This article was originally published in
Clinical Nutrition 2007;26(6):364-70
and is available from http://www.sciencedirect.com/science//journal/02615614

A COST UTILITY ANALYSIS OF MULTIVITAMIN AND MULTIMINERAL SUPPLEMENTS IN MEN AND WOMEN AGED 65 YEARS AND OVER

Mary M Kilonzo[ab], Luke D Vale[ab], Jonathan A Cook[b], Anne C Milne[b], Audrey I Stephen[b], Alison Avenell[b] and The MAVIS Trial Group *

a. Health Economics Research Unit, University of Aberdeen
b. Health Services Research Unit, University of Aberdeen

*Members of the group listed at the end of paper

Cost utility analysis of mineral and vitamin supplements

Correspondence to:
Ms Mary Kilonzo
Health Services Research Unit/Health Economics Research Unit
University of Aberdeen
Foresterhill
Aberdeen
AB25 2ZD
UK
Email address: m.kilonzo@abdn.ac.uk
Telephone: +44-1224-551906
Fax number: +44-1224-550926

Abstract

Background and Aims

As people age there is a progressive dysregulation of the immune system that may lead to an increased risk of infections, which may precipitate hospital admission in people with chronic heart or respiratory diseases. Mineral and vitamin supplementation in older people could therefore influence infections in older people. However, the evidence from the available randomised controlled trials is mixed. The aim of the study was to assess the relative efficiency of multivitamin and multimineral supplementation compared with no supplementation.

Methods

Cost-utility analysis alongside a randomised controlled trial. Participants aged 65 years or over from six general practices in Grampian, Scotland were studied. They were randomised to one tablet daily of either a multivitamin and multimineral supplement or matching placebo. Exclusion criteria were: use of mineral, vitamin or fish oil supplements in the previous three months (one month for water soluble vitamins), vitamin B_{12} injection in the last three months.

Results

Nine hundred and ten participants were recruited (454 placebo and 456 supplementation). Use of health service resources and costs were similar between the two groups. The supplementation arm was more costly although this was not statistically significant (£15 per person, 95% CI -3.75 to 34.95). After adjusting for minimisation and baseline EQ-5D scores supplementation was associated with fewer QALYs per person (–0.018, 95% CI -0.04 to 0.002). It was highly unlikely that supplementation would be considered cost-effective.

Conclusions

The evidence from this study suggests that it is highly unlikely that supplementation could be considered cost-effective.

Keywords

Cost effectiveness; Nutrition; Quality of life; Randomised controlled trial; Oral nutritional supplementation; Vitamins and Minerals.

Introduction

As people age there is a progressive dysregulation of the immune system.[1] This decline in immunity may lead to an increased risk of infections, which may precipitate hospital admission in people with chronic heart or respiratory diseases.[2] A further consequence may be the depletion of nutritional reserves, which may also be sub-optimal for the prevention of future infections.[3] Mineral and vitamin supplementation in older people could therefore influence infections in older people. However, the evidence from the available randomised controlled trials (RCTs) is mixed.[4-8] These trials were generally of small size and none included an economic evaluation.

We undertook a large randomised placebo controlled trial of multivitamin and multimineral supplementation in doses commonly provided in over-the-counter preparations amongst people aged 65 years and older, examining the effects on morbidity from infections.[9] Part of this study involved the prospective collection of participant-specific resource use and health-related benefits for the twelve-month period following randomisation. This paper reports a cost-utility analysis undertaken from the perspective of the UK National Health Service (NHS) of supplementation versus no supplementation.

Methods

Design

Details of the design of the RCT are available elsewhere.[9] In brief this was a pragmatic randomised double-blind, placebo-controlled trial. Nine hundred and ten participants were recruited from six general practices in Grampian, Scotland, between February and December 2002 and randomised to either placebo (n = 454) or a multivitamin and multimineral supplement (n = 456) and were followed up for 12 months. Of these 32 withdrew from the study (18 placebo and 14 supplement). Furthermore, 77 stopped taking the tablets but did not withdraw from the trial (39 placebo, 38 supplement).

