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
A computer-assisted antibiotic-dose monitor to check the renal function of every patient each day and to identify patients who may be receiving excessive dosages of antibiotics. Each morning during the 12-month intervention period, the antibiotic-dose monitor checked the renal function of all patients who were receiving any of five targeted antibiotics (vancomycin, gentamicin, imipenem, cefazolin, and cefuroxime). Pharmacists received a computer listing of patients who may have been receiving excessive dosages. The antibiotic-dose monitor suggested an alternate dosage and a pharmacist contacted the patient's physician if the suggested change in the dosage was appropriate. The renal function was determined using the Cockcroft-Gault equation to estimate the creatinine clearance based on the patient's serum creatinine, ideal body weight, gender, age, height, and weight. The computer program calculated an optimal 24-hour dosage for the prescribed antibiotic, adjusted by the patient's estimated renal function and based on the adult guidelines from the American College of Physicians.

Type of intervention
Treatment and secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study included patients aged 18 years or older, who were admitted to the study hospital, had received at least one of five targeted antibiotics, had a serum creatinine or a urine creatinine clearance test result before antibiotic therapy, and were never admitted or transferred to the shock/trauma/respiratory intensive care unit.

Setting
Hospital (tertiary care centre). The economic analysis was carried out in Utah, USA.

Dates to which data relate
Effectiveness and resource use data corresponded to the two-year pre-intervention period (April 1993 to March 1995) and the one-year intervention period (April 1995 to March 1996). The price year was 1995-96.

Source of effectiveness data
The evidence for the final outcomes was based on a single study.

Link between effectiveness and cost data
Costing appears to have been performed retrospectively 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 consisted of 4,483 patients with a mean age of 60 years who received one or more of the study antibiotics during the one-year intervention period, compared with 8,901 with a mean age of 60 years during the two-year pre-intervention period.

Study design
This was a non-randomised study with historical controls, carried out in a single centre. The duration of the follow-up appears to have been until discharge from hospital. No information was provided regarding the loss to follow-up. The study antibiotics were selected because they were identified as five of the leading antibiotics causing adverse drug events (ADEs) at the study hospital and because the dosage of these agents should be modified according the patient's renal function.

Analysis of effectiveness
The principle (intention to treat or treatment completers only) used in the analysis of effectiveness was not explicitly specified. The clinical outcome measures were the proportion of patients receiving an excessive dosage, the number of days that patients received excessive dosages of antibiotics, the number of ADEs secondary to antibiotics, and significant changes in renal function. Length of hospitalisation and mortality were used to assess whether patient care was compromised due to lower antibiotic dosages. The outcome measures were compared between the two study groups adjusting for age, gender, diagnosis-related groups, medical service, nursing acuity, and mortality by using a linear regression analysis. The comparability of the study groups in terms of baseline characteristics was not addressed.

Effectiveness results
The effectiveness results were as follows:

During the intervention period, 44% (1,974 patients) were identified as receiving an excessive antibiotic dosage on at least one day versus 50% during the pre-intervention period, (p<0.001).

During the intervention period, the patients received excessive dosages for an average of 2.9 days, compared with 4.7 days, (p<0.001) during the pre-intervention period.

There were 14 ADEs (0.3%) secondary to the five study antibiotics during the intervention period, compared with 82 (0.9%) for the two-year pre-intervention period, (p<0.001).

The overall renal function changes for patients from both time periods were similar.

It was found that significantly more patients identified as receiving excessive dosages had experienced decreases in renal function, compared with patients who were not identified as receiving excessive dosages (25% versus 12% during pre-intervention period and 23% versus 16% during intervention period; p<0.001).

The average length of hospital stay was decreased from 7.0 +/- 8.6 days in the pre-intervention period to 6.6 +/- 7.4 in the intervention period.

The decrease in mortality rate was from 2.9% in the pre-intervention period to 2.3% in the intervention period.

