=241)	Cost-effectiveness study embedded in a randomized controlled trial	CHS criteria for frailty ($\geq$3 of the following: weak grip, slow gait, exhaustion, low energy expenditure, and weight loss)	12-month interdisciplinary, multifactorial intervention targeting the components of frailty, delivered by an interdisciplinary team	Usual care	**3 months (n=):** EQ-5D: Mean $\pm$ SD deviation Intervention: 0.56$\pm$0.31 Control: 0.47$\pm$0.34 *P*=0.24 **12 months (after treatment) (n=216):** EQ-5D: Mean $\pm$ SD deviation Intervention: 0.49$\pm$0.32 Control: 0.47$\pm$0.34 *P*=0.74 216 of the 241 randomized participants completed the study
Favela et al, 2013[31]	Frail adults aged >60 years, living in Mexico with health insurance supplied by the Mexican Social Security Institute (n=133)	Randomized controlled trial	Frailty index score $\geq$0.14. Count of different symptoms, illnesses, and other conditions (n=34). Frailty index score = number of items present/ number of total items	Weekly nurse home visits over a 9-month period including alert buttons vs nurse home visits alone	Usual care	This information was requested from the authors No statistically significant difference between groups on the different domains of the SF-36 Intervention nurse home visits including alert buttons: n=39 Intervention nurse home visits: n=37 control: n=39

(*Continued*)

Table 1 (*Continued*)

Reference	Study population	Design	Definition of frailty	Intervention	Control group	Results
Giné-Garriga et al, 2013[32]	Frail adults, 80–90 years old, selected from a primary health care center in the Barcelona area (n=51)	Randomized controlled trial	Frail when (a) more than 10 seconds to perform a rapid-gait test; (b) could not stand up five times; or (c) if found frail by the (Fried) exhaustion criterion	12-week functional circuit training program: combination of functional balance and lower body strength-based exercises twice a week	Usual care with health education meetings once a week	**12 weeks:** Mean ± SD deviation SF-12 PCS/SF-12 MCS Intervention (n=22): 35.59±4.41/38.37±7.14 Control (n=19): 29.80±3.74/31.14±8.56 *P*<0.001/*P*=0.001 **36 weeks:** Mean ± SD deviation SF-12 PCS/SF-12 MCS Intervention (n=18): 36.52±4.47/33.94±6.18 Control (n=7): 29.26±3.05/30.53±7.41 *P*<0.001
Hempenius et al, 2013[22] Hempenius et al, 2016[21]	Frail patients, aged >65 years who were undergoing elective surgery for a solid tumor in the Netherlands (n=297)	Randomized controlled trial	GFI score >3. The GFI screens for loss of function and resources in four domains: physical, cognitive, social and psychological	Preoperative geriatric consultation, an individual treatment plan targeting risk factors for delirium, daily visits by a geriatric nurse during the hospital stay and advice on managing any problems encountered	Usual care	Univariate binary logistic regression analysis, outcome score of the SF-36 were dichotomized as same/better or worse scores Intervention (n=127) Control (n=133) **At discharge:** Positive effect on following domains of SF-36: • bodily pain (OR: 0.49, 95% CI: 0.29–0.82) **3 months after discharge:** SF-36-MCS: OR 0.84 (95% CI: 0.50–1.42) Intervention (n=106) Control (n=121)
Hoogeboom et al, 2010[33]	Frail elderly aged ≥70 years with hip osteoarthritis awaiting total hip replacement in the Netherlands (n=21)	Pilot randomized controlled trial	Score of ≥2 on the CSHA Clinical Frailty Scale; the Clinical Frailty Scale ranges from 1 (robust health) to 7 (complete functional dependence on others)	A short (3–6 weeks) preoperative tailor-made, therapeutic exercise program at least twice a week. Patients were encouraged to exercise at home	Usual care	**Preoperative:** HOOS QoL: Mean ± SD deviation Intervention (n=10): 36.3±15.8 Control (n=10): 43.3±15.4 Adj mean diff. (95% CI): −1.2 (13.0–10.7) No statistically significant differences between groups
Hoogendijk et al 2016[34]	Community-dwelling frail older adults aged ≥65 years recruited through 35 primary care practices in the Netherlands (n=1,147)	Stepped wedge cluster randomized controlled trial	PRISMA-7 score of ≥3 PRISMA-7 is a brief 7-item questionnaire containing risk factors for functional decline	Geriatric Care Model (GCM): a geriatric in-home assessment by a practice nurse, followed by a tailored care plan. Complex patients were reviewed in multidisciplinary consultations	Usual care	**6 months:** Measurement: B (95% CI), *P*-value SF-12 MCS: –0.22 (–0.91–0.46), *P*=0.52 SF-12 PCS: 0.25 (–0.53–1.03), *P*=0.53 EQ5D: 0.01 (–0.01–0.03), *P*=0.37 **12 months:** Measurement: B (95% CI) SF-12 MCS: 0.34 (–0.55–1.22), *P*=0.46 SF-12 PCS: 0.–0.37 (–1.38–0.64), *P*=0.47 EQ5D: 0.01 (–0.01–0.04), *P*=0.24 **18 months:** SF-12 MCS: 0.06 (–1.08–1.20), *P*=0.92

