Early switch from intravenous to oral antibiotics: guidelines and implementation in a large teaching hospital

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
Short intravenous antibiotic therapy followed by oral antibiotic treatment as an alternative to intravenous administration for the entire treatment course for patients suffering from serious infections. This switch strategy (also known as sequential antibiotic therapy) was based on published guidelines and determined by members of the study group. IV-oral switch occurred after at least 48-72 hours of iv therapy.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population was based on patients suffering from serious infections that required the administration of antibiotics. Details of the criteria for suitability for iv-oral switch are specified in the paper.

Setting
The economic study was conducted in a large teaching hospital in Amsterdam, the Netherlands.

Dates to which data relate
Clinical effectiveness data were based on studies published between 1989 and 1997. The effectiveness of the iv-oral switch guidelines was based on a single study conducted between 1996 and 1997. The price year was 1990.

Source of effectiveness data
The impact of the introduction of guidelines for the identification of patients that were candidates for an early iv-oral switch was analysed in a single study. The authors also made an assumption of equivalent clinical effectiveness for the intervention and comparator (based on published findings).

Link between effectiveness and cost data
The costing was undertaken prospectively on the same sample as that used in the effectiveness (in terms of switching between intravenous and oral antibiotics) analysis.

Study sample
The study sample was based on patients hospitalised in Internal Medicine, Surgery or Pulmonology wards, two months
before (inventorial phase) and 2 months after (implementation phase) the introduction of the clinical guidelines. These wards were selected because of their high antibiotic use. During the inventorial phase, 271 patients were followed up (control group), while during the implementation phase 234 patients were followed up. No power calculations were reported.

Study design
This was a non-randomised study with historical controls carried out at a single centre. The study might also be categorised as a before-after study (before and after the implementation of the clinical guidelines), but the group of patients followed before and after this implementation was not the same. The patients were selected on the basis of their hospitalisations in wards with high antibiotic use. All patients hospitalised in these wards were included in the analysis and as such no patients were lost to follow-up.

Analysis of effectiveness
The analysis was based on treatment completers only. In this study no clinical trial was performed to assess the clinical effectiveness of intravenous followed by oral antibiotics, but the question of whether the implementation of clinical guidelines for the iv-oral switch was likely to increase the percentage of candidates for an oral switch who actually switched was investigated.

Effectiveness results
In the inventorial phase an iv-oral switch would have been justifiable in 97/230 (42%) of courses where antibiotics were started intravenously. 52 (54%) of the 97 patients who met the criteria switched to the oral therapy. The median day on which the switch was made was day 6 (range: 2 - 28).

In the implementation phase, 80/182 (44%) patients met the criteria for the switch and 66/80 (83%) were actually switched (difference from baseline phase = 29%; 95% CI: 16 - 42%; p < 0.001). The median time to switch was 4 days (range: 2 - 16).

7 of the 66 patients who were switched during the implementation phase were readmitted to the hospital within 6 weeks after termination of the antibiotic course. However, readmittance was for non-infectious disorders. The intervention was not associated with an increase in readmittance due to infectious disorders.

Clinical conclusions
A substantially greater number of patients were candidates for early iv-oral switch using the guidelines and this occurred earlier.

Methods used to derive estimates of effectiveness
This study had, in effect, two parallel outcomes of interest. The principal area of concern related to the effectiveness of achieving a switch from intravenous to oral antibiotics, as reported above. However, in terms of the clinical outcomes associated with each strategy, the authors made assumptions based on the literature.

Estimates of effectiveness and key assumptions
All clinical trials found in the literature by the authors reported equal efficiency for the two treatment strategies.

Measure of benefits used in the economic analysis
The findings supported the view that the clinical effectiveness of the two alternatives was equal. Therefore the principal benefit was expressed in monetary terms (cost-minimisation analysis) The monetary benefits of the implementation of clinical guidelines for an early iv-oral switch were calculated taking into account the following factors:
the percentage of patients who met the criteria for the switch who actually switched before and after the introduction of the guidelines; and

the median time the switch was made.