Clinical conclusions
There was a significant decrease in the rate of ADEs secondary to the five antibiotics during the intervention period. This further supports the concept that many ADEs are caused by excessive dosages and are preventable. The fact that during the intervention period significantly fewer patients received excessive antibiotics dosages compared with the pre-intervention period suggests an educational effect provided by the pharmacists following up on the drug-dosage monitor.
Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only individual clinical outcomes were reported.

Direct costs
Costs were not discounted due to the short time frame of the cost analysis. Some quantities (antibiotic doses, grams, and defined daily doses (DDDs)/1000 patient days) were reported separately from the costs. The cost analysis covered the costs of antibiotic therapy. The perspective adopted in the cost analysis was not explicitly specified. The acquisition costs of the antibiotics during the pre-intervention period were adjusted to equal those during the intervention period. The price year was 1995-96. The cost analysis did not cover the cost of one to one-and-a-half hours of pharmacists' time needed to follow up on an average of seven alerts per day.

Statistical analysis of costs
A linear regression analysis was used to compare the groups in terms of acquisition costs, and antibiotic-related quantities, controlling for age, gender, diagnosis-related groups, medical service, nursing acuity, and mortality.

Indirect Costs
Indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
Not applicable.

Cost results
The mean (SD) antibiotic cost was $92.96 (185) in the pre-intervention period versus $80.62 (149) in the intervention period, (p<0.003). The corresponding values for the patients who received excessive antibiotic therapy were $128.11 (238) in the pre-intervention period and $98.06 (176) in the intervention period, (p<0.004).

Synthesis of costs and benefits
Costs and benefits were not combined since the intervention was the dominant strategy.

Authors' conclusions
Many patients’ experience decreases in renal function after antibiotics are ordered. The use of the computer-assisted antibiotic-dose monitor appears to be a promising method to help reduce the excessive use and cost of antibiotic therapy and reduce the number of ADEs secondary to antibiotics.

CRD COMMENTARY - Selection of comparators
The strategy of not using the computer-assisted antibiotic-dose monitor was explicitly regarded as the comparator. This allowed the active value of the intervention to be evaluated.
Validity of estimate of measure of effectiveness
The internal validity of the effectiveness results cannot be reasonably assured due to the non-randomised nature of the study design, the use of historical controls, and the fact that no power calculations were performed to justify the sample size. Furthermore, comparability of the study groups was not addressed and the principle used in the effectiveness analysis was not specified. However, adjustments were made for some of the known confounding variables, and the study sample appears to have been representative of the study population.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The analysis was therefore one of cost-consequences design.

Validity of estimate of costs
Positive aspects of the cost analysis, which enhanced its validity, were as follows: the price year was given and adjustment was made for the acquisition costs; statistical analysis was performed on antibiotic-related resource use and cost data. However, the following limitations of the cost analysis apply: the perspective adopted in the cost analysis was not specified; unit costs were not reported; costing was conducted retrospectively; the cost analysis was not comprehensive as some of the important cost components (such as the pharmacists' time, as mentioned by the authors, and costs of antibiotic-related adverse events) were omitted from the cost calculations; the effects of the alternative modalities on indirect costs (productivity loss) were not addressed. In consequence, the cost results may not be generalisable outside the study setting.

Other issues
Given the limitations of the study design, lack of sensitivity analysis, and lack of comprehensive cost analysis, the study results may need to be treated with some degree of caution. The issue of generalisability to other settings was addressed by noting that the computer program was limited in its ability to identify excessive antibiotic dosages for patients who have creatinine or creatinine clearance test results and who are aged 18 years or over. The issue of generalisability to other countries was not addressed, although appropriate comparisons were made with other studies. The issue of the degree to which the study sample was representative of the study population was not addressed in the authors' comments.

Implications of the study
Continuous quality improvement is a constant search for small opportunities to improve patient care. With this concept in mind, the antibiotic-dose monitor was updated to monitor all formulary antibiotics that should be adjusted by renal function; it is now operational at eight other hospitals owned by Intermountain Health Care.

The authors note that the computer logic of the program will need to be expanded and tested before it can be used for neonatal and paediatric patients.

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