Monotherapy versus multi-drug therapy for the treatment of perforated appendicitis in children

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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.

Health technology
The authors assessed monotherapy treatment for children with perforated appendicitis. Monotherapy consisted of a 100 mg/kg dose of the piperacillin-tazobactam (PT) component given every 8 hours if the patient was younger than 12 years old, and a 4 g dose given every 8 hours if the patient was older than 12 years old. Treatment lasted for 10 to 14 days. Further details about the patients’ treatment were reported in the paper.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised children with perforated appendicitis.

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and cost data were collected between 1 January 1998 and 31 December 2001. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

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

Study sample
The authors did not report that power calculations were carried out to estimate the impact of chance on the results. The sample was selected by including all children with perforated appendicitis who had been admitted to the study hospital between the dates of the study and had undergone operation within the first 24 hours of admission. In total, 94 patients were included. There were 51 patients in the PT group (56.9% male) and 43 in the MD group (67.4% male). The patients in the PT group were aged 9.2 (+/- 4.0) years and the duration of their symptoms was 54.7 (+/- 34.7) hours. The patients in the MD group were aged 9.5 (+/- 3.3) years and the duration of their symptoms was 54.7 (+/- 27.6)
hours. There were no reports of patients excluded for any reason. There was no evidence of whether the study sample was representative of the study population.

**Study design**
The analysis was based on a retrospective cohort study, with data gathered from medical records. Patients were assigned to the two groups according to the antibiotic regimen they received, which depended on the surgeon's preferences. The study was carried out at a single centre, the Children's Hospital of Pittsburgh, University of Pittsburgh School of Medicine, Pittsburgh, (PA). Each patient was followed up until the first clinic visit, usually 1 to 2 weeks after discharge.

**Analysis of effectiveness**
The analysis was conducted on the basis of the actual antibiotic regimen received. The primary health outcomes were the overall complication rates and the numbers of patients experiencing antibiotic-related complications and readmissions. The groups were reported to be comparable at baseline in terms of their age, gender, duration of presenting symptoms, initial white blood cell count and length of hospitalisation.

**Effectiveness results**
The overall complication rate was 8% in the PT group and 32% in the MD group.

Patients in the MD group were more likely to suffer from a complication than those in the PT group, (14 of 43 MD patients versus 4 of 51 PT patients; p=0.002), and more likely to suffer from an antibiotic complication (10 of 43 MD patients versus 4 of 51 PT patients; p=0.04).

There were no statistically significant differences in the number of patients readmitted (4 MD patients versus 1 PT patient, p=0.17).

**Clinical conclusions**
Monotherapy would appear to be more effective in the treatment of children with perforated appendicitis. It resulted in a significantly lower number of patients experiencing overall complications and antibiotic-related complications than those treated with MD therapy.

**Measure of benefits used in the economic analysis**
The authors did not estimate a summary measure of benefits. The study was therefore categorised as a cost-consequences analysis.

**Direct costs**
The authors did not report the perspective adopted, although they appear to have been concerned with the costs to the health care provider or third-party payer as they were interested in inpatient and outpatient charges. However, it was unclear whether overheads and similar costs element relevant to these perspectives were included. The costs were derived from actual patient records and authors' assumptions about the duration of home antibiotics (based on that presented by the most common home care agency employed in the study setting). Charges taken from the accounting department at the study setting were used instead of unit costs; a cost-to-charge adjustment was not performed. As the time horizon for each patient was short, discounting was not necessary in this study. A price year and any attempts to reflate prices were not reported to have been used. The total price was not broken down beyond total inpatient and outpatient charges.

**Statistical analysis of costs**
Statistical comparisons of the costs were reported, although only for estimated inpatient costs.
**Indirect Costs**
The indirect costs were not estimated.

**Currency**
US dollars ($).

**Sensitivity analysis**
There was no report of sensitivity analyses being carried out to estimate the impact of uncertainty on the results.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
For the PT group, the total average inpatient charges were $19,191 (standard deviation, SD=7,433) and the outpatient charges were $2,460.

For the MD group, the total average inpatient charges were $20,703 (SD=11,306) and the outpatient charges were $4,349.

The difference in inpatient charges between the study groups was not significant, (p=0.5)

**Synthesis of costs and benefits**
Not relevant.

**Authors' conclusions**
Monotherapy would appear to be more effective and more cost-effective than multi-drug (MD) therapy (at least in the outpatient setting) since it reduced complications without significant differences in charges.

**CRD COMMENTARY - Selection of comparators**
MD therapy was reported to be standard practice in the study setting, although the authors commented that recent evidence demonstrating the benefits of PT prompted a protocol of PT to be adopted. The authors' choice of technologies enabled a real world comparison relevant to their own setting to be adopted. You should decide if the treatments considered in the study are relevant treatments for children with perforated appendicitis in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis was based on a retrospective cohort study of patients, with the grouping determined by the surgeon. This non-randomisation and selection according to preferences introduces the possibility of selection bias, and thus can lead to substantial within-group similarities and between-group variation. However, comparisons of the groups at baseline suggested that patients in the two groups were comparable at baseline. One limitation the authors highlighted was the limited sample size, which reduces the ability to detect statistically significant results. An interesting supplement to the study would have been to identify the surgeons' reasons for assigning patients to each of the groups. The study sample might have been representative of the study population as it comprised all children entering the study setting and receiving antibiotic treatment following perforated appendicitis. The sample was reported to be consistent with those assessed in similar studies. Statistical analyses were carried out to compare the individuals at baseline and the study outcomes.
Validity of estimate of measure of benefit
The authors did not estimate a summary measure of benefit. The study was therefore categorised as a cost-consequences analysis. The reader is referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above), given that the health benefits are reflected in the disaggregated effectiveness outcomes.

Validity of estimate of costs
A limited cost analysis was undertaken. The perspective of the analysis was not reported, which makes it difficult to assess whether all the relevant cost elements were incorporated into the analysis. The authors appear to have been concerned with the costs to the health care provider or third-party payer by incorporating inpatient and outpatient costs, although not all cost elements relevant to either of these perspectives were incorporated (e.g. the costs of readmissions). The authors acknowledged that this might have biased the results. The authors were able to provide a brief description of some of the main cost components involved with the technology, although the analysis did not provide details of the main cost-drivers; this would make extrapolation to different settings difficult. Statistical comparisons were reported only for inpatient charges. Given the short time horizon, discounting was appropriately not performed. Nevertheless, the study data were collected over a 3-year period and, therefore, the costs should have been reflated to a specific price year. Charges instead of costs were used for the cost estimation. No adjustments to reflect the true cost of the treatment options were made.

Other issues
The authors mentioned that the overall complication rate for the MD group was higher than that presented in other studies. The issue of generalisability was not addressed explicitly. The cost analysis was not sufficiently detailed to consider the generalisability of the results. The results do not appear to have been presented selectively. The conclusions were a good reflection of the results presented and were consistent with the objective and design of the study.

Implications of the study
The authors recommended that “the use of monotherapy for children with perforated appendicitis who have undergone adequate source control should be considered the treatment of choice”. They suggested a prospective analysis would be required to validate their results. In addition, a more thorough costing analysis might be considered a natural step forward.

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