A detailed description of the clinical outcomes are reported elsewhere.[9] All people aged 65 years and over were eligible unless their general practitioners (GPs) considered them too unwell to participate. Participants were excluded if they had used oral mineral, vitamin or fish oil supplements in the previous three months (one month in the case of water soluble vitamins only), or vitamin B_{12} injection in the last three months. Written informed consent was collected from participants and the Grampian Research Ethics Committee gave approval for the study. Participants were randomised to one tablet daily of either a commercially available multivitamin and multimineral supplement (800mcg vitamin A, 60mg vitamin C, 5mcg vitamin D, 10mg vitamin E, 1.4mg thiamin, 1.6mg riboflavin, 18mg niacin, 6mg pantothenic acid, 2mg pyridoxine, 1mcg vitamin B_{12}, 200mcg folic acid, 14mg iron, 150mcg iodine, 0.75mg copper, 15mg zinc, 1mg manganese) or matching placebo.

Measurement of costs

Estimation of NHS resource use

In over 94% of cases the use of health services resources in primary care was collected principally from a review of primary care notes by a member of the trial team (AM or AS) using a data abstraction form linked to a Microsoft Access database™. These data were supplemented with participant information elicited from a patient diary when detailed information was provided (e.g. the participant gave exact details of an antibiotic prescription received from their GP not detailed in the primary care notes), and for the few cases where the health authority had removed the primary care notes of the participants who had died. The data collected from primary care records related to the number and type of antibiotic prescriptions in primary care (and total number of days that antibiotics were prescribed); number of primary care contacts; number of hospital admissions (in total and those related to infection); number of days in hospital with infection; total number and number of infection-related outpatient visits; adverse events reported by participants; compliance with trial medication (from monthly diary report in all participants and tablet count at six and twelve months in a random sample of 10% of participants). Hospital data were obtained from computerised patient administration systems, hospital and primary care notes.

All analyses of outcomes including the economic evaluation were conducted on an intention to treat basis. Table 1 describes the main elements of resource use in the trial.

Derivation of costs

Average unit costs of each aspect of resource use were obtained from reliable and widely used published sources for inpatient and day case admissions, outpatient and primary care contacts and antibiotic use.[10-13] The cost of the multivitamin and multimineral supplement was based on the purchase cost. Costs were derived using unit costs for 2003 UK £ sterling. Data describing the resource utilisation of participants were combined with estimates of unit costs for each of the areas of management considered. This allowed estimation of total cost for each participant, as well as the average cost for each area of resource utilisation and average total cost.

As unit costs differ between, for example type and place of contact, the estimates of resource utilisation used for the estimation of cost were more disaggregated than those used in the analysis described above. The main unit costs used in the analysis are reported in Table 1.

Missing cost data were rare (about 0.5%) and assumed to be missing completely at random. The incremental (difference) in mean cost between groups was based on an analysis of covariance adjusting for the factors used in minimisation (i.e. treatment, gender, age 74-84y, age 85y and above, and residence type).

Derivation of Quality Adjusted Life Years (QALYs)

The health outcomes of the economic evaluation were expressed in terms of quality adjusted life years (QALYs); other clinical endpoints are reported in the main trial report.[9] QALYs have been used in order to reflect the effect of supplementation on an individual's health related quality of life. QALYs were estimated from the participant's responses to the EuroQol (EQ-5D) questionnaire collected at baseline, six and 12 months. The EQ-5D is a generic measure of health status that defines health in terms of five dimensions: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each of these dimensions has three levels: no, moderate or extreme problems. The combinations of these dimensions and levels provide 243 possible health states. The responses of participants were converted into utilities using a tariff scale derived from a sample of UK general public.[14] The approach used to generate QALYs has been extensively validated and has recently been recommended for decision making by the National Institute for Health and Clinical Excellence (NICE) UK.[15]

As the number of missing QALY responses was less than 10%, missing data were assumed to be missing completely at random (that is non-responders do not differ systematically from responders). An alternative approach was also adopted that imputed the missing data using the mean responses of those that did provide a response. The incremental QALYs between groups were based on analysis of covariance, adjusting for the factors used in minimisation (i.e. treatment, gender, age 74-84, age 85 and above, and residence type), and EQ-5D baseline scores.

Assessment of cost-effectiveness

Data reported as mean costs for both cases and controls were derived for each item of resource use and then compared using unpaired t-tests. Using the estimates of incremental cost and QALYs, the incremental cost per QALY ratio (ICER) was estimated to assess the likelihood of the intervention being more cost effective. Decisions about the acceptability of a technology as an effective use of NHS resources are based primarily on the cost-effectiveness estimate of below an ICER of £20,000 per QALY.[15] As the data were not normally distributed non-parametric bootstrapping was used to estimate credible limits around the difference in cost for each area of resource use, mean total cost, and mean QALYs.[16] No discounting of costs and effects was performed, as the time horizon was only one year.

