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Original article

Cost-effectiveness of oral nutritional supplements in older malnourished care home residents

Marinos Elia [a,*], Emma L. Parsons [a], Abbie L. Cawood [a], Trevor R. Smith [b], Rebecca J. Stratton [a]

[a] Faculty of Medicine, University of Southampton, Southampton General Hospital, Tremona Road, Southampton, SO16 6YD, UK

[b] Department of Gastroenterology, University Hospitals Southampton NHS Foundation Trust, Southampton General Hospital, Tremona Road, Southampton, SO16 6YD, UK

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SUMMARY

Background & aims: Malnutrition is common in care home residents, but information on the cost-effectiveness of nutritional interventions is lacking. This study, involving a randomised trial in care home residents, aimed to examine whether oral nutritional supplements (ONS) are cost-effective relative to dietary advice.

Methods: An incremental cost-effectiveness analysis was undertaken prospectively in 104 older care home residents (88 ± 8 years) without overt dementia, who were randomised to receive either ONS or dietary advice for 12 weeks. Costs were estimated from resource use and quality adjusted life years (QALYs) from health-related quality of life, assessed using EuroQoL (EQ-5D-3L, time-trade-off) and mortality. The incremental cost-effectiveness ratio (ICER) was calculated using 'intention to treat' and 'complete case' analyses.

Results: The ONS group gained significantly more QALYs than the dietary advice group at significantly greater costs. The ICER (extra cost per QALY gained), adjusted for nutritional status, type of care, baseline costs and quality of life, was found to be £10,961 using the 'intention to treat' analysis (£190.60 (cost)/0.0174 (QALYs); n = 104) and £11,875 using 'complete case' analysis (£217.30/0.0183; n = 76) (2016 prices). Sensitivity analysis based on 'intention to treat' data indicated an 83% probability that the ICER was ≤£20,000 and 92% that it was ≤£30,000. With the 'complete case data' the probabilities were 80% and 90% respectively.

Conclusion: This pragmatic randomised trial involving one of the oldest populations subjected to a cost-utility analysis, suggests that use of oral nutritional supplements in care homes are cost-effective relative to dietary advice.

1. Introduction

Disease-related malnutrition (DRM) is a condition in which malnutrition can cause and/or result from disease, and is common and costly [1]. In care homes DRM predisposes residents to infections, pressure ulcers and greater number of days in bed [2], with detrimental effects on quality of life (QoL). The burden is a particular problem in ageing populations because the prevalence of malnutrition generally increases with age. For example, the Nutrition Screening Week Surveys in the UK, which used the 'Malnutrition Universal Screening Tool' ('MUST') in 474 care homes, found the prevalence of malnutrition (those with undernutrition with a score of 1 (medium risk) or more (high risk)) to be 27% in those less than 70 years, 34% in those 70–84 years and 39% in those 85 years and over [3]. Increasing age was also more likely to be associated with underweight and weight loss [3]. In addition, those who were malnourished lost more weight than those without malnutrition. Therefore, it is surprising that there is only very limited information in care homes about the effects of nutritional interventions on functional outcomes, such as QoL [4,5] which is of paramount importance to the residents, their relatives, and the caring health care professionals. In addition, although QoL and quality adjusted life years (QALYs) can be used to assess the cost-

* Corresponding author. Faculty of Medicine, University of Southampton, Mailpoint 113, Southampton General Hospital, Tremona Road, Southampton, SO16 6YD, UK.

E-mail address: m.elia@soton.ac.uk (M. Elia).

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effectiveness of nutritional interventions, such as oral nutritional supplements (ONS) or dietary advice, these type of cost-utility analyses in care home residents have not been widely reported. A recent systematic review examining the economic aspects of using standard (not-disease specific) ONS [6] identified only one paper on the cost-effectiveness of nutritional interventions in care homes, and this was in relation to the extra cost required to increase energy intake [7], rather than to increase QoL or QALYs. Community studies in free-living subjects were also identified, but these were often retrospective cost analyses [6] based on investigations that were initially designed to address non-economic outcomes. The result was that relevant economic information was missing, and data obtained from one country were frequently applied to another, despite the existence of different health and social care systems, providing different care at different costs to citizens with different priorities who apply different weightings to the components of quality of life [8]. These factors increase the risk of bias, compromising study validity. In the review ONS was defined as a commercially available, ready to consume, multi-nutrient (complete or incomplete) liquid or semi-solid product produced by specialist medical nutrition manufacturers, but disease-specific ONS were excluded (see also classification of ONS by ESPEN) [9]. Although studies of nutritional support with cost-effectiveness analyses have been carried out both in and outside the hospital setting, including those involving diet, parenteral nutrition, enteral nutrition and standard or disease specific ONS (see reviews [6,10–14]), the paucity of information in care homes highlighted the need [6] to carry out prospective cost-utility analyses with ONS.