						SF-12 PCS: 0.01 (−1.29–1.30), *P*=0.99 EQ5D: 0.03 (0.00–0.06), *P*=0.06 **24 months:** SF-12 MCS: −0.80 (−2.31–0.72), *P*=0.30 SF-12 PCS: −0.11 (−1.83–1.61), *P*=0.90 EQ5D: 0.01 (−0.03–0.05), *P*=0.63 782 (68.2%) frail older adults completed the full 24-month study period
Kircher et al, 2007[38]	Frail patients who were hospitalized in hospitals with a geriatric evaluation and management (GEM) team in Germany, at least 65 years old (n=345). Patients from hospitals without this team formed an external comparison group (n=90)	Randomized controlled trial	≥2 of the criteria proposed by Lachs et al (measuring vision, hearing, arm and leg function, urinary incontinence, nutrition, mental status, depression, instrumental and basic activities of daily living, environmental hazards, and social support systems)	Comprehensive geriatric assessment and management in the form of consultations and follow-up provided by the GEM team	Control group: Usual care Comparison group: usual care in other hospitals (without GEM team present)	**3 months follow up:** QoL Philadelphia Geriatric Center Morale Scale: Mean (SD) GEM group (n=122): 7 (6–10) Control group (n=107): 8 (6–9) Comparison group (n=60): 9 (7–9) **12 months follow up:** QoL Philadelphia Geriatric Center Morale Scale: Mean (SD) GEM group (n=83): 8 (7–9) Control group (n=78): 8 (7–10) Comparison group (n=29): 8 (6–9) No statistically significant differences between groups
Langlois et al, 2013[39]	Frail older adults, aged 61–89 years (n=83; 34 frail older adults and 38 non-frail older adults)	Matched-control group design	Participants were categorized as frail if they met at least two of the three following diagnostic criteria: (a) three of the five symptoms defined by Fried et al, (b) a score of ≤28/36 on the modified Physical Performance Test, (c) identified as frail according to the geriatrician's judgment based on the frailty index. To be classified as non-frail, participants could not meet any of these three frailty criteria	Physical exercise-training program consisted of 12 weeks of 1-hour exercise session 3 days a week	Participants were instructed to maintain their current level of activity. After participating in the study, they were offered the opportunity to join a physical training program	**After 12 weeks:** QoL Systemic Inventory questionnaire Global QoL: Main group effect: F(1, 68)=3.97, *P*=0.05 Z score change frail elderly: 0.09 Leisure activities Main group effect: F(1, 68)=9.13, *P*=0.004 Z score change frail elderly: 0.35 Perception of physical capacity Main group effect: F(1, 68)=5.76, *P*=0.019 Z score change frail elderly: 0.44 Social/family relationships Main group effect: F(1, 68)=4.41, *P*=0.039 Z score change frail elderly: 0.14 Perceived physical health Main group effect: F(1, 68)=4.40, *P*=0.040 Z score change frail elderly: 0.27 No group × frailty interactions were reported. Significant differences between groups on these domains. Intervention (n=36) Control (n=36)

