Cost-effectiveness analysis of adjunct VSL#3 therapy versus standard medical therapy in pediatric ulcerative colitis

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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.

CRD summary
The study examined the cost-effectiveness of adding the probiotic VSL#3 to standard medical therapy for children with moderate-to-severe ulcerative colitis. The authors concluded that the addition of VSL#3 was not cost-effective, but small changes in the quality of life after surgery could make it cost-effective. The cost-effectiveness framework was valid, the sources of evidence were robust, and alternative scenarios were considered, but the authors’ conclusions were dependent on their model assumptions.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of adding the probiotic VSL#3 to the standard medical therapy for paediatric patients with new moderate-to-severe ulcerative colitis.

Interventions
Standard medical therapy plus VSL#3 was compared with standard medical therapy alone. VSL#3 was a specific blend of high-dose probiotics, containing 450 billion live bacteria of eight strains per sachet. Standard medical therapy consisted of mesalazine and intravenous or oral steroids. After the failure of either treatment, escalating therapy of mesalazine, azathioprine, and infliximab was administered.

Location/setting
USA/out-patient secondary care.

Methods
Analytical approach:
The analysis was based on a Markov model, with a lifetime horizon and a hypothetical cohort of 10-year-old children with ulcerative colitis. The authors stated that a societal perspective was adopted.

Effectiveness data:
The clinical inputs were identified by a review of electronic databases and clinical trial registries. Studies were selected by their quality (randomised trials were given priority) and their relevance to paediatric ulcerative colitis. Means or medians were calculated to pool evidence from multiple sources. The treatment effects for medical therapy, for VSL#3, and for most escalating therapies were from clinical trials of both children and adults. The efficacy of treatment (response rate while on therapy) was the primary input for the model. Large observational studies were used where clinical trials were not available.

Monetary benefit and utility valuations:
The utility values were from published sources that used the time trade-off and standard gamble methods to elicit preferences for the health conditions associated with ulcerative colitis.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at an annual rate of 3%.
Cost data:
The economic analysis included the costs of drugs, hospitalisations, out-patient visits, procedures such as ileal pouch anal anastomosis (IPAA), and laboratory services. The costs of drugs were based on their average wholesale prices, while other medical costs were estimated using national reimbursements from the Centers for Medicare and Medicaid Services or average reimbursement rates from eligible patients at a large medical centre. All costs were in US $ and a 3% annual discount rate was applied. The price year was 2009.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on all the model inputs, using both published and arbitrarily assumed ranges of values.

Results
The expected lifetime costs were $203,317 with standard therapy and $212,582 with additional VSL#3. The QALYs were 24.93 with standard therapy and 25.05 with VSL#3. The incremental cost per QALY gained with VSL#3 over standard therapy was $79,910, which was above the commonly cited cost-effectiveness threshold of $50,000 per QALY gained.

The most influential inputs were the cost of colectomy plus IPAA, the maintenance cost after surgery, the probability of developing pouchitis after surgery, and the quality of life after a colectomy plus IPAA. High surgical and after-surgery costs, a high probability of developing pouchitis, and a low quality of life after surgery made VSL#3 cost-effective. The quality of life after surgery was the most sensitive input and only small reductions (from 0.89 to 0.86) made VSL#3 cost-effective.

Authors' conclusions
The authors concluded that the addition of VSL#3 to standard medical therapy was not cost-effective, but small changes in the quality of life after an IPAA could make it cost-effective.

CRD commentary
Interventions:
The selection of the comparators was appropriate as conventional medical therapy was the usual care for paediatric patients with ulcerative colitis. A description of escalating medical therapy was given.

Effectiveness/benefits:
A systematic review of the literature was appropriately conducted to identify published studies for the clinical data. Valid criteria were used to select the relevant sources. Most of the data were from clinical trials, but they had small samples that often contained adults rather than children. This was acknowledged by the authors as a possible limitation to the analysis. Most of the parameters were varied in the sensitivity analysis. QALYs were an appropriate benefit measure, given the impact of ulcerative colitis on quality of life. The utility values were from studies that appear to have used valid instruments.

Costs:
The economic analysis was restricted to the costs of the medical services for the two treatments. Non-medical costs should have been included for a societal perspective. This would have analysed indirect costs, such as the wage losses of caregivers. The unit costs and quantities of resources were not presented separately, and the costs were reported as category totals and were not broken down to individual items. The sources for the economic data reflected typical US accounting systems for third-party payers. The price year was reported, allowing reflation exercises. The costs were treated deterministically, but the impact of variations in economic inputs was investigated in the sensitivity analyses.

Analysis and results:
The results were clearly reported. An incremental approach was appropriately used to combine the costs and benefits of the two treatments. A deterministic approach was used to assess uncertainty, and the results were clearly reported. The authors stated that the main issues of their analysis were the poor quality of clinical data for VSL#3 for ulcerative colitis in children and the need for some assumptions. The model results appear to be specific to the USA and will be difficult to transfer to other settings. They were strongly dependent on some model parameters.
Concluding remarks:
The cost-effectiveness framework was valid, the sources of evidence were robust, and alternative scenarios were considered, but the authors' conclusions were dependent on their model assumptions.

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