A cost-utility analysis of multivitamin and multimineral supplements in men and women aged 65 years and over


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study examined the use of over-the-counter multivitamin and multimineral supplements to reduce the risk of infections in elderly people. Supplements included 800 microg vitamin A, 60 mg vitamin C, 5 microg vitamin D, 10 mg vitamin E, 1.4 mg thiamin, 1.6 mg riboflavin, 18 mg niacin, 6 mg pantothenic acid, 2 mg pyridoxine, 1 microg vitamin B12, 200 microg folic acid, 14 mg iron, 150 microg iodine, 0.75 mg copper, 15 mg zinc and 1 mg manganese.

Type of intervention
Primary and secondary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised individuals aged 65 years or older, unless their general practitioner (GP) considered them too unwell.

Setting
The setting was primary care. The economic study was carried out in the UK.

Dates to which data relate
The recruitment of patients involved in the effectiveness and cost analyses took place between February and December 2002. The price year was 2003.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the analysis of effectiveness.

Study sample
Initially, a sample of 910 participants was enrolled. There were 454 individuals (47% women) in the control group and 456 participants (48% women) in the intervention group. The median age was 71 years (interquartile range, IQR: 68.0 to 76.9) in the control group and 72 years (IQR: 68.0 to 76.0) in the intervention group. Individuals were recruited by their GPs, who decided whether patients were too unwell to participate. Participants who had used oral mineral, vitamin or fish oil supplements in the previous 3 months or vitamin B12 injections in the last 3 months were excluded.

Study design
This was a prospective, pragmatic, randomised, double-blind placebo-controlled trial that was carried out in six general
practices in Grampian, Scotland. The length of follow-up was 12 months. Of the individuals initially enrolled, 32 withdrew from the study (18 in the placebo group and 14 in the supplement group) and 77 (39 in the placebo group and 38 in the supplement group) stopped taking tablets although they remained in the study.

Analysis of effectiveness
The primary health end point used in the current analysis was the change in the EuroQol (EQ-5D), which was used to evaluate the patients’ quality of life (QoL) over the study period. Three measurements were made (baseline, 6 and 12 months). The analysis of the clinical study was conducted on an intention to treat basis. The baseline comparability of the study groups was not explicitly discussed in this paper, but the randomised design of the clinical trial and the large sample size should have ensured that there were no statistically significant differences at baseline.

Effectiveness results
The mean values of QoL changed from 0.75 (+/- 0.23) at baseline to 0.77 (+/- 0.22) at both 6 and 12 months in the intervention group, and from 0.78 (+ 0.19) at baseline to 0.80 (+/- 0.19) at both 6 and 12 months in the control group.

After adjusting for minimisation factors and baseline estimates, differences between the groups did not reach statistical significance.

Clinical conclusions
The effectiveness analysis showed that QoL was similar between the two groups.

Measure of benefits used in the economic analysis
The summary benefit measure used was the quality-adjusted life-years (QALYs). These were estimated using the QoL values derived from the clinical trial. Discounting was not required because of the short time horizon of the analysis (12 months).

Direct costs
The analysis of the costs was carried out from the perspective of the NHS. It included the costs associated with mineral and vitamin supplements, antibiotic prescriptions, primary care contacts, hospital admissions, days in hospital with infection, infection-related outpatient visits, and adverse events. The unit costs and the quantities of resources used were presented separately for several items. Much of the resource use data were derived from a review of primary care notes. These data were supplemented with participant information recorded in a patient diary. Consumption of hospital resources was obtained from computerised patient administration systems, hospital and primary care notes. The costs came from typical NHS sources such as the British National Formulary, Personal Social Services Research Unit, the UK Department of Health and the Scottish Health Service. Discounting was not relevant and was not performed. The price year was 2003.

Statistical analysis of costs
Cost-differences were tested for statistical significance using an analysis of covariance and adjusting for factors such as treatment, gender, age 74 to 84 years, age 85 years and older, and residence type. Imputation of missing values was performed using a random approach, although missing data on resource use were very rare (less than 1%).

Indirect Costs
Productivity costs were not considered.

Currency
UK pounds sterling (£).
Sensitivity analysis
A univariate sensitivity analysis was carried out to assess the impact of changes in the cost estimates on the results of the analysis. The authors stated that plausible variations were used for inpatient and outpatient services. Bootstrapping was performed to assess the probability of the intervention being cost-effective at different willingness-to-pay values.

Estimated benefits used in the economic analysis
The expected mean QALYs per patient over the 12-month study period were 0.771 (+/- 0.22) (median 0.796) in the intervention group and 0.789 (+/- 0.20) (median 0.796) in the placebo group.

The mean adjusted difference in QALYs was -0.018 (95% confidence interval, CI: -0.04 to 0.002). Thus, the placebo was associated with more QALYs, although the difference failed to reach statistical significance.

Cost results
The mean cost per patient was 90 (median 38; IQR: 17 to 87) in the treatment group and 75 (median 21; IQR: 0 to 74) in the control group.

The cost difference was 15 (+/- 9.86).

The higher costs of the intervention group were totally due to the cost of minerals and vitamins. The other categories of costs were similar between the groups.

Synthesis of costs and benefits
The costs and benefits were not combined in a cost-utility ratio as the incremental analysis showed that placebo was the dominant strategy, in that it was both more effective and less expensive than the intervention. Further, bootstrapping indicated that that the probability that supplements were associated with an incremental cost per QALY gained lower than the threshold of 20,000 was very low (1%). The sensitivity analysis did not alter the conclusions of the analysis.

Authors' conclusions
It was highly unlikely that the use of multivitamin and multimineral supplements in elderly people would be cost-effective.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear and appropriate in that no intervention represented the current strategy in the elderly. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data came from a well-conducted clinical trial, a design that is usually associated with a high internal validity. Although the primary trial was published in a companion paper, and more detailed information on randomisation will probably be found in the primary publication, the large sample of patients recruited, the use of intention to treat, the double-blind assessment, and the multi-centre design should have ensured the robustness of the clinical estimates. The use of wide inclusion criteria enhances the representativeness of the sample of individuals. However, the authors pointed out that the patient sample might not be representative of older people living in nursing homes. Appropriate statistical analyses (analysis of covariance) were conducted to take potential differences in baseline characteristics between the groups into consideration.

Validity of estimate of measure of benefit
QALYs would appear to be an appropriate benefit measure as they capture the impact of the interventions on both
quality of life and survival, which may both be relevant for the individuals considered in the study. The instrument used to elicit patient preferences has been widely used and validated in several settings. However, the QALYs were calculated using a short timeframe (one year), whereas the use of a long follow-up would have been more appropriate.

**Validity of estimate of costs**
The analysis of the costs was carried out credibly, the authors providing extensive information on the unit costs, quantities of resources used and sources selected to obtain the data. This will enable the analysis to be repeated in other settings. Statistical analyses of the costs were performed and the impact of using alternative cost estimates was investigated in the sensitivity analysis. The price year was reported, which will facilitate reflation exercises in other time periods.

**Other issues**
The authors stated that, in general, their findings conformed with those from other studies, although no direct comparison was made. The issue of the generalisability of the study results to other settings was not explicitly addressed, and the results of the sensitivity analysis were not extensively reported. Thus, the results seem to be relevant primarily to the authors' setting. The study referred to older individuals not currently taking supplements and this was reflected in the authors' conclusions.

**Implications of the study**
The study results do not support the use of multivitamin and multiminerl supplements in the elderly.

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