Since these systematic and economic reviews became available, we have published a pragmatic randomised trial that compared the effects of ONS and dietary advice on QoL in care home residents in England. This trial, involving participants suffering from a variety of chronic diseases and malnutrition (undernutrition) identified using 'MUST', found that ONS improved QoL to a significantly greater extent than dietary advice [4]. The study was part of a larger program of work that not only aimed to prospectively collect data on QoL, the primary outcome variable, but also on secondary outcomes including resource use and costs. The present paper used data from this original work to undertake a cost-utility analysis and specifically examine whether the use of ONS in care home residents, with a wide variety of diseases and clinical conditions is cost effective relative to dietary advice.

2. Methods

2.1. General

Details of the study design and methodology, including the randomisation procedure and inclusion and exclusion criteria, are described elsewhere [4]. The trial was registered with clincaltrials.gov on 10th August 2007, using the clinical trials identifier, NCT00515125 (http://www.clinicaltrials.gov/ct2/show/NCT00515125?term=nutrition+support&rank=60), and ethical approval was obtained from the Southampton Research Ethics Committee. In brief, residents who were able to provide informed consent were recruited from care homes in Hampshire, England between August 2007 and March 2010. The participants with a variety of diseases [4], mainly cardiovascular and neurological, were randomised to receive either ready-made ONS (1.5–2.4 kcal/ml; range of styles, flavours, volumes; Nutricia Ltd) aiming to increase ad libitum intake by at least 600 kcal/day and 16 g protein, or dietary advice designed to encourage the intake of high energy and protein foods, snacks and drinks with the aid of a diet sheet. The ONS group only received advice about the choice, timing and amount of ONS to be consumed. Both groups of participants were seen by a dietitian at baseline and at 6 weeks to receive advice about implementing their respective intervention. The dietitian also had discussions with care home staff, and the agreed goals were included in the notes and care plans of individual residents. Both interventions were pragmatic in that they aimed to reproduce routine practice in care homes of the region. Among the data recorded were age, gender, disease category, type of care received (nursing or residential) and malnutrition risk (medium + high risk) according to the 'Malnutrition Universal Screening Tool' ('MUST') [15], the most commonly used malnutrition screening tool in the UK. 'MUST' was developed with the following definition of malnutrition in mind: a state of nutrition in which a deficiency or excess (or imbalance) of energy, protein, and other nutrients causes measurable adverse effects on tissue/body form (body shape, size and composition) and function, and clinical outcome [15]. In this paper the term 'malnutrition' is used to refer to undernutrition according to 'MUST', although the instrument was developed to also identify obesity (BMI >30 kg/m^2). QALYs and costs were calculated during the 12 week intervention period, so that a cost-utility analysis could be carried out.

2.2. Cost

The costs of the interventions included the dietetic costs [16] and the costs of the ONS where relevant, as specified in the study protocol. An assessment was also made of the cost of health care utilization during the 12 week intervention as well as during the 12 week period before the intervention commenced (baseline period). The assessment included the following: the number of General Practitioner (GP) visits, the number of district nurse and practice nurse visits, attendance at hospital accident and emergency units as well as hospital outpatient attendances and hospital admissions. Among the specific resources considered were the following: outpatient appointments for gastroenterology, orthopaedics, ophthalmology, neurology, radiography, phlebotomy, chiropody, physiotherapy, audiology, and general medical outpatients. Any endoscopy, visits by district nurses, and visits to a specialist respiratory centre were also recorded. Costs were calculated from the number and type of resources used (according to the history and care home records) and unit costs. The unit costs were based on data published by the Personal Social Services Research Unit (PSSRU), University of Kent using 2009 prices (2008/9) [16], uplifted by 11% to reflect 2016 prices. At the time of writing this paper, the latest PSSRU report on the cost of Hospital and Community services (prices and payments) [17] indicated that inflation had increased by 9.7% between 2008/9 and 2014/15. A further increment for 2015/16 [18] was made, to bring the total inflation to ~11%. This total increment (~11%) was also based on the harmonized index of consumer prices for Medical and Paramedical Services in the UK (Eurostat), which was 10.8% between January 2009 and July 2016 [18]. Discounting was not used because the intervention period did not exceed one year. The costs during the intervention period were adjusted for malnutrition risk (medium and high 'MUST' categories), type of care, baseline QoL, and baseline healthcare costs.

