Effect of changes in antibiotic prescribing on patient outcomes in a community setting: a natural experiment in Australia

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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 prescription of antibiotics in a community setting, before and after an Australian government directive, was under evaluation.

Type of intervention
Other: Policy (prescribing behaviour).

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with an episode of care (EOC) for otitis media (OM), acute sinusitis, lower respiratory tract infection (LRTI) and acute exacerbation of chronic bronchitis (AECB). Specific inclusion or exclusion criteria were not reported.

Setting
The setting was the community. The economic study was carried out at the University of Adelaide, Australia.

Dates to which data relate
The effectiveness data were gathered between 1994 and 1998. The dates to which the resource use data related were not reported. The price year was also 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 study was based on population data. The study database contained information about 34,242 patients who were treated by one of the 22 general practitioners (GPs) issued from four Australian general practices between July 1994 and June 1998. There were 15,303 antibiotic prescriptions provided to 9,921 patients and 318,234 recorded patient visits. The intra-and inter-reliability of the data-entry staff (k) was greater than 0.85 for both. Patient numbers were added together for each antibiotic, both before and after the letter from the HIC was distributed. The number of patients given AC at least once was 738 before the letter and 810 after the letter. The number of patients given...
amoxicillin at least once was 1,284 before the letter and 1,521 after the letter. For cefaclor, the numbers of patients were 1,141 (before the letter) and 1,886 (after the letter), respectively.

**Study design**
A time-series design was used to identify the temporal relationship between the effects of the HIC letter on patient outcomes and prescription share (i.e. the percentage of the antibiotics ordered when compared with other antibiotics in connection with an episode of sinusitis, OM, LRTI or AECB). To assess how representative the patients were of the Australian population, the age and gender profiles of the database patient sample were compared with the national Australian general practice attendees for the middle year of the study, 1997. The study period was 1994 to 1998.

**Analysis of effectiveness**
All of the patients included in the study were accounted for at analysis. Both patient outcomes and process-of-care outcomes were considered in the study. The patient outcomes included uninitiated return visits to the GP within 2 weeks of receiving the antibiotic, hospitalisation, and referral to a specialist. The process-of-care outcomes included computed tomography scan of sinus and chest, chest radiography, and pathology tests, spirometry, bronchoscopy and sinuscopy. An outcome was considered to be related to a specific antibiotic if it occurred within the EOC in which the antibiotic was prescribed.

The overall patient sample and the national Australian general practice attendees were comparable in age and gender profiles.

**Effectiveness results**
There were 1,854 adverse outcomes in the period before the letter, and 3,271 in the period after the letter.

The rate of patient and process-of-care outcomes per 100 EOC remained the same for amoxicillin, at 3.8 before and after the letter. The rate changed from 9.3 to 11.5 for macrolides, from 6.9 to 7.1 for cefaclor, from 9.0 to 9.6 for cephalixin, and from 7.9 to 11.3 for AC.

Of all EOCs that involved AC before the letter, 0.14 per 100 EOCs had a hospitalisation. Of all EOCs that involved AC after the letter, 1.84 per 100 EOCs had a hospitalisation, (p=0.0011).

For the EOCs in which the macrolides cefaclor, cephalixin and amoxicillin were given alone, there were no significant changes in the rate of each outcome.

When all EOCs for which at least two of these antibiotics were given as a total group were analysed, there were significant increases in the rate of adverse outcomes per 100 other antibiotic-related EOCs for the following:
- hospitalisation, 0.44 before the letter and 0.86 after the letter, (p=0.0054);
- radiologic investigations, 3.27 before the letter and 4.87 after the letter, (p=0.00001); and
- pathologic investigations, 2.73 before the letter and 3.62 after the letter, (p=0.005489).

There was a significant association between the increase in the rate per month for all outcomes and the decrease in AC-prescription share, (p=0.011), with a 3-month lag.

There was also a significant association between AC-prescription share and the overall outcome rate weighted by relative cost, (p=0.0024).

The rate of patient outcomes, including return visits, was not significantly associated with AC-prescription share.