(*Continued*)

Table 1 (*Continued*)

Reference	Study population	Design	Definition of frailty	Intervention	Control group	Results
Latham et al, 2003[35]	Frail patients aged 65 and older admitted to geriatric rehabilitation units in New Zealand and Australia (n=243)	Randomized controlled trial	Frail patients were those who had one or more health problems or functional limitations from a list of indicators that included dependency in an activity of daily living (ADL), prolonged bed rest, impaired mobility, or a recent fall	Single dose of vitamin D 10 weeks of high-intensity quadriceps resistance exercise three times a week started in the hospital and continued at home	Placebo tablet Social home visits (attention)	**3-month follow-up:** PCS SF-36: Mean (95% CI): Resistance exercise (n=112): 34 (32–36) Attention control (n=110): 35 (33–37) Vitamin D (n=108): 35 (33–37) Placebo (n=114): 35 ± (33–36) No statistically significant differences between groups
Looman et al, 2014[24] Looman et al, 2016[23]	All GP patients aged ≥75 years of the 3 GP practices in the experimental (n=222) and 6 GP practices in the control group (n=224)	Quasi-experimental study	GFI score ≥4	Preventive integrated care model: Comprehensive assessment of care needs with EASYcare. Treatment goals were translated into a multidisciplinary treatment plan	Usual care	**3 months follow-up:** **Intervention** group (n=205), control group (n=212) measurement, mean int. group, mean control group, *P*-value General QoL (based on RAND-36): 40.56, 40.95, *P*=0.14 EQ-6D-mobility: 1.73, 1.71, *P*=0.44 EQ-6D-self-care: 1.48, 1.39, *P*=0.30 EQ-6D-daily activities: 1.73, 1.71, *P*=0.29 EQ-6D-pain/discomfort: 1.81, 1.79, *P*=0.78 EQ-6D-anxiety/depression: 1.46, 1.46, *P*=0.38 EQ-6D-cognitive functioning: 1.49, 1.51, *P*=0.75 ICECAP-role: 2.56, 2.68, *P*=0.69 ICECAP-enjoyment: 2.81, 2.68, *P*=0.61 ICECAP-security: 3.25, 3.18, *P*=0.12 ICECAP-control: 2.53, 2.68, *P*=0.83 ICECAP-attachment: 3.08, 2.86, *P*=0.03 **12 months follow-up:** Intervention group (n=222), control group (n=224) measurement: mean int. group, mean control group, *P*-value General QoL (based on RAND-36): 42.66, 39.92, *P*=0.06 EQ-5D: 0.66, 0.65, *P*=0.73 ICECAP-attachment: 3.00, 2.75, *P*<0.001 ICECAP-security: 3.32, 3.28, *P*=0.45 ICECAP-role: 2.57, 2.54, *P*=0.66 ICECAP-enjoyment: 2.73, 2.66, *P*=0.30 ICECAP-control: 2.55, 2.61, *P*=0.27