2.3. Effectiveness (utility)

The health benefit (effectiveness) was measured as the number of QALYs gained during the intervention period, and was calculated using standard procedures [19] based on a combination of QoL and mortality. Therefore, residents who died during the intervention period were included in the analysis [8] (but were excluded from a previous paper [4] which reported QoL only in those who survived). Health related QoL was assessed using the five domains of EuroQoL

(EQ-5D-3L) health questionnaire. Details of the standardised instrument, including the availability of its questionnaire and scoring sheet in various languages and formats for computers, smart phones and carrying out telephone interviews are available on the website of the EuroQol organisation (http://www.euroqol.org/home.html) together with user guides, frequently asked questions and a new version of the questionnaire (EQ-5D-5L). EuroQoL EQ-5D-3L, a standardised instrument for measuring health outcome, has been used to assess QoL in a wide range of clinical conditions and the effects of various interventions, including those with drugs and nutrition. In this study, the results of the domains were amalgamated to establish an overall score using the UK time-trade-off (TTO) data, which was then used to calculate QALYs, a measure of both QoL and quantity of life (or survivorship, with death corresponding to a QoL score of zero and a gain of zero QALYs over time). The best imaginable health state (highest score across all 5 domains of EQ-5D), with a maximum overall QoL score of 1.0, results in a gain of 1 QALY over one year and 0.25 QALYs over a quarter of a year (a QoL score of 0.5 over the same periods would correspond to a gain of only half of these QALYs). The number of QALYs gained was adjusted for the same variables as those used to adjust costs (see above).

2.4. Cost-effectiveness (cost-utility) analysis (CEA)

Cost effectiveness during the 12 week intervention period was assessed using both 'intention to treat' analysis (according to the originally designated group) and 'complete case' analysis. The latter included only residents who had complete data on costs and QALYs during the intervention period, and a complete set of covariates to adjust these costs and QALYs (baseline healthcare costs, QoL, 'MUST' category, and type of care). Multiple imputation was used to replace missing data during the intervention period so that 'intention to treat' analysis could be carried out. The missing data from both groups was mainly due to ill health which prevented measures being taken [4]. The imputation model included age, gender, designated group, type of care, 'MUST' category, QALYs gained during the 12 week intervention period, costs during the same 12 week period, and baseline costs and QoL (TTO). All variables were used as predictor variables, but QALYs gained and costs during the 12 weeks intervention period were also used as dependent variables.

The CEA was undertaken using two methods: one based on the central limit theorem and the other on bootstrapping [20]. According to the central limit theorem, sample means, such as those for costs and effectiveness, converge to normal distributions as sample size increases, even when the data are skewed. The true standard errors, which are used to construct the cost-effectiveness acceptability curves, can be shown to be accurately predicted by both methods, when sample sizes are >50, even when the data are highly skewed [20]. From these analyses the incremental cost-effectiveness ratio (ICER; extra costs per extra QALY gained or 'cost/QALY') was calculated. Cost-QALY relationships were used to establish confidence ellipses and probabilistic sensitivity analysis was undertaken to establish cost-effectiveness acceptability curves (CEACs). The probability that the intervention was cost-effective was tested against two thresholds (£20,000 and £30,000 per QALY gained) to correspond to the lower and upper values of the range used in England by the National Institute of Health and Care Excellence [21–23].

2.5. Statistics

Sample size calculations were based on QoL [4]. The chi squared test and independent sample t-test were used to compare baseline characteristics between groups. The general linear model (univariate analysis of variance) was used to adjust costs and QALYs during the intervention period for confounding variables (see Sections 2.2 and 3.3). The imputation (see Section 3.4) was carried out using SPSS version 18.0 (Chicago). Statistical analyses were also undertaken using SPSS version 22.0 (Chicago). Measures of variation are expressed as mean ± standard (SD), or mean ± standard error (SE) to reflect the results obtained from statistical modelling.

