Initiating insulin treatment in insulin-requiring type 2 diabetic patients: comparative efficiency and cost of outpatient and inpatient management

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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.

Health technology
Outpatient approach to initiating insulin therapy in insulin-requiring Type 2 diabetic patients.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Type 2 diabetic patients aged 40 to 70 years, with a body mass index of less than 30 kg/m^2 and a persisting fasting blood glucose level above 1.8 g/l (9.9 mmol/l). Patients excluded from the study were pregnant women and patients with severe neuropathy, blindness or a history of ketoacidosis.

Setting
Hospital and community. The economic analysis was carried out in France.

Dates to which data relate
Effectiveness and resource use data corresponded to patients admitted to the study institution between August 1993 and March 1994. The price year appears not to have been reported.

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

Link between effectiveness and cost data
Costing was prospectively conducted 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 114 patients who were randomly assigned to start insulin therapy on an inpatient or outpatient group basis. A total of 104 patients were included in the final analysis, 54 in the inpatient group with a mean (SD) age of 58 (1) years and 50 in the outpatient group with a mean (SD) age of 57.8 (1.1) years.

Study design
This was an open, pragmatic, randomised study of two parallel groups recruited from 19 French hospitals. The duration of the follow-up was 3 months after the initiation of the insulin therapy. Regarding loss to follow-up rate, it was reported that 10 patients initially recruited were not evaluated since 3 failed to satisfy the inclusion criteria, 4 did not start treatment, 2 were lost to follow-up and 1 discontinued the treatment because of suspected allergy to insulin. A centralised randomisation protocol was used to assign patients to the study groups. Visits were scheduled for both groups after one month, two months and three months of treatment. All patients had been treated for at least one month prior to the study with an adapted diet, maximum doses of sulphonylurea (3 tablets/day) and metformine in 80% of cases.

**Analysis of effectiveness**

The principle used in the analysis of effectiveness appears to have been treatment complaters only. The primary health outcome measure was glycemic control (HbA1c measurement) of diabetes after three months of treatment. All adverse events and acute complications were recorded, particularly all episodes of hypoglycaemia or hyperglycaemia with ketonuria. The covariance analysis using Schuirmann’s method was used to adjust for the effects of difference in HbA1c levels at the study inclusion. A subgroup analysis was performed based on the number of patients who achieved at least a 15% reduction of their HbA1c 3 months after starting insulin. The study groups were comparable in terms of baseline demographic and clinical characteristics (except for the fact that HbA1c levels were significantly different between the two study groups; 10.17 (SD, 0.19%) in the inpatient group versus 10.87 (0.22%) in the outpatient group, (p=0.019) despite a correct randomisation procedure).

**Effectiveness results**

The effectiveness results were as follows:

After three months, the mean (SD) HbA1c level was 8.80 (0.16%) for the inpatient group and 9.56 (0.20%) for the outpatient group.

Covariance analysis showed equivalent glycemic control at 3 months in both groups (adjusted means (SD) with respect to the inclusion values: 9.00 (1.14%) %) for the inpatient group versus 9.37 (1.14%) for the outpatient group; equivalence hypothesis: p=0.01).

A low and similar incidence of episodes of hypoglycaemia or hyperglycaemia with ketonuria was observed (67.9% for the inpatient group versus 57.4% for the outpatient group (p=0.2) for proportion of patients with one or more episodes of hypoglycaemia and 0% for the inpatient group versus 3.7% for the outpatient group (p=0.24) for hyperglycaemia with ketonuria).

Average weight gain was similar in both groups (2.8 kg).

Adverse events, probably or possibly attributable to the treatment, were essentially local reactions at the injection site, which were evenly distributed between both groups.

Analysis of the number of patients who reached at least a 15% reduction of their HbA1c 3 months after starting insulin showed no difference between the groups (21 in each study group), and the number of hypoglycaemic episodes was comparable in these subgroups.