The savings arising from the introduction of clinical guidelines were then calculated.

**Direct costs**
The only direct costs included in the analysis were the preparation, administration and purchase costs per iv and oral dose of antibiotics. Quantity and costs were reported separately. No discount rate was applied since the period of follow-up was only 4 months. The costs were calculated on the basis of the hospital data. The price year was 1990.

**Statistical analysis of costs**
No statistical analysis of costs was performed.

**Indirect Costs**
No indirect costs were included in the analysis.

**Currency**
Dutch guilder (Dfl) converted to US dollars ($).

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

**Estimated benefits used in the economic analysis**
See effectiveness results above.

**Cost results**
The preparation and administration costs for an iv dose of antibiotics was conservatively estimated at Dfl 10 ($5). The costs for administering one oral dose were negligible. In the patients meeting the criteria for iv-oral switch, the total number of iv administrations during the inventorial phase (97 courses) was 2,620, compared with 1,240 during the implementation phase (80 courses). The purchase costs of all antibiotics used were Dfl 18,442 in the inventorial phase and Dfl 7,156 in the implementation phase.

**Synthesis of costs and benefits**
Taking an average of 90 courses amenable for an early switch in 2 months, the potential number of iv administration that could have been avoided was (90/97 x 2620)-(90/80 x 1240) = 1036, in 2 months or over 6000 in a year, leading to potential savings in administration costs of 6000 x fl 10 = Dfl 60,000 (US$30,000) per year. Again, taking an average of 90 courses per 2 months the potential savings in purchase costs were equal to Dfl 9,059 (90/97 x 18442 90/80 x 7156) in 2 months or Dfl 54,000 (US$27,000) per year.

**Authors' conclusions**
The authors believe that the literature provides sufficient evidence, in terms of clinical effectiveness, for an iv-oral switch if the condition of the patients has improved after a few days. Given the evidence of this analysis they stated that the implementation of clinical guidelines for an iv-oral switch is likely to lead to monetary savings. Electronic drug-ordering systems, which can provide computer-assisted decision support, might be an additional aid in streamlining the
use of antibiotics.

**CRD COMMENTARY - Selection of comparators**
The comparator was clearly identified and justified (pre-guidelines), which allowed the monetary benefits of the intervention (guidelines) to be assess

**Validity of estimate of measure of benefit**
The study design, whilst being appropriate for the study question, may have been hampered by the use of historical controls and a lack of randomisation. The validity of the effectiveness (benefit) measure could have been improved by a prospective, randomised approach which would have eliminated some of the problems inherent in the before-after design adopted (different patient cohorts, selection bias and the possible presence of confounding variables). The assumption of equivalent clinical effectiveness appears to be justified based on what was reported in the literature, although it is difficult to judge if a systematic review was undertaken and if all relevant studies had this particular finding. The authors strongly suggest that this is, however, the dominant finding of similar studies.

**Validity of estimate of costs**
The economic analysis was clearly presented and explained. Some categories of costs, however, have not been considered in the analysis. Additional savings, for example, might have been achieved by the earlier discharge of patients in the case of oral treatment. On the other hand, the costs of the study doctor, or of other means to ensure the implementation of the guidelines, were not included in the analysis. Sensitivity analyses taking account of these missing data would have been helpful in increasing the robustness and generalisability of the cost results.

**Other issues**
The main issue raised from this study is related to the generalisability of the results. The authors referred to other studies to compare their results, and found similar outcomes; but the use of sensitivity analyses would have been helpful in this respect. Moreover, in this specific case a study doctor implemented the clinical guidelines whereas, in other circumstances, hospital pharmacists or specially trained nurses might be involved in this intervention programme, leading to additional costs.

**Implications of the study**
The implementation of clinical guidelines for an early iv-oral antibiotic switch should be encouraged as it should offer economic benefits without adversely affecting clinical effectiveness.

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