Sensitivity analysis

Sensitivity analysis is necessary to assess the robustness of the qualitative conclusion and identify where areas where research needed to more precisely estimate the values of those variables to which the result is sensitive.[17] The variables that were considered uncertain in this study related to the cost of the different services used.

Therefore one-way sensitivity analysis was conducted using plausible variations in the cost of inpatient and outpatient services.

Results

Description of the participants (Table 2)

The median age of intervention and placebo groups was 72 and 71 years respectively. Four percent of participants were aged 85 years or older, 3% lived in nursing homes. More than half took three or more different drugs daily, 30% had heart disorders, 19% had chest disorders and 29% were at risk of either iron, folate, vitamin C or vitamin D deficiency.

The supplemented group had 150 hospital admissions during the trial, of which 22 were for the treatment of infection. The figures for the placebo group were 125 and 23, respectively. The differences between groups were not statistically significant ($P > 0.05$).[9]

Costs

The summary of the mean cost per patient of the two interventions is presented in Table 3. This table summarises both resource use and costs and shows that the main determinant of incremental cost was the cost of the supplements. The mean total cost per patient in the multivitamin and multimineral supplement arm was £90 (standard deviation (SD) £155, median £38) and of the placebo arm £75 (SD £142, median £21). The difference in mean cost was £15 (95% CI -£4 to £35).

Quality-adjusted life years

Table 4 reports the EQ-5D scores for each arm of the trial at baseline, six and 12 months. Also reported are the differences between arms in EQ-5D score at six and twelve months. From these data it was estimated that the mean QALYs were 0.771 (SD 0.22, median 0.796) for the multivitamin and multimineral supplement arm and 0.789 (SD 0.20, median 0.796) for the placebo arm. The mean difference in QALYs after adjusting for minimisation and baseline EQ-5D scores was –0.018 (95% CI –0.04 to 0.002) i.e. the placebo arm was associated with more QALYs, although the difference was not statistically significant.

Estimation of cost-effectiveness

In terms of mean incremental cost per QALY the placebo intervention was dominant (less costly and at least as effective). Furthermore, the results of the bootstrapping exercise indicated that it was highly unlikely (1% likelihood) that supplements could provide additional benefits at a price considered affordable by society.

Sensitivity analysis

The total costs were derived in several ways: by imputing the missing costs, including all outpatient and in-patient costs. Sensitivity analyses were carried out for outpatient service costs included the costs of day cases and accident and emergency visits. The inpatient costs were also calculated based upon all hospital admissions and imputed speciality costs. These results were not sensitive to any of the changes around costs made in the sensitivity analyses performed.

Discussion

The use of a multivitamin and multimineral supplement, similar to many of the products available over the counter, is unlikely to be cost-effective in this population for the UK. This conclusion was not affected by any of the sensitivity analyses performed or the inclusion of a stochastic analysis of costs and QALYs. This latter approach has been advocated in situations where no difference in outcomes has been detected to quantify the likelihood that a more costly intervention could also be more effective.[15] In our situation this likelihood was found to be very low (estimated at 1%). Interventions with a cost per QALY of £20,000 are generally recommended for use in the UK NHS. Multivitamin and multimineral supplementation is highly unlikely to meet this criterion.

The trial population is representative of the elderly population living in the community but included very few people aged 85 years or over or living in nursing homes, many of whom may be of higher risk of nutritional deficit.[18] However, people already taking supplements were also excluded and these people have been shown to have healthier diets.[17]

The method used to elicit QALYs might have failed to capture some beneficial aspect of multivitamin and multimineral supplementation. However, there appeared to be no evidence of a difference when health was measured using the SF-12 nor in the number of infection days per person.[9] These results are in concordance with those from similar trials[6,8] although some evidence of borderline effectiveness has been reported.[19,20] There was also a high proportion of people with zero costs in each section as resource utilisation was quite low.

Conclusions

In conclusion, regular use of commonly available multivitamin and multimineral supplements by older people living in the community not already taking supplements is unlikely to be cost-effective. It is unclear whether this conclusion also holds for older people or those living in nursing home care.

The MAVIS Trial Group are: Dr Marion K Campbell PhD CStat, Prof Philip C Hannaford MD FRCGP, Dr Geraldine McNeill PhD MB ChB, Dr Craig R Ramsay PhD BSc, Prof D Gwyn Seymour MD FRCP(UK), Ms Kathryn Brownie, Ms Janice Cruden, Ms Gladys McPherson, Ms Clare Robertson, Ms Joanne Warner.