Metzelthin et al, 2014[25] Metzelthin et al, 2015[26]	Community-dwelling frail older people, aged ≥70 years in the south of the Netherlands, recruited from GP practices (n=346)	Cluster randomized controlled trial	GFI score ≥5 points	Proactive primary care approach which included an in-home assessment and interdisciplinary care based on a tailor-made treatment plan	Usual care	**6-month follow-up:** EQ-5D based on NL tariff: mean ± SD Intervention group (n=171): 0.68±0.19 Control group (n=145): 0.73±0.17 *P*=0.34 **12-month follow-up:** Intervention group (n=157): 0.69±0.18 Control group (n=141): 0.72±0.16 *P*=0.81 **24-month follow-up:** Intervention group (n=143): 0.68±0.17 Control group (n=127): 0.69±0.19 *P*=0.97 Also data available based on UK tariff: no statistically significant differences between groups no significant group by time interaction effects of the intervention group on QoL
O'Connell et al, 2011[19] Srinivas-Shankar et al, 2010[20]	Intermediate frail or frail community-dwelling men aged ≥65 years with low testosterone levels, recruited by advertisements or mailed invitations from family practice registers in England (n=274)	Randomized controlled trial	Based on the criteria of Fried: unintentional weight loss, self-reported exhaustion, low physical activity, slow walk time and low handgrip strength. Intermediate frail: 1 or 2 criteria, frail: 3 or more criteria of Fried	6 months testosterone gel (25 or 75 mg daily)	Placebo	**6 months (after treatment):** AMS somatic subscale: mean ± SD deviation Intervention (n=130): 12.7±4.3 Control (n=132): 13.8±4.7 *P*=0.04 AMS psychological subscale: mean ± SD deviation Intervention (n=130): 8.2±3.5 Control (n=132): 7.6±3.2 *P*=0.83 **12 months:** AMS somatic subscale: Mean ± SD deviation Intervention (n=104): 14.1±4.4 Control (n=104): 15.1±5.4 *P*=0.08 AMS psychological subscale: mean ± SD deviation Intervention (n=104): 7.6±3.6 Control (n=104): 8.2±3.9 *P*=0.091
Oosting et al, 2012[36]	Frail patients, aged >65 years, scheduled for elective total hip arthroplasty in the Netherlands (n=30)	Pilot randomized controlled trial	Score of 2 or higher on the frailty index ISAR which consists of six self-report questions on functional dependence, recent hospitalization	A preoperative program to train functional activities and walking capacity twice a week for 3–6 weeks during supervised sessions	Usual care which consisted of a single group information session	**Before admission (t1):** HOOS: Mean ± SD deviation Intervention (n=15): 77.0±10.1 Control (n=13): 80.4±11.1 **6 weeks after discharge (t3):** HOOS: Mean ± SD deviation

(*Continued*)

Table 1 (*Continued*)

Reference	Study population	Design	Definition of frailty	Intervention	Control group	Results
			impaired memory and vision and polymedication.	and instructions to additionally train 4 times/week at home and use a pedometer		Intervention (n=14): 53.2±16.4 Control (n=12): 49.2±16.1 No statistically significant differences between groups
Van Hout et al, 2010[37]	Frail elderly, age ≥75 years and listed as primary care patient, living at home in the Netherlands (n=651)	Randomized controlled trial	Frail: self-reported score in the worst quartile of at least two of six COOP-WONCA charts	Preventive home visiting program, with seven key characteristics including assessment of health risks and care needs an individually tailored care plans and nurse home visits	Usual care	SF-36 physical component: mean ± SD deviation **6-month follow-up:** Intervention (n=244): 31.4±9.3 Usual care (n=229): 32.1±9.4 **18-month follow-up:** Intervention (n=215): 30.7±9.2 Usual care (n=209): 32.2±9.3 SF-36 mental component: mean ± SD deviation **6-month follow-up:** Intervention (n=244): 44.5±10.5 Usual care (n=229): 45.4±10.6 **18-month follow-up:** Intervention (n=215): 43.9±11.2 Usual care (n=209): 45.2±11.2 No statistically significant differences between groups
Yuri et al, 2016[41]	Frail older people aged ≥65 years, living in the community in Izumi, Osaka, Japan (n=143)	A cluster nonrandomized controlled trial	The 25-item Kihon Checklist has seven domains: activities of daily living, physical strength, nutritional status, oral function, houseboundness, cognitive function and depression risk. According to Japanese frailty criteria, eligibility for this study was defined as having one or more of the following: "low physical strength," "low nutritional status," "low oral function," or "generally frail" status	Standard preventive care program in combination with life goal-setting support (SPCP + LGST)	Standard preventive care program (SPCP): physical exercise classes, oral care and nutrition education	QoL: 5 point Likert scale. group: mean (SD) Baseline: Intervention: 3.14±0.78 Control: 3.23±0.84 3 months Intervention (n=65): 3.81±0.80; P=0.001* Control (n=61): 3.30±0.81; P=0.970 6 months Intervention (n=53): 3.50±0.74; P=0.078 Control (n=52): 3.23±0.91; P=1.000 9 months Intervention (n=42): 3.36±0.66; P=0.415 Control (n=47): 3.23±0.91; P=1.000 Time × group interaction effect P=0.022

Notes: [a]MeanΔint.group, meanΔcontrol group: mean change in score between baseline and discharge/12 months. Mean change in score given for the intervention group and the control group. [b]MeanΔint.group, meanΔcontrol group: mean change in score between discharge and 12 months.

