Nitrofurantoin compares favorably to recommended agents as empirical treatment of uncomplicated urinary tract infections in a decision and cost analysis

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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.

CRD summary
This study examined the clinical and economic impact of nitrofurantoin as first-line treatment for uncomplicated urinary tract infections, compared with other antibiotics and considering antibiotic resistance. The authors concluded that nitrofurantoin appeared to be a reasonable alternative to trimethoprim-sulphamethoxazole or fluoroquinolones, given the rates of antibiotic resistance among uropathogens in the USA at the time. The analysis used a cost-minimisation approach, despite differences in treatment efficacy. Within the limitations of this approach, the authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the clinical and economic impact of nitrofurantoin as first-line treatment for uncomplicated urinary tract infections (UTIs) compared with other antibiotics and considering antibiotic resistance.

Interventions
The three treatments were a three-day course of generic trimethoprim-sulphamethoxazole, a three-day course of generic fluoroquinolone (ciprofloxacin), and a five-day course of generic nitrofurantoin macro-crystals.

Location/setting
USA/out-patient.

Methods

Analytical approach:
The analysis used a cost-minimisation framework, based on a decision-tree model that was identified by a literature review of published models. A short time horizon was considered. The authors stated that the perspective of the health service payer was adopted.

Effectiveness data:
The clinical data were identified by a systematic review of articles in MEDLINE, EMBASE, and the Cochrane Library. Where data were available from multiple sources, the mean value was selected. The key endpoint was the cure rate for the UTIs.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The rates of cured infection were the key outcome of the treatments.

Cost data:
The economic analysis included the costs of the drugs, hospitalisations, physician visits, out-patient treatment for pyelonephritis, urinalysis and urine culture, and self-treatment of vaginal yeast infection. These costs were based on a systematic review of the literature and a survey of costs from national and local sources. The antibiotic costs were their
average wholesale prices from the 2010 Red Book. Other costs were from published studies, Medicare, commercial laboratories, and national pharmacies, and fees from the American Hospital Association. All costs were in US dollars ($).

Analysis of uncertainty:
One-and two-way sensitivity analyses were carried out on the model inputs. The ranges were mainly from published sources; otherwise, a range from half to double the base-case estimate was used. A threshold approach was used to identify those changes that would affect the cost-minimisation decision.

Results
The rate of clinical cure was 0.55 with trimethoprim-sulphamethoxazole resistant infection treated with trimethoprim-sulphamethoxazole, 0.91 with trimethoprim-sulphamethoxazole sensitive infection treated with trimethoprim-sulphamethoxazole; 0.78 with fluoroquinolone-resistant infection treated with fluoroquinolone, 0.94 with fluoroquinolone-sensitive infection treated with fluoroquinolone, 0.67 with nitrofurantoin-resistant infection treated with nitrofurantoin, and 0.89 with nitrofurantoin-sensitive infection treated with nitrofurantoin.

Nitrofurantoin was cost-minimising when the rate of fluoroquinolone resistance exceeded 12%. At this rate, the mean total cost of empirical treatment with either drug was $159. When the resistance rate was below 12% fluoroquinolone was preferred.

Nitrofurantoin was cheaper than trimethoprim-sulphamethoxazole at a trimethoprim-sulphamethoxazole resistance rate above 17%, otherwise the latter was preferred.

Fluoroquinolone was preferred over trimethoprim-sulphamethoxazole when the rate of trimethoprim-sulphamethoxazole resistance was above 10%.

Comparing all three treatments, nitrofurantoin was cost-minimising when trimethoprim-sulphamethoxazole resistance exceeded 17% and fluoroquinolone resistance exceeded 12%. With lower rates of trimethoprim-sulphamethoxazole and fluoroquinolone resistance, trimethoprim-sulphamethoxazole or a fluoroquinolone was the cheapest drug, depending on prevalence of resistance to these two antibiotics.

The sensitivity analyses showed that the costs of the antibiotics were key drivers of the model, as expected.

Authors’ conclusions
The authors concluded that nitrofurantoin appeared to be a reasonable alternative to trimethoprim-sulphamethoxazole or fluoroquinolones for treating uncomplicated UTIs, given the rates of antibiotic resistance among uropathogens in the USA at the time.

CRD commentary
Interventions:
The authors justified their selection of the comparators. Trimethoprim-sulphamethoxazole was the preferred antibiotic, given its efficacy and low cost, but increasing resistance had discouraged its use. Fluoroquinolone was an alternative treatment, but was not recommended for uncomplicated UTIs to avoid the development of uropathogen resistance. Nitrofurantoin had been used as an alternative treatment, without developing high resistance.

Effectiveness/benefits:
A systematic review was performed to identify the inputs for the cost-minimisation analysis, but the methods and other details of the studies used were not reported. The mean values were not weighted by features, such as sample size, and the authors did not discuss the homogeneity of the studies. These issues should be considered when assessing the validity of the clinical data.

Costs:
The cost categories appear to have reflected the stated perspective of the third-party payer. It appears that all the relevant cost items were included and only rare events were not considered. Some unit costs together with ranges found
in the literature were reported, while fewer resource use data were provided. The authors did not describe in detail the sources for the cost data, but it appears that standard US sources were generally used. The cost data were varied in the sensitivity analysis and this showed the impact of the drug costs. The price year was not explicitly reported, but might have been 2010.

Analysis and results:
The results were selectively reported, without the total costs and giving only the findings of the threshold analyses. The uncertainty was investigated in a deterministic analysis and the results were selectively presented. The authors stated that a limitation of their analysis was the high variability in values found in the literature and the lack of some data for the model. It was stated that this was the first model comparing the three antibiotics for UTIs. The findings appear to be specific to the authors’ context and cannot be generalised to other settings.

Concluding remarks:
The analysis used a cost-minimisation approach, despite differences in treatment efficacy. Within the limitations of this approach, the authors’ conclusions appear to be valid.

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