3. Results

3.1. Baseline characteristics

Although baseline data were available on all 104 residents recruited into the study (mean age 88 ± 8 y; 86% female; 45% nursing and 55% residential care), complete data on QALYs and costs during the intervention period were available in only 76 (73%) of residents with a variety of diseases. Table 1 shows the baseline characteristics according to type of analysis ('intention to treat' and 'complete case' analysis) as well as the type of intervention (ONS and dietary advice). None of these comparisons were found to be significant. For example, the baseline QoL (TTO) in the 76 residents with complete data during the intervention period was 0.528 ± 0.375 (SD) compared to 0.509 ± 0.404 in the 28 residents without complete data during the intervention period. The associated baseline costs (those incurred during the 12 weeks before enrolment into the study (2009 prices)) were £158 ± 204 (n = 76, as shown in Table 1) and £151 ± 218 (n = 28, not shown in Table 1) respectively. There were also no significant differences between the ONS and dietary advice groups in any of the other baseline characteristics (Table 1), irrespective of whether the comparisons involved 'intention to treat analysis' (n = 104), 'complete case analysis' (n = 76) (Table 1), or 'incomplete case analysis' (n = 28) (data not shown). Finally, the reasons for missing data during the 12 week intervention period, did not differ significantly between the ONS and dietary advice groups [4]. Only 7% of the overall population was aged less than 75 years and almost half 90 years and over. The baseline QoL score (TTO) for all subjects was 0.52 [4], with no significant age-related decline. Among those aged 70–90 years the mean score was 0.61, below that of the general population of England, with a score of 0.80 at 70 years declining to 0.65 at 90 years (insufficient data for people older than 91 years to allow further comparisons) [22]. The results are consistent with observations that subjects with different diseases have QoL scores that are usually about 0.15 below that of the general population [22].

3.2. Resources used and costs

Most of the recorded resources used during the 12 week intervention period (ONS + dietary advice group; mean ± SD) involved GP visits (number of visits = 0.587 ± 1.146 per resident for the 'intention to treat' analysis, compared to 0.750 ± 1.277 per resident for the 'complete case' analysis), nurse visits (0.192 ± 1.150 compared to 0.266 ± 1.340 per resident) and outpatient appointments (0.125 ± 0.735 compared to 0.171 ± 0.855 per resident). There were only two short stay hospital admissions (one in the ONS group and one in the dietary advice group), and only one attendance at the accident and emergency department (dietary advice group). These affected both the 'intention to treat' and 'complete case' analyses. No significant differences were found between ONS and dietary advice groups in any of the individual resources used.

The overall healthcare costs, after adjustment for confounding variables, were significantly higher in the ONS group than the dietary advice group (Table 2) by about £172 ± 50 (SE) per resident in the 'intention to treat' analysis and by £196 ± 53 in the 'complete

Table 1
Baseline characteristics by type of analysis[a] and type of intervention.

	ONS	Dietary advice	Both groups
Intention to treat analysis (all residents)			
Residents: n	53	51	104
Age (y): mean ± SD	89 ± 7	87 ± 9	88 ± 8
Gender			
Male: n (%)	8 (15.1)	7 (13.7)	15 (14.4)
Female: n (%)	45 (84.9)	44 (86.3)	89 (85.6)
'MUST' category			
Medium risk: n (%)	22 (41.5)	26 (51.0)	48 (46.2)
High risk: n (%)	31 (58.5)	25 (49.0)	56 (53.8)
Type of care			
Nursing care: n (%)	27 (50.9)	20 (39.2)	47 (45.2)
Residential care: n (%)	26 (49.1)	31 (60.8)	57 (54.8)
Quality of life (TTO): mean ± SD	0.509 ± 0.384	0.537 ± 0.381	0.523 ± 0.381
Cost over 3 months before intervention (£): mean ± SD	170.7 ± 196.0	140.9 ± 218.2	156.1 ± 206.7
Complete case analysis at 12 weeks			
Residents: n	41	35	76
Age (y): mean ± SD	89 ± 7	87 ± 9	88 ± 8
Gender			
Male: n (%)	8 (19.5)	6 (17.1)	14 (18.4)
Female: n (%)	33 (80.5)	29 (82.9)	62 (81.6)
'MUST' category			
Medium risk: n (%)	16 (39.0)	20 (57.1)	36 (47.5)
High risk: n (%)	25 (61.0)	15 (42.9)	40 (52.6)
Type of care			
Nursing care: n (%)	22 (53.7)	15 (42.9)	37 (48.7)
Residential care: n (%)	19 (46.3)	20 (57.1)	39 (51.3)
Quality of life (TTO): mean ± SD	0.504 ± 0.392	0.556 ± 0.357	0.528 ± 0.375
Cost over 3 months before intervention (£): mean ± SD	162.7 ± 194.0	152.8 ± 217.8	158.1 ± 204.0

ONS = oral nutritional supplements; 'MUST' = 'Malnutrition Universal Screening Tool'; TTO = Time trade off.
[a] The baseline characteristics were recorded (not imputed). 'Complete case' analysis refers to the analysis of the complete (non-imputed) dataset, which is used to calculate costs and QALYs over the 12 week intervention period, including the complete dataset of confounding variables (covariates) used to adjust the costs and QALYs.