Abbreviations: ADL, activity of daily living; CHS, Cardiovascular Health Study; CSHA, ; COOP-WONCA, ; GEM, geriatric evaluation and management; GFI, Groningen Frailty Indicator; GP, general practitioner; HOOS QoL, Hip disability and Osteoarthritis Outcome Score - quality of life subscale; HUI-3, Health Utilities Index-3; ICECAP, Investigating Choice Experiments for CAPability measure for Older people; ISAR, Identification of Seniors At Risk; Mean int. group, mean score of intervention group (at the described follow-up period); QoL, quality of life; SF-12 MCS, Short form-12 mental health composite scale; SF-12 PCS, Short form-12 physical health composite scale; SF-36 MCS, Short form-36 mental health composite scale; WHOQOL-BREF, WHO Quality of Life-BREF.

domain bodily pain was still present after one-year follow-up (P=0.01). The outpatient geriatric care had a positive effect on: energy (P=0.009), mental health (P=0.001), and general health (P=0.01). When mean changes of scores of the intervention and control group between discharge and 1-year follow-up were compared, only the improvement in the score for the mental health dimension remained significant (P=0.004). Ekerstad et al[40] reported a statistically significant difference between groups for four of the eight dimensions of the HUI-3 questionnaire (speech, ambulation, cognition and pain).

Exercise programs

Three of the six studies which examined the effect of an exercise program on quality of life reported no statistically significant difference between groups.[33,35,36] Giné-Garriga et al[32] reported a statistically significant difference between groups concerning the physical composite score (PCS) and the mental composite score (MCS) on the SF-12, after 12 and 36 weeks. After 12 weeks the average score of the PCS of the intervention group and the control group was 35.59 (SD 4.41) and 29.80 (SD 3.74) ($P<0.001$) respectively. Langlois et al[39] reported a statistically significant difference in favor of the intervention group in several domains of the Quality of Life Systemic Inventory questionnaire: global quality of life, leisure activities, perception of physical capacity, social/family relationships, and perceived physical health. Yuri et al[41] reported a statistically significant improvement in the quality of life measured with a five point Likert scale.

Other interventions: testosterone gel, nurse home visits with alert buttons or acupuncture

The study describing a testosterone gel intervention vs placebo gel reported a statistically significant difference on the somatic subscale 6 months after treatment (P=0.04),[20] which was not sustained 12 months after treatment (P=0.08).[19,20] Favela et al[31] examined the effect of 1) weekly nurse home visits in combination with alert buttons and 2) only nurse home visits, and reported that none of the interventions had a statistically significant effect on quality of life. Likewise, van Hout et al[37] reported no statistically significant effect of nurse home visits on quality of life. Chan et al[28] reported statistically significant improvement on several domains of the WHOQOL-BREF after an acupressure intervention.

Discussion

This systematized review provides an overview of the effects of different health care interventions for frail elderly on quality of life. The reported effects seem low, but the findings were inconsistent and the study designs were very heterogeneous in the design. Ten intervention studies reported no statistically significant difference between the intervention and control groups. Seven studies reported a statistically significant effect on subdomains of quality of life and two studies reported a statistically significant effect of the intervention on the overall quality of life score.

Two previous reviews have focused in particular on the effect of exercise interventions for frail elderly.[42,43] One of these, the systematic review by Chou et al,[42] concluded that exercise interventions had no effect on quality of life, but the results of the meta-analyses suggest that exercise increased gait speed, improved balance, and improved ADL performance of frail elderly.[42] The other, a review by Theou et al,[43] reported that exercise improved quality of life in four of the ten studies. The conclusions of these two reviews correspond with our results, namely inconclusive results concerning the effect of exercise interventions on frail elderly's quality of life.

