Elective penicillin skin testing and amoxicillin challenge: effect on outpatient antibiotic use, cost, and clinical outcomes

Macy E

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
Elective penicillin skin testing (PenSTs) in advance of acute antibiotic need and (optional) amoxicillin challenge (AC) in patients with negative skin test responses. Patients were previously entered in a study of new penicillin reagents and received at least 1 prescription drug over a 2-year period.

Type of intervention
Treatment and secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients who were health plan members over a 2-year period and who obtained at least 1 prescription medication from a health plan pharmacy.

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

Dates to which data relate
Effectiveness and resource use data were collected between 16 November 1994 and 15 November 1995. The price year was 1995.

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

Link between effectiveness and cost data
Costing was retrospectively performed on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size. The study sample initially consisted of 237 subjects chosen from a total of 255 patients who were health plan members for the year before and after PenSTs; one outlier was excluded from the study, thus 236 patients remained. A total of 196 subjects with a mean (SD) age of 40 (22.4) years had negative PenST responses versus 40 patients with a mean (SD) age of 28.8 (23.1) years who had positive PenST responses. Of the 196 patients having negative PenST responses, 146 with a mean (SD) age of 37.4 (22.4) years self-selected to undergo AC, while the group with no AC (n=50) had a mean (SD) age of 47.7 (21.0) years.
Study design
The study was a retrospective before and after study, carried out in 8 centres. The duration of follow-up was 1 year. There appears to have been no loss to follow-up. Cephalosporin was prescribed to those patients allergic to penicillin class antibiotics (PCAs) with no history of adverse reaction to it and in the case of clinical indication.

Analysis of effectiveness
The principle used in the analysis of effectiveness seems to have been intention to treat. The clinical outcome measures were classes of antibiotics dispensed, antibiotic use, outpatient visit rate, and adverse reactions. As the study design was 'before-and-after' the same patient sample underwent both the intervention and the comparator. It was reported that there were significant differences between the negative and positive PenST subjects in terms of demographics, especially age.

Effectiveness results
A significant difference between the year before and the year after the PenSTs was observed in terms of classes of antibiotics dispensed, both to the patients with positive and negative test response (p=0.001)(data not shown in the paper).

A fall of 28% in antibiotic use was observed between the year before the PenSTs (779 courses dispensed to 191 patients) and the year after the PenSTs (558 courses dispensed to 169 patients).

No change was observed in the outpatient visit rate after PenST, but a shift from primary to specialty care occurred in the year after PenST (51.9% of outpatient visits to primary care in the year before PenST versus 39.1% in the year after PenST, (p=0.0001)).

A total of 3.3% (3 cases) unrechallenged mild adverse reactions occurred in 93 patients with negative skin test responses having received 188 therapeutic courses of penicillin during the year after PenST.

Six cases of adverse reactions occurred in 146 subjects with negative skin test responses undergoing optional amoxicillin challenge (AC), four of these being resolved by prescribing a penicillin analogue in the next year without reaction.

One delayed reaction was observed in 15 patients with positive PenST responses with 33 prescriptions for oral cephalosporin during the year after PenST.

Clinical conclusions
"This article provides evidence that elective PenSTs are safe and will convince physicians to once again prescribe PCAs in individuals with negative PenST responses. There are significant changes in the types of antibiotics prescribed during the year after a negative PenST response. Even when multiple courses of PCAs are used in individuals with negative PenST responses, there are low rates of subsequent adverse reactions." "It was found that AC had no effect on the frequency of patients receiving PCAs during the year after a PenST." "Data presented in this paper also lends support to the widespread clinical practice of oral cephalosporin use in patients who have positive PenST responses".

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported.

Direct costs
Costs were not discounted despite having been incurred over a 2-year period of time. Quantities were reported separately from the costs. Cost items were reported separately. The cost analysis covered the costs of acquisition and
pharmacy dispensing of antibiotics. The perspective adopted in the cost analysis was that of the health plan. The source of the resource use data was the medical records. The source of (average) cost data was the health plan providing the antibiotics. The date of the price data was 1995.

**Statistical analysis of costs**

Costs before and after PenSTs were compared using the paired t test. Cost between patients with positive and negative PenST responses (having non-normal distribution) was compared using the Wilcoxon test.

**Indirect Costs**

Not considered.

**Currency**

US dollars ($).

**Sensitivity analysis**

Not conducted.

**Estimated benefits used in the economic analysis**

Not applicable.

**Cost results**

A total cost of $17,211.88 was observed for the year before PenST versus $11,648.27 in the year after PenST for 236 patients.

The corresponding average costs were $72.93 (95% CI: $57.41-$88.45) for the year before PenST versus $49.36 (95% CI: $38.93-$59.79) for the year after PenST (p=0.0015).

The corresponding average values for the patients with positive PenST responses were $81.58 (95% CI: $67.99-$95.17) for the year before PenST and $48.03 (95% CI: $37.20-$58.86) for the year after PenST (p=0.03).

The corresponding values for the patients with negative PenST responses were $71.17 (95% CI: $53.59-$88.84) for the year before PenST and $49.63 (95% CI: $38.04-$61.22) for the year after PenST (p=0.01).

**Synthesis of costs and benefits**

Not combined.

**Authors' conclusions**

The author concluded that elective penicillin skin testing done by an allergist was associated with unexpected declines in the number and cost of antibiotics used the year after testing, but only modestly lowered the average cost per antibiotic. Adverse reactions to penicillin in subjects with negative skin test responses were infrequent, and amoxicillin challenge did not affect outcomes.

**CRD COMMENTARY - Selection of comparators**

The reason for the choice of the comparator (no PenST) is clear. You, as a database user, should consider whether this applies to your own setting.
Validity of estimate of measure of benefit
The internal validity of the effectiveness results cannot be guaranteed due to the retrospective observational study design. The study was a cost-consequences analysis.

Validity of estimate of costs
Quantities were reported separately from the costs. Some details of methods of cost estimation were given. The author adopted a health plan perspective, therefore, patients costs were not included in the analysis. Cost results may not be generalisable to other settings or countries.

Other issues
The issue of generalisability to other settings or countries was not addressed. Appropriate comparisons were made with other studies.

Implications of the study
"A randomized trial is planned to help answer (some of unanswered) questions."

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