Table 2
Health care costs and QALY's gained during the intervention period.[a]

	ONS group	Dietary advice group	P value
'Intention-to-treat' analysis (n = 104)			
Total costs			
2009 prices (£)	339.4 ± 31.0	167.7 ± 34.0	<0.001
2016 prices (£)	376.7 ± 34.0	186.2 ± 37.8	<0.001
QALYs	0.1302 ± 0.0084	0.1128 ± 0.0086	0.033
'Complete case' analysis (n = 76)			
Total costs			
2009 prices (£)	369.6 ± 35.7	173.8 ± 38.7	<0.001
2016 prices (£)	410.3 ± 39.5	192.9 ± 42.9	<0.001
QALYs	0.1399 ± 0.0056	0.1216 ± 0.0060	0.031

[a] The results are presented as mean ± SE and are adjusted for malnutrition risk ('MUST' categories), type of care, baseline QoL and baseline healthcare costs during the 12 weeks before intervention. Calculations of incremental costs and QALYs, and ICERs based on the results presented in the Table (to 1 decimal point for costs and 4 decimal points for QALYs) are subject to small rounding errors (see text for ICER results using 2016 prices).

case' analysis using 2009 prices (£191 ± 55 and £217 ± 59 respectively using 2016 prices). The higher expenditure was largely due to the cost of the ONS (£162.30/resident; 2009 prices). Without this cost and that of the dietitian, who advised both groups about the intervention (i.e. the combined direct costs of the intervention; see Methods – General), the remaining costs did not differ significantly between groups. In the 'complete case' analysis, hospital costs accounted for only a quarter of the total 'non-interventional' costs. Neither the total hospital costs nor its components (inpatient costs, outpatient visits and accident and emergency (A & E) costs) differed significantly between groups. Similarly, neither the total non-hospital costs nor its components differed significantly between groups. The total hospital and non-hospital costs combined were dominated by GP visits (£86 per patient using 2009 prices and £95 using 2016 prices), which accounted for 65% of the total expenditure (after exclusion of those directly associated with the intervention).

3.3. QALYs

Both the 'intention to treat' analysis and the 'complete case' analysis found that the ONS group gained significantly more QALYs during the intervention than the dietary advice group (Table 2). There were two deaths in the ONS group and four in the dietary advice group.

The changes in QALYs were associated with a significant increase in weight (but not 'MUST' categories) in the ONS group and not the dietary advice group. For further details and relationship between weight change and quality of life see reference [4].

3.4. Cost-effectiveness analysis

Working with the central limit theorem and 2009 prices, the adjusted ICER (extra cost per QALY gained or 'cost per QALY') was found to be £9857 according to the 'intention to treat' analysis, and £10,698 according to the 'complete case' analysis (£10,941 and £11,875 respectively using 2016 prices; calculations based on data shown in Table 2, but see footnote about rounding). The relationships between the mean additional QALYs gained and the mean additional costs incurred by the ONS group (over and above those for the dietary advice group) are shown diagrammatically by the large black dots located in the right upper (north-east) quadrant of the cost-effectiveness plane of Fig. 1 (*upper*). This figure also shows the 50%, 75% and 95% confidence ellipses established using the central limit theorem and also the distribution of individual results (small grey dots) established using bootstrapping methodology. Visual inspection shows an overall consistency between the results obtained by the two methodologies (Fig. 1 (*upper*)) and also