Several possible explanations for the lack of evidence of the effectiveness of the health care interventions have been proposed by the authors of several studies included in this review. First, the intervention and control treatments might not be very different. As health professionals will already be aware of the risks involved in treating frail elderly patients,[22] usual care often had many matching elements to the geriatric evaluation and management (GEM) intervention program and other multidisciplinary interventions. Therefore, the effectiveness of these interventions appeared to be limited.[22,24–26,29,38] Second, inadequate implementation of an intervention will affect research results.[25,26,37,38] Several articles on the Dutch National Care Program for Elderly[44–46] indicated that the efficacy of a multidisciplinary intervention aimed at frail older people depended on adequate implementation of the intervention. Inadequate implementation occurred when eg, only part of the protocol was followed, application of the full protocol was perceived as time consuming, the protocol was perceived as difficult or because health care professionals requiring more training to apply the protocol.[25,37,38,47,48] During process evaluation of the multidisciplinary treatment program of Metzelthin et al,[25] professionals did report that they did not always follow the whole protocol due to time constraints or its complexity. Adequate implementation of the protocol is not only dependent on the professional, but also on the frail elderly. If a protocol is time-consuming or difficult to perform for the elderly, inadequate implementation or loss to follow-up may be the result. Third, group size might be decisive for a study's results; two studies were pilot, randomized controlled trials with few participants.[33,36] A similar trial with adequate sample sizes might result in different findings.

A major limitation of the present review was the heterogeneity of the included studies. The studies used different frailty measurements, different health care interventions and different outcome measurements for quality of life, which made it difficult to compare the results and to draw conclusions.

Furthermore, we focused only on the outcome quality of life. We did not describe adverse effects of the intervention. For that matter, most of the studies did not describe adverse effects. The testosterone gel intervention, however, is controversial. It is unclear if short-term testosterone treatment leads to long-term effects and there are concerns about its possible adverse effects, such as increased PSA and prostate cancer progression, as stated in the editorial comment on one of the articles.[49] Furthermore, high intensity resistance exercise might lead to musculoskeletal injury. In the study of Latham et al,[35] eighteen people (15%) in the exercise group had musculoskeletal injuries compared with five (4%) in the control group (RR 3.6, 95% CI 1.5–8.0). The other studies did not describe any adverse effects. The strength of this review is that this study included all health care interventions, which resulted in an overview of all assessed health care interventions and their results.

Conclusion

In conclusion, this review found conflicting and inconsistent results concerning the effects of health care interventions for frail elderly on quality of life. Most of the included studies, however, reported no differences between intervention and control groups. As the population of older people will continue to grow, it will be important to pursue the search for effective health care interventions, not only regarding quality of life, but also other outcomes. Different aspects should be taken into consideration in order to make progression and improve quality of life among frail elderly in daily practice. It might be needed to adjust interventions enhancing the quality of the interventions and increasing the difference between the intervention and usual care. It is important to assure proper implementation of an intervention. It might be needed to adjust outcome measurements.

Author contributions

All authors contributed toward data analysis, drafting and critically revising the paper, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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Supplementary material

Embase and Medline (OvidSP) search strategies

Embase (Embase and Medline)

('frail elderly'/de OR ((frail* AND (elder* OR old* OR aged OR geriatr* OR octogenar*)) OR (impair* NEXT/1 elder*)):ab,ti) AND ('quality of life'/exp OR ((qualit* NEAR/3 (life OR liv*)) OR QOL OR HRQL):ab,ti)

Medline (OvidSP)

("Frail Elderly"/ OR ((frail* AND (elder* OR old* OR aged OR geriatr* OR octogenar*)) OR (impair* ADJ elder*)).ab,ti.) AND ("Quality of Life"/ OR ((qualit* ADJ3 (life OR liv*)) OR QOL OR HRQL).ab,ti.)