Cost-benefit analysis and prediction of 24-hour proteinuria from the spot urine protein-creatinine ratio


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 measurement of proteinuria using the urine protein-creatinine (Up/Uc) ratio from a spot urine sample was compared with urine protein measured in a sample collected over 24 hours.

Type of intervention
Screening.

Economic study type
Cost-benefit analysis.

Study population
The study population comprised patients with glomerular diseases of different aetiology attending an outpatients department. Patients were eligible for inclusion in the trial if they had a daily proteinuria of more than 200 mg per 1.73 m2 body surface area (BSA). Patients were excluded from the study if they had a urinary tract infection or tubular proteinuria (multiple myeloma, polyclonal gammapathy), or if they were unable to collect their urine correctly. The authors stated that they sought to examine the equivalence of the two tests over a wide range of proteinuria values.

Setting
The setting was secondary care. Although not directly stated, the economic study appears to have been carried out at Christchurch Hospital in Canterbury, New Zealand.

Dates to which data relate
The dates during which the effectiveness and resource use data were collected were not given. The price year was also not stated. The paper was submitted for publication in 2000.

Source of effectiveness data
The evidence for the final outcomes was derived from a single study.

Link between effectiveness and cost data
The costing was not undertaken on the patient sample. Instead, the costing was based on disease-related group (DRG) scoring and relative value scale-based payment.

Study sample
No power calculation was reported. The unselected sample was formed from 200 consecutive, eligible patients who consented to participate in the study. The authors did not justify the choice of the patient sample, nor did they report
whether any patients refused to participate in the study. Of the 200 patients selected, 5% were excluded from the study because they had a urinary tract infection or tubular proteinuria. A further 10% were excluded because they made repeated errors in the collection of their urine. From the 170 patients included in the study, a sub-group of 50 was chosen randomly to provide a further series of specimens on the third day of the study. The method by which this sub-group was selected was not described. Urine samples were rejected if the total daily creatinine excreted was less than 20 mg/kg in men and less than 15 mg/kg in women, and the participants were then required to repeat the urine collection on a subsequent day.

**Study design**
This was a cross-sectional study undertaken at an unspecified number of sites. As the urine tests were performed concurrently, there was no possibility that the test order could bias the results. Blinding was not relevant. All 170 patients included in the final analysis gave two spot urine samples and a 24-hour urine collection. Both tests were performed on the same day. There was no follow-up of the participants beyond specimen collection.

**Analysis of effectiveness**
The comparison of the tests was based on two evaluations. First, the correlation \( r \) between the Up/Uc ratios and the 24-hour proteinuria was examined. Second, the level of agreement between the actual 24-hour proteinuria and Up/Uc ratios and the predicted 24-hour proteinuria from the Up/Uc ratios were analysed using a concordance correlation coefficient and the limits of agreement on a Bland-Altman plot (see Other Publications of Related Interest).

**Effectiveness results**
The correlation between the Up/Uc ratios from the spot urine tests and the 24-hour proteinuria was \( r=0.97 \) for the first test, and \( r=0.99 \) for the second test and for the average of the two tests. However, the 95% confidence intervals were wide at the extreme levels of proteinuria. Using two spot readings did not improve the precision of prediction. Concordance coefficients were 0.98 and 0.97 for Up/Uc1 and Up/Uc2 respectively.

**Clinical conclusions**
Irrespective of the level of renal function, a good correlation and precision of agreement were shown between the 24-hour proteinuria and the Up/Uc ratios from the spot urine tests across the whole range of proteinuria, but wide confidence intervals were observed at extreme levels. Using a second spot urine sample did not improve the predictive power.

**Modelling**
A decision analysis model was used to calculate the costs of the medical consequences associated with every diagnostic outcome.

**Measure of benefits used in the economic analysis**
The authors said that a cost-benefit analysis was undertaken. It appears that a human capital method was utilised as there was no valuation of the health states that resulted from each test outcome, but productivity costs were included. See the 'Direct Costs' and 'Indirect Costs' sections (below).

**Direct costs**
The net costs of each test outcome were derived using a decision analysis model that incorporated the following direct costs:

- overheads (presumably the cost of providing the test and the outpatient service),
- repeated admissions,
costs due to complications,
relocation,
transport, and
personal costs, which were presumably borne by the patient.