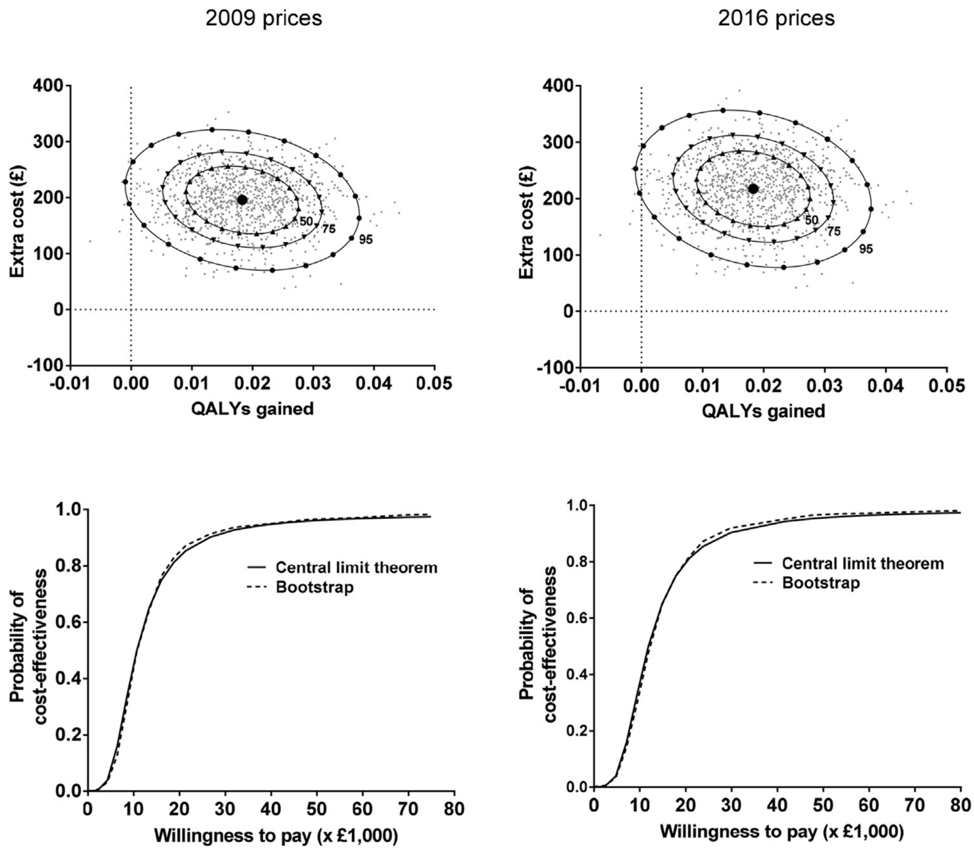

Fig. 1. (*upper*) 'Cost-QALY' relationships showing the mean extra cost and mean extra QALY's gained (ONS minus dietary advice group, represented by the large central black dots), the 50, 75, and 95% confidence ellipses established using the central limit theorem, and the individual results established by bootstrapping (small grey dots). (*lower*) Cost-effectiveness acceptability curves established using the central theorem (solid line) and a typical bootstrapped result (dotted line). The data were calculated using 2009 prices (*left*) and 2016 prices (*right*).

consistency in the associated cost-effectiveness acceptability curves (CEACs) which closely overlapped with each other (Fig. 1 (*lower*)). Furthermore, when bootstrapping was repeated five times using 'complete case' data, the bootstrapped ICER was found to be 100.1 ± 1.0% (SD) of that obtained by the central limit theorem. The associated CEACs obtained by bootstrapping also showed small deviations in the probabilities of cost-effectiveness relative to those obtained by the central limit theorem (e.g. −0.7 ± 1.2% for <£20,000/QALY and −0.4 ± 1.2% for <£30,000; the negative values indicate the results obtained by bootstrapping were less than those obtained by the central limit theorem). The corresponding results based on 'intention to treat' analysis did not differ significantly from those based on 'complete case' analysis. The actual values obtained by the central limit theorem using 2009 and 2016 prices are shown in Table 3.

With both the 'intention to treat' and 'complete case' analysis, the CEACs, established using 2009 prices and the central limit theorem (Fig. 1 and Table 3), indicated a 86% and 83% probability respectively that the 'cost per QALY' was ≤£20,000, and 93% and 92% that it was ≤£30,000 (corresponding to lower and upper values of the threshold range ('willingness to pay') respectively used by the National Institute for Health and Care Excellence (NICE)) [22,23]. There was little change in these probabilities when they were calculated using 2016 prices and the same threshold values (only 1–3% lower; Fig. 1 and Table 3).