The rate of process-of-care outcomes was significantly associated with AC-prescription share also at the 3-month lag, (p=0.006).
After the first visit, there was no significant increase in the proportion of EOCs with a patient outcome before and after the letter, \( (p=0.1776) \). There was a significant increase in the proportion of EOCs with a process-of-care outcome after the letter, \( (p<0.0001) \). There was a significant increase in the proportion of EOCs in which tetracyclines were prescribed, \( (p=0.0304) \).

There was a significant increase in the proportion of EOCs that involved a patient outcome before and after the letter (2.3% before and 6.1% after; \( p<0.0001 \)).

There was also a significant increase in the proportion of EOCs with a process-of-care outcome after the letter (4.3% before and 10.2% after; \( p<0.0001 \)).

**Clinical conclusions**
The policy initiated created unintentional changes in prescribing behaviour, and a trend towards poorer patient outcomes.

**Measure of benefits used in the economic analysis**
No summary benefit measure was used in the economic evaluation. The study was, in effect, a cost-consequences analysis.

**Direct costs**
The cost/resource boundary of the study was reported to be that of the community. The direct costs included in the analysis were for referral to a specialist, return visits, hospitalisation, pathology test, radiology and other tests. Discounting was not reported, although the costs were incurred during 4 years. The resource use data were estimated using actual data coming from the study database. Median costs were taken from the national HIC schedule for pathologic and diagnostic-imaging services and the tertiary-hospital case-mix table. The resource quantities and the costs were reported separately. The price year was not reported.

**Statistical analysis of costs**
Statistical analyses of the costs were not carried out.

**Indirect Costs**
The indirect costs were not included.

**Currency**
Australian dollars (Aus$).

**Sensitivity analysis**
Sensitivity analyses were not performed.

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

**Cost results**
The total costs were not reported. However, the authors reported the relationship between patient and process-of-care outcomes and costs.
When the rates of patient outcomes were weighted by the cost, there was a significant association with AC-prescription share, \( p=0.0114 \) when excluding return visits and \( p=0.0081 \) when including return visits.

There was a significant association between process-of-care outcomes weighted by relative cost, and AC-prescription share, \( p=0.0242 \) at the 3-month lag.

**Synthesis of costs and benefits**

Not relevant.

**Authors’ conclusions**

The Australian government directive targeted at amoxicillin with clavulanic acid (AC) resulted in more conservative behaviour of general practitioner (GPs), increased cost to the government, and a general trend towards poorer patient outcomes.

**CRD COMMENTARY - Selection of comparators**

The choice of the comparator was justified, as it represented the standard prescription of antibiotics before the Australian government directive. You should decide whether it represents a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**

A time-series design was used, which was appropriate for the study question. Power calculations were not carried out. All patients receiving antibiotics on a database of computerised medical records were included in the study. Statistical analyses were undertaken to compare the patient outcomes and process-of-care outcomes. The overall patient sample and the national Australian general practice attendees were comparable at baseline in terms of the age and gender profiles. However, since data on bacterial resistance were unavailable, confounding factors may be high for this parameter. The main drawback of the study was that no health outcomes were really estimated, except health care use (return visits, referral to a specialist and tests). A more appropriate health outcome measure would have been the measure of morbidities.

**Validity of estimate of measure of benefit**

No summary benefit measure was used in the analysis because, in effect, a cost-consequences analysis was carried out.

**Validity of estimate of costs**

The perspective of the study was stated. As such, it appears that all the relevant categories of costs have been included in the analysis. Details on the unit costs and quantities of resources used were reported, which may ease transferability of the economic analysis to other settings. However, the price year was not reported, which limits deflation exercises. The cost estimates were derived from national sources and were specific to Australia. Discounting was not carried out, even though the costs were incurred during 4 years. The main drawbacks of the cost analysis were that total costs were not reported, and statistical and sensitivity analyses were not performed on the costs. Consequently, the external validity of the study may be low.

**Other issues**

The authors did not compare their results with those from other published studies. They also did not address the issue of the generalisability of the study results to other settings. The results were not reported selectively and the effectiveness conclusions reflected the scope of the study. The authors did not report any limitations of their study. Sensitivity analyses were not performed to account for variability in the cost or effectiveness data. Consequently, caution should be exercised when extrapolating the study results to different contexts.
Implications of the study
The authors recommended that national policies aimed at changing the prescribing behaviour of GPs need to carefully analyse the likely effect on clinicians, patients, and the health system before being initiated.

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