The expected net costs were determined by multiplying the probabilities of the complications, biopsies and end-stage renal disease occurring with the associated costs and summing. The costs and resource use were not reported separately. Resource use was estimated by DRG and relative value scale-based payment. The cost data were derived from actual data supplied by agencies within the national public health service. Discounting of the costs was relevant and a rate of 5% was applied. The date to which the price data related was not reported.

**Statistical analysis of costs**
No statistical analysis of the costs was reported.

**Indirect Costs**
Lost productivity costs were included in the analysis as a societal perspective was taken. These were discounted at a rate of 5%. The source of the data was not clearly reported, but it was inferred that the data were derived from actual data supplied by agencies within the national public health service. The date to which the price data related was not reported.

**Currency**
New Zealand dollars (NZ$).

**Sensitivity analysis**
No sensitivity analysis was reported.

**Estimated benefits used in the economic analysis**
No health outcomes were valued in this paper.

**Cost results**
The total average costs per patient for each of the four diagnostic outcomes were not reported. The average costs of some of the major health events were reported in a model.

**Synthesis of costs and benefits**
The optimum threshold for abnormal and nephrotic proteinuria was determined by identifying the optimum operating characteristic (ROC) curve. This was the point where the curve intersected a line with a slope incorporating disease prevalence (0.35) and the cost outcomes of diagnostic decisions. By this method it was established that the best thresholds (cut-off points) for detecting normal and nephrotic proteinuria (where average costs were minimised and average benefits maximised) occurred at Up/Uc ratios of 0.26 (normal) and 3.20 (nephritic), respectively.

**Authors’ conclusions**
A good correlation and precision of agreement were shown between the proteinuria from a 24-hour urine collection and the urine protein-creatinine (Up/Uc) ratios from the spot urine tests, across the whole range of proteinuria. The ‘cut-off’ value of 0.26 of Up/Uc1 for 24-hour proteinuria less than 0.25 g/1.73 m2 body surface area (BSA) per day
differentiates normal versus abnormal proteinuria with a sensitivity of 96% and specificity of 89%. Similarly, a Up/Uc ratio of 3.70 was the optimal threshold for differentiating nephrotic from non-nephrotic range proteinuria for 24-hour proteinuria greater than 3.5 g/1.73 m² BSA per day.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used. The 24-hour urine collection is more inconvenient and more unreliable (because of collection errors) than the urine spot test. You should decide if this represents a valid comparator for proteinuria testing in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a cross-sectional design, which was appropriate given the study question. The study sample was representative of the study population. All of the patients provided specimens for both tests. Both tests were performed on the same day, thus eliminating the possibility of bias due to the order of the tests. No power calculations were reported. Hence, it is not possible to ascertain whether the results obtained were due to chance.

Validity of estimate of measure of benefit
No summary measure of benefit was derived. A cost-benefit analysis was undertaken and the reader is therefore referred to the cost results and associated commentary.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included in the analysis. The cost information was not provided in detail, so it was unclear whether some relevant costs might have been omitted from the analysis. The cost of performing the 24-hour urine collection and the spot urine test were not considered, as the authors did not intend to compare the costs of the two methods. The costs and resource use were not reported separately. Resource use was gauged by DRG and relative value scale-based payment. A sensitivity analysis of the quantities was not conducted, which may limit the interpretation of the study findings. A statistical analysis of the prices was not performed. Discounting was undertaken appropriately. The price year was not reported.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. They noted that the generalisability of their findings on the optimum thresholds for abnormal and nephrotic range proteinuria was limited since the cost analysis incorporated New Zealand values. The authors did not present their results selectively. The study sought to examine the equivalence of the two tests over a wide range of proteinuria values and this was reflected in the authors' conclusions.

Implications of the study
The authors concluded that spot urine tests and 24-hour urine collections can be used interchangeably. The best thresholds for detecting normal and nephrotic proteinuria (given New Zealand prevalence and cost conditions) occur at Up/Uc ratios of 0.26 (normal) and 3.20 (nephrotic), respectively.

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Other publications of related interest

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