The cost-effectiveness of endoscopic injection of dextranomer/hyaluronic acid copolymer for vesicoureteral reflux
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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
This study evaluated the cost-effectiveness of endoscopic dextranomer plus hyaluronic acid copolymer injection, for children aged two to three years, with vesicoureteral reflux, persisting for longer than one year. The authors concluded that endoscopic injection was as effective as or more effective than open surgery, at a lower cost. The study was well reported, but limited and reliant on many structural assumptions. The evidence was from 2001, and may not be relevant to current clinical practice and health systems.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study evaluated the effects on the costs and cure rates of endoscopic dextranomer plus hyaluronic acid copolymer, as an endoscopic injection, for children aged two to three years, with grade III vesicoureteral reflux, persisting for more than one year.

Interventions
Three scenarios for endoscopic injection were considered. For scenario one, endoscopic injection was given to 75% of children who were not cured after six years on antibiotics. For scenario two, endoscopic injection was given to 90% of children who were not cured on antibiotic therapy each year, and the other 10% underwent surgery. For scenario three, all children with unresolved reflux after one year of antibiotics, were offered endoscopic injection, with up to 70% of parents accepting it. For all three scenarios, 75% of patients who were not cured at six years, received injection.

The comparator was usual practice, defined as prophylactic antibiotic treatment, followed by ureter reimplant open surgery, for half the patients who were not cured at six years, or no further antibiotics, for the other half. Antibiotic treatment consisted of trimethoprim-sulphamethoxazole, followed by nitrofurantoin.

Location/setting
USA/out-patient care.

Methods
Analytical approach:
The economic evaluation was based on a six-year decision model. The states in the model were based on information from experts and the published literature. The authors did not state the perspective.

Effectiveness data:
The primary measure of effectiveness was the percentage of children who were cured, defined as grade 0 or I reflux, at six years. The effectiveness of endoscopic injection was calculated from 140 patients, with 208 ureters with grade III reflux, who were treated in Sweden. It was assumed that 98% of patients were reflux free after surgery, based on a physician survey. Other key clinical inputs for the model, such as spontaneous resolution and surgical intervention rates, were from two long-term follow-up studies, other published studies, and a survey of paediatric urologists and nephrologists.

Monetary benefit and utility valuations:
Measure of benefit:
The measures of benefit were the percentage and number of patients who were cured (grade 0 or I reflux, for both ureters) at six years.

Cost data:
The resource use for usual care was from a survey of 27 paediatric urologists and nephrologists. This provided the frequency, type of visit, and test performed, while patients were on antibiotic therapy, and the preoperative and postoperative management for ureter reimplantation surgery. The annual cost of antibiotic prophylaxis was estimated using Current Procedural Codes for the tests, the Physician Fee Schedule for physician visits, and an online drug price list. The costs of endoscopic injection were from the accounts of a Philadelphia hospital, modified by a cost-to-charge ratio. The costs of surgery included initial visit, operating theatre fees, anaesthesia, physician fee, and in-patient bed costs. The percentage of bilateral surgery was reduced from that in the Philadelphia hospital to nearer that in the USA, as these were very different. All costs were reported in US $. Future costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
The authors conducted sensitivity analyses by varying the resolution and failure by gender, the proportion of bilateral interventions, and the costs of reimplantation and endoscopic injection, and using a 10% discount rate. An analysis was conducted assuming a 10% reflux relapse rate with endoscopic injection.

Results
Over six years, usual practice resulted in a discounted cost per patient of $7,815, with 12.0% of patients not cured. Scenario one, 75% injection at six years, resulted in discounted costs of $7,246, with 11.2% of patients not cured. Scenario two, 90% injection each year, decreased the discounted costs to $6,130, with 10.6% of patients not cured. Scenario three, 70% injection at one year, had a discounted cost of $7,697, with 4.0% of patients not cured.

Scenario two was less costly and more effective (dominant) than usual care and scenario one. Scenario three was most effective, but more costly than the other two scenarios.

Sensitivity analyses showed that the costs were higher for girls than for boys. Most sensitivity analyses did not change the cost-effectiveness relationships between interventions, except when decreasing the cost of surgery, which favoured usual care, over the injection interventions.

Authors’ conclusions
The authors concluded that endoscopic dextranomer plus hyaluronic acid copolymer injection was as effective as or more effective than open surgery, at a lower cost.

CRD commentary
Interventions:
The interventions were generally well described and appear to have been appropriate. The most appropriate comparator, usual care, was included. The authors mentioned other viable options, such as glutaraldehyde cross-linked bovine collagen injection, but did not include them due to safety issues or a lack of long-term data.

Effectiveness/benefits:
The search and selection methods for the effectiveness data were not reported, so it is not clear whether the best available evidence was used. The treatment protocols were based largely on assumptions, which may or may not reflect clinical practice. The authors acknowledged that their primary outcome (grade 0 or 1 reflux, at six years) was an intermediate outcome, which was chosen due to lack of long-term effectiveness and cost data. The true outcome of interest was the long-term avoidance of severe health problems and renal scarring. They recommended that future analyses should focus on prevention of renal scarring, rather than reflux cure rates.

Costs:
The costs suggest that a hospital perspective was adopted. They were reported with sufficient detail, and appear to have been from appropriate sources. The price year was not reported, which hinders comparison with other studies. The
process of the survey, used to derive the resource data, was well described and appears to have been rigorous. The authors compared some physician-reported resource use to that in published studies, which was an appropriate validation. While the elicitation of expert opinion for the costs appears to have been done well, the elicited costs remain considerably uncertain, and this was not reflected in the analysis.

Analysis and results:
The authors acknowledged that the time horizon of the analysis was short, and failed to capture the expected differences in long-term effects and costs. A full incremental analysis was not conducted. As usual care, and scenario one, were dominated by scenario two, they should not have been considered in the final analysis. The proper comparison was scenario three against scenario two. The model had many assumptions, which resulted in considerable uncertainty, which was only partly assessed in one-way sensitivity analysis, and the measures of variance were not reported. A rigorous probabilistic sensitivity analysis could have assessed the overall parameter uncertainty. The authors conducted a thorough comparison of their results with those of similar economic evaluations, and appropriately acknowledged their study limitations. The effectiveness evidence was from 2001, and so may not be relevant to current clinical practice and health systems.

Concluding remarks:
The study was well reported, but limited due to a short time horizon, a lack of sensitivity analysis, and a reliance on structural assumptions. The authors' conclusion should be used with caution.

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