Collaborators in primary care:
Ellon Health Centre: Dr Alan Donaldson, Dr Ian MacKay, Dr Duncan McKerchar, Dr Ian Simpson, Dr Martin Pucci, Dr Rosamund Bell, Dr Peter Brown, Dr Pilar Murphy, Dr Huber Kam, Dr Anne Pearson, Ms Caroline Cumming
Gilbert Road Medical Group: Dr John Corse, Dr Douglas Orr, Dr Linda Sandilands, Dr James Scott, Dr Murdoch Shirreffs, Dr Sheena Tuttle, Dr Jane White, Dr Gordon Wilson, Ms Jane Harvey, Ms Hilary Andrew
Inverurie Health Centre: Dr James Beattie, Dr James Black, Dr Victor Johnston, Dr David Hood, Dr Jacqueline MacDonald, Dr Sally Harkness, Dr Fiona McKay, Dr David Rutledge, Dr Fiona Baxter, Dr Gillian Brewis, Dr Richard Gordon, Ms Eunice Connon, Ms Wilma Hadden
Macduff Health Centre: Dr Iain Brooker, Dr Alison Barbour, Dr Pat Hoddinott, Mrs Murial Barclay, Ms Joy Thom
Peterhead Health Centre: Prof Lewis Ritchie, Dr Kenneth Strachan, Dr Patricia Donaldson, Dr Joyce Robertson, Dr John Stout, Dr Ian Small, Dr Gregor Bruce, Dr David Kennedy, Dr Bruce Strachan, Dr Graham Strachan, Dr Dale Fenwick, Ms Michelle Bibby, Ms Ethel Wilson, Ms Fiona Begg
Queen's Road Medical Group: Dr Iain Duthie, Dr Geoff Clarke, Dr Fiona Garton, Dr Eunice Connon, Dr Paul Davidson, Dr Iain Stirling, Dr Theresa Suttle, Dr Stuart Watson, Dr Belinda Porter, Ms Shona Nairn, Ms Loraine Horsburgh, Ms Rosie Jamieson

Data Monitoring and Safety Committee group members:
Dr Adam Coldwells (chair), Dr Barbara Golden, Prof Lewis Ritchie.

Funding/Support: we are very grateful to The Health Foundation (formerly PPP Healthcare Medical Trust) for funding this trial (ISRCTN 66376460). The Health Services Research Unit and Health Economics Research Unit are funded by the Chief

Scientists Office of the Scottish Executive Health Department. The views expressed are those of the authors.

Statement of the independence of researchers from funders: The study funders had no role in the study design; collection, analysis, and interpretation of data; writing of the report; and in the decision to submit the paper for publication.

Acknowledgements: We thank all the participants for their help with this study, the staff of the general practices and medical records at Aberdeen Royal Infirmary, and the Data Monitoring and Safety Committee group.

Ethical approval: ethical approval was obtained from the Grampian Research Ethics Committee.

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Table 1: Methods of data collection and outcomes

Variables		**Average unit cost**
Minerals and vitamins		£17.20
GP consultations	Per surgery consultation (9.36 mins)[11]	£20
	Per telephone consultation (10.8 mins)[11]	£23
	Per home visit (13.2 mins)[11]	£61
Nurse	Per consultation[11]	£8
	Per home visit[11]	£18
Dentist	General dentist appointment[13]	£6.65
Antibiotics prescribed	Cost of actual antibiotic (British National Formulary)[12]	Varied
Contacts with other care providers		
Out patient appointments	ISD Scotland National Statistics[10]	£73
A and E contact	Ref costs (minor injuries within A&E)[10]	£37
Day case	ISD Scotland[10]	£334
Inpatient stay	Personal Social Services Research Unit (PSSRU) [11]	£147

10,11,12,13 refer to references.