In addition to the probabilistic sensitivity analyses described above, it is possible to undertake simple non-probabilistic sensitivity analyses using only the average reported values for costs and QALYs, and hypothetically assuming that they are systematically

Table 3
Sensitivity analysis indicating the probability (%) that the threshold is below £20,000 and £30,000 per QALY gained.[a]

Type of analysis and year of pricing	Threshold value for extra cost/QALY gained	
	£20,000	£30,000
	%	%
'Intention to treat' analysis		
2009 prices (mean ± SD)[b]	86 ± 5	93 ± 3
2016 prices (mean ± SD)[b]	83 ± 6	92 ± 3
'Complete case' analysis		
2009 prices (mean)	83	92
2016 prices (mean)	80	90

[a] All the results are based on the central limit theorem, which, unlike bootstrapping, produces exactly the same result when a given set of data are reanalysed. The mean 'cost per QALY' was found to be £9857 and £10,698 using the 'intention to treat' analysis and 'complete case' analysis respectively using 2009 prices, and £10,941 and £11,875 respectively using 2016 prices.

[b] Unlike the 'complete case' analysis which produced a single mean result when the central limit theorem was used, the 'intention to treat' analysis involving 5 sets of imputations produced 5 sets of mean results, which are summarized as a grand mean (mean of means) ± SD.

over- and/or under-estimated (calculations based on the fact that the 'extra cost/QALY gained' is proportional to deviations in the assumed average extra cost and inversely proportional to the calculated average extra QALYs gained). For example, it can be shown using the 'intention to treat' data and 2009 prices (£9857/QALY) that the average cost would have to increase by 203%–304% to reach the threshold range of £20,000–£30,000 per QALY gained (183–274% using 2016 prices).

4. Discussion

The results of this pragmatic randomised trial of malnourished, older care home residents, with a range of diseases, are consistent with the variety of clinical and functional benefits of ONS reported in other settings and patient groups [24–27]. The further economic analysis suggests that ready-made ONS can be cost-effective relative to dietary advice, adding to reports demonstrating cost savings from appropriately managing malnutrition primarily with ONS, in a combination of settings [1], as well as in the care home settings [28,29]. This cost-effectiveness was associated with an improvement in QoL, assessed with a generic tool (EQ-5D-3L; see reference [4] for the sensitivity of the tool to the intervention) at an extra cost.

The study adds to the limited available information on cost-utility ('cost per QALY') in care homes, which includes physical exercise [30], pharmacotherapy follow-up [31], fracture prevention program [32], vaccination [33], and enteral tube feeding [34]. The present study also raises certain clinical and economic issues related to the care of older care home residents and the choice of cost-effective thresholds for use in older people.

Although expenditure in the ONS group was greater than in the dietary advice group (mainly due to the cost of ONS; with no significant differences in resource use), this also produced more health benefits, measured in QALYs. Overall, ONS were considered to be cost-effective relative to dietary advice for two reasons. First, the mean 'cost per QALY' (2009 prices) was found to be £9875 using the 'intention to treat' analysis and £10,698 using the 'complete case analysis', both of which are substantially below the operational threshold range of £20,000–£30,000 currently used by NICE [22,23]. Second, the associated sensitivity analyses indicated that there was a high probability that the ICER was <£20,000 (86% using 'intention to treat' analysis, and 83% using 'complete case' analysis), and substantially higher when the threshold was <£30,000 (93% and 92% respectively). This conclusion was confirmed using 2016 prices (Table 3), which reduced the probability of cost-effectiveness obtained with 2009 prices by only 1.2–3.6%.

In considering the thresholds used by NICE, a House of Commons Health Committee concluded that they are 'not based on empirical research and not directly related to the budget' [35]. Therefore, Claxton et al. [22] undertook a large analysis based on historic, observational data, in order to empirically establish the likely thresholds actually used by the National Health Service in routine practice, while using the fixed budgets allocated to them. Using 2008-10 mortality data with 2008 prices the authors suggest that the most relevant 'central' threshold was £12,936 per QALY, or only about half of that used by NICE. However, their study involved individuals aged 1–74 years (in contrast to the present study in which only 7% of participants were younger than 75 years), and calculations based on mortality (in contrast to the present study which was predominantly based on quality of life), which, as the authors acknowledged, ignore the impact of expenditure aimed at chronic care. Nevertheless, the present study of residents receiving care for a variety of conditions and chronic diseases, found that the 'cost per QALY' was low enough to remain below the cost-effective threshold of £12,936.