**Clinical conclusions**

The results concerning effectiveness, safety and general patient satisfaction with the outpatient strategy provide strong arguments in favour of the widespread adoption of this method of initiation of insulin therapy in insulin-requiring Type 2 diabetes. Patients who started insulin treatment on an outpatient basis achieved as good a reduction in HbA1c levels as those who were hospitalised as inpatients with comparable safety profiles. However, metabolic results as a whole were quite disappointing, which may be attributable in part to the fact that over 90% of Type 2 diabetic patients in France are followed only by their general practitioner, reference to diabetologist being delayed as long as possible.
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. As the health outcomes were comparable, it appears that the economic study was conducted as a cost-minimisation analysis.

Direct costs
Costs were not discounted due to the short time frame of the cost analysis. Some quantities were reported separately from the costs. Some cost items were reported separately. Cost analysis covered the direct costs of initial hospital stay, additional clinical tests, and paramedical care. The perspective adopted in the cost analysis appears not to have been reported. The price year appears not to have been specified. The cost analysis did not cover the costs of treating associated diseases since the treatment period was not defined.

Statistical analysis of costs
It was reported that Student’s t test or Wilcoxon’s rank sum t-test was used to compare the study groups in terms of quantitative variables (and presumably costs).

Indirect Costs
The total number of lost workdays was reported, but valued in monetary terms. Excluded from these figures were the days of initial hospitalisation and the time taken off work for the monthly visits.

Currency
French francs (Ffr). The conversion rate was US$1 = Ffr6.

Sensitivity analysis
No sensitivity analysis was conducted.

Estimated benefits used in the economic analysis
Not applicable.

Cost results
The mean total cost per patient was Ffr 15,231 in the inpatient group versus Ffr 3,296 in the outpatient group.

Synthesis of costs and benefits
Costs and benefits were not combined since the economic study was carried out as a cost-minimisation analysis.

Authors’ conclusions
Insulin-requiring Type 2 diabetic patients can be effectively and safely started on insulin as outpatients, and this approach to initiating insulin therapy is cost-effective.

CRD COMMENTARY - Selection of comparators
A justification was given for the choice of the comparator (the inpatient strategy). It was the traditional practice in France at the time of the study. You, as a database user, should consider which health technology is used widely in your own setting.
Validity of estimate of measure of effectiveness
The internal validity of the effectiveness results is likely to be high due to the randomised nature of the study design. However, it may have been weakened by the fact that no power calculations were performed and that the effectiveness analysis was performed on the basis of treatment completers only. The study groups were comparable in terms of baseline demographic and clinical characteristic, except for HbA1c levels. This despite a correct randomisation procedure; a covariance analysis was performed to adjust for this difference between the two study groups. The study sample appears to have been representative of the study population (a population of middle-aged Type 2 diabetes patients).

Validity of estimate of measure of benefit
The analysis of benefits appears to have been based on the therapeutic equivalence of treatment alternatives. The economic analysis therefore included only costs.

Validity of estimate of costs
The validity of the cost results may have been enhanced by the following positive features of the cost analysis: some quantities were reported separately from the costs; the effect of alternative procedures on time off work was addressed (although it was not evaluated in monetary values); and statistical analyses were performed on some resource consumption and cost data. However, the validity of the cost results may have been adversely affected by the following characteristics: adequate details of methods of cost estimation were not given; the price year was not specified and it is not clear whether the cost data were adjusted for inflation; it is not clear whether charge data were used or actual costs; the cost results may not be generalisable outside the study setting.

Other issues
The authors' conclusions appear to be justified given the uncertainties in the data. The issue of generalisability to other settings or countries was not addressed. Some comparisons were made with other studies. The question of whether the study sample was representative of the study population was addressed in the authors' general comments; it was reported that the patients recruited to the study were familiar with diabetes, had been diagnosed as Type 2 diabetic patients for an average of 13 years, and had been treated with diet and oral hypoglycaemic agents for approximately 12 years on average. Furthermore, the fact that randomisation was well-accepted by patients was indicative of their general willingness to participate.

Implications of the study
The extension of outpatient management and, consequently, the avoidance of hospitalisation, could allow insulin therapy to be initiated earlier in the course of diabetic disease, when insulin-resistance is less severe. Indeed, the common French national policy of starting insulin treatment only on an inpatient basis presents several medical, psychological and economic disadvantages. The message of this study is of particular importance for southern European and Latin countries.

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