Table 2: Description of participants. Values are numbers (percentages) unless stated otherwise

Characteristics	Supplement group	Placebo group
	n=456	n=454
Median (interquartile range) age (years)	72 (68.0-76.0)	71 (68.0-76.0)
Aged ≥85	19 (4)	16 (4)
Women	217 (48)	214 (47)
Mean (SD) body mass index (kg/m^2)	28.2 (4.2)	27.9 (4.1)
	n=456	n=453
Current smoker	57 (13)	63 (14)
Current No of different drugs taken:	n=455	n=453
0-2	205 (45)	234 (52)
3-6	198 (44)	164 (36)
>6	52 (11)	55 (12)
Past and present chronic conditions:	n=456	n=454
Hypertension	188 (41)	172 (38)
Heart disorders	137 (30)	130 (29)
Chest disorders	86 (19)	87 (19)
Diabetes	37 (8)	42 (9)
Cancer	46 (10)	46 (10)
Cerebrovascular disease	31 (7)	22 (5)
Chronic infection present at recruitment	42 (9)	38 (8)
Injection in past year to prevent influenza	432 (95)	423 (93)
Place of residence:		
Community	440 (97)	439 (97)
Nursing home	16 (3)	15 (3)
Housing tenure:		
Owner occupier	340 (75)	332 (73)
Public sector tenant*	88 (19)	92 (20)
Other	28 (6)	30 (7)
Nutrient at high risk of being deficient†:		
Iron	73 (16)	37 (8)
Folate	25 (6)	21 (5)
Vitamin C	58 (13)	59 (13)
Vitamin D	70 (15)	49 (11)
At risk for any of above	145 (32)	117 (26)

*For example, council house tenant.
†On basis of micronutrient risk scores, see: http://www.foodfrequency.org/naq

Table 3 Resource use and mean cost per patient

	Area of resource use‡	**Treatment number***		**Control number***		**Difference****	
		Resource	Cost	Resource	Cost	Resource	Cost
NHS Primary Services	Minerals and vitamins	12 months supply	£17.20	0	0	12 months supply	£17.20
	Antibiotics prescribed (number of prescriptions)	1.37 (1.0) [0,2]	£11.72(0)[0,8.6]	1.42 (0.0) [0,2]	£9.56 (0.9)[0,7.4]	0.97{0.05}	£2.16 {1.86}
	GP consultations (visits)						
	At home	0.22 (0)[0,0]	£13.5(0)[0,0]	0.24 (0)[0,0]	£14.71(0)[0,0]	0.02{0.6}	£1.51{3.64}
	At surgery	1.4(1.0)[0,2]	£27.64(0)[0,0]	1.3(0.0)[0,2]	£26.90(0)[0,0]	0.04{0.14}	£0.74{2.95}
	Telephone	0.07(0)[0,0]	£1.63(0)[0,0]	0.05(0)[0]	£1.11(0)[0,0]	0.02{0.21}	£0.51{0.051}
	Contacts with other primary care providers (visits)						
	Nurses at home	0.12(0)[0,0]	£2.19(0)[0,0]	0.14(0)[0,0]	£2.55(0)[0,0]	0.02{0.11}	£0.36{1.90}
	In surgery	0.08(0)[0,0]	£0.64(0)[0,0]	0.16(0)[0,0]	£1.29(0)[0,0]	0.08{0.08}	£0.66{0.61}
	Dentist	0.01(0)[0,0]	£0.08(0)[0,0]	0.00(0)[0,0]	£0.03(0)[0,0]	0.00{0.00}	£0.06{0.05}
	Unknown	0.06(0)[0,0]	£1.60(0)[0,0]	0.12(0)[0,0]	£3.12(0)[0,0]	0.06{0.03}	£1.16{0.93}
NHS Secondary Services	Out patient appointments (visits)	0.08 (0) [0,0]	£7.21(0)[0,0]	0.09 (0)[0,0]	£7.77 (0)[0,0]	0.01{0}	£-0.56{2.96}
	Inpatient stay (days)	0.05(0)[0,0]	£7.14 (0)[0,0]	0.05(0)[0,0]	£7.48 (0)[0,0]	0{0}	£-0.34 {2.89}
TOTAL COSTS			£90(38)[17,87]		£75(21)[0,74]		£15{9.86}

‡There are very many zero values as resource utilisation was very low * Data reported as mean (median) [inter-quartile range] ** Data reported as mean difference {Std error difference}

Table 4 EQ-5D scores

	Treatment n = 456	Control n = 454	Adjusted difference*	CI	P value
Baseline	0.75 (0.23)	0.78(0.19)			
6 months	0.77(0.22)	0.80(0.20)	-0.014	[-0.034, 0.006]	0.18
12 months	0.77(0.22)	0.80(0.19)	-0.018	[-0.04, 0.002]	0.08

() Standard deviations

* Difference adjusted for minimisation factors and baseline EQ-5D