This study involved one of the oldest groups of individuals (88 ± 8 years) ever subjected to a cost-utility analysis (cost/QALY) based on data from a randomised trial. There have been some objections to applying the same cost-effectiveness thresholds to adults of all ages and conditions. For example, Williams' 'fair innings' argument is based on the notion that everyone is entitled to a 'normal' lifespan of health: anyone failing to achieve this has been cheated, whereas anyone getting more than this is living on borrowed time. Therefore, it was suggested that there should be greater discrimination against older people than considerations based only on efficiency objectives [36]. Similarly, the concept of 'disability adjusted life years' (DALYs) [37,38], developed and promoted by the World Health Organization, involves a smaller weighting for older people than those in 'middle age' (who are considered to take care of older and the younger people), which can arguably be regarded as a form of discrimination against older people. However, it is difficult to establish a universally accepted definition of 'fairness', especially in an ageing population. Since society can be judged on moral grounds by the way it treats the young, the old and those with disease and disability, concepts of 'fairness' emerging from such considerations may not necessarily harmonize with those based on economic concepts alone. Taken together these considerations suggest that the 'cost per QALY' thresholds for older people in England should be reviewed, particularly since the NICE guidance methods have not changed since 2004 [21,22]. During this time there have been changes in healthcare budgets, price inflation and technology, all of which can influence the choice of threshold. During the same time period, new, increased thresholds have been introduced for certain groups of patients, such as those receiving end of life treatments [39] and those receiving the drug Herceptin©, Roche (trastuzumad) for the treatment of breast cancer [40]. These increased thresholds imply the need to sacrifice other more cost-effective services, including those affecting older people.

Other studies involving interventions with ONS in the community found that the largest overall healthcare expenditure involved hospital care. A recent economic review on this subject found that hospitals accounted for over 60% of the total expenditure and sometimes considerably more than 60% [6], while GPs accounted for a much smaller proportion. In contrast, the present study found GP expenditure to be responsible for about two thirds of the total National Health Service expenditure, while hospitals accounted for only a quarter of the expenditure. This may be because care home residents were already receiving much of the needed care in their care homes, which frequently included nurses, obviating at least some of the need for hospital care. In addition, any variations or differences in care needs within or between groups may be met by the routine care provided in care homes.

One of the limitations of the study is that the 'complete case' analysis involved only 73% of residents, raising the possibility of attrition bias. However, comparisons of baseline resident characteristics did not suggest selection bias, either when all the residents were divided into those who had complete and incomplete data during the intervention period, or when only those with complete data were divided into the ONS and dietary advice groups. Furthermore, it is reassuring that the overall results, including the ICERs, obtained by the 'complete case' and 'intention to treat' analyses agreed closely with each other. The close agreement of the CEACs established using two different methods, one based on the central limit theorem and the other on bootstrapping, which rely on different principles, also adds confidence in the use of each method as well as to the results of the study as a whole. Another study limitation is that only residents without overt dementia were studied, although some had intermittent confusion which resulted in incomplete data collection. This means that the majority of care home residents, who have a diagnosis of dementia, were not studied, although it is recognised that establishing the QoL in patients with overt dementia can be problematic. Finally, the trial did not include a control group (routine care only), which means that the cost-effectiveness of ONS or dietary advice, or a combination of both interventions relative to routine care could not be assessed. Therefore, caution should be taken not to interpret the results of this study as indicating that dietary advice in general has no effect in care homes. This is not only because of the lack of a control group receiving routine care, but also because it is possible that a more

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intense or different type of dietary advice, possibly in combination with ONS, could enhance dietary intake, QoL and QALYs. The results could also be influenced by the care pathways used, subject characteristics and nutritional status.

In summary, this cost-utility analysis involving one of the oldest age groups of malnourished people participating in a randomised pragmatic trial suggests that use of ready-made ONS in care home residents can produce a cost-effective outcome relative to dietary advice (improved QoL and gains in QALYs at a cost that is within the generally acceptable range for 'willingness to pay'). These results can be used to highlight to payers and other health and social care decision makers the cost effectiveness of oral nutritional supplements, so that informed choices can be made about which treatments to use and/or fund.

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Statement of authorship

ME, RJS and ALC designed the RCT.

Study oversight was provided by ME, RJS, ALC and TRS.

ELP conducted the research (data collection).

ME and ELP analysed the data and ME drafted the paper for modification by other co-authors.

ME has primary responsibility for the final content.

Conflict of interest statement

ALC and RJS, both of whom hold honorary research posts with the University of Southampton, are also employed part time by Nutricia. ME, ELP, and TRS declared no conflicts of interest.

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