Using a genetic, observational study as a strategy to estimate the potential cost-effectiveness of pharmacological CCR5 blockade in dialysis patients

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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 assessed the cost-effectiveness of C-C chemokine receptor type five (CCR5) deletion 32 screening and pharmacological CCR5 blockade, for dialysis patients with systemic inflammation. It used data from a genetic association study that mimicked the randomisation process of a clinical trial. The authors concluded that the screen and treat strategy was potentially cost-effective and further study was worthwhile. The methods were valid, the sources were robust, and the uncertainty was considered. The authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study assessed the cost-effectiveness of C-C chemokine receptor type five (CCR5) deletion 32 screening and pharmacological CCR5 blockade, in dialysis patients with systemic inflammation. The data were from a genetic association study that mimicked the randomisation process of a clinical trial.

Interventions
The intervention was screening for the CCR5 deletion 32 polymorphism, followed by treatment for dialysis patients with the CCR5 insertion/insertion genotype, who had systemic inflammation, using pharmacological CCR5 blockers. The comparator was no screening.

Location/setting
Netherlands/secondary and tertiary care.

Methods
Analytical approach:
The analysis was based on a Markov model, with a 10-year time horizon. The authors stated that it was carried out from the perspective of the third-party health care payer.

Effectiveness data:
Most of the clinical data were from a published multicentre, prospective follow-up study that was part of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD). This study enrolled 413 patients with incident (new or consecutive) end-stage renal disease, who were treated at one of 38 Dutch dialysis centres between 1998 and 2001. It provided data on the genotype distribution and the efficacy of CCR5 blockers. Patients were followed-up until their death or until June 2007. Inflammation-associated mortality was a key clinical input and the data were from this study. Additional published sources were used for other inputs.

Monetary benefit and utility valuations:
The health utility values were collected from patients in the NECOSAD study, using the European Quality of life (EQ-5D) instrument. The utilities for transplanted patients were from a Swedish study.

Measure of benefit:
Life-years and quality-adjusted life-years (QALYs) were the summary benefit measures. A 1.5% annual discount rate was applied.
Cost data:
Two main cost categories were considered; intervention-related costs and unrelated future costs. The intervention costs included the genetic screening test for the CCR5 deletion 32 polymorphism, drugs for CCR5 blockade (including value added tax and prescription fees), cardiovascular and non-cardiovascular deaths, and transplantation graft failures. These costs were generally from official prices and a Dutch study. Transplantation failures included the costs of dialysis and renal transplant care, which were from official sources. In general, the resource quantities were from the NECOSAD study. The base-case analysis considered only the intervention-related costs. All costs were in Euros (EUR) and were discounted at an annual rate of 4%. The price year was 2009.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on all the model inputs, varying them by ±25% of their base-case values. The discount rate was varied from zero to 3%. In a probabilistic analysis, predetermined distributions were assigned to the model inputs. A threshold analysis was performed on the combined influence of drug effectiveness and the costs of pharmacological CCR5 blockade.

Results
The expected costs were EUR 1,863 with no screening, and EUR 8,482 with screening and treatment. The expected life-years were 5.71 with no screening, and 6.07 with screening and treatment. The QALYs were 4.36 with no screening and 4.67 with screening and treatment.

Compared with no screening, the incremental cost was EUR 18,557 per life-year gained or EUR 21,896 per QALY gained. When assuming no transplantation effect, these estimates were EUR 18,494 per life-year gained or EUR 24,642 per QALY gained. When unrelated future costs were included (mainly due to future dialysis), these estimates rose to EUR 37,400 per life-year gained or EUR 44,127 per QALY gained.

There was considerable uncertainty in these results. The sensitivity analysis showed that the main drivers of the screen and treat strategy were the costs of pharmacological CCR5 blockade and their effectiveness in reducing the mortality.

Authors' conclusions
The authors concluded that the screen and treat strategy was potentially cost-effective and further study was worthwhile.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the proposed intervention (screen and treat) was compared against the usual care (no screening).

Effectiveness/benefits:
The clinical data appear to have been from a valid source; the authors justified their use of an observational study, based on genetic association. There were difficulties in carrying out a randomised trial and this genetic association approach limited potential selection bias from an observational study. The authors stated that observational studies of a genetic polymorphism associated with a well-characterised functional phenotype, could be considered equivalent to clinical trials, with randomisation at conception. More information on this study was presented in a companion paper. Its multicentre nature and the large number of patients included should have ensured high internal validity. Life-years and QALYs were valid benefit measures, which captured the impact of the disease on patients' health. Quality of life was particularly relevant for dialysis patients. An appropriate instrument was used to elicit the preferences for health conditions.

Costs:
The cost categories reflected the perspective of the third-party payer. The resource use was from the patients who provided the clinical data, which should have ensured that the data reflected the Dutch situation. The unit costs were generally from standard Dutch sources. The resource quantities and unit costs were not presented separately. An alternative analysis was conducted including the future costs of dialysis and this showed their dramatic impact on the cost-effectiveness results. Other costs were varied in the sensitivity analyses. The price year and discount rate were
reported.

Analysis and results:
The results were clearly presented for both the base case and the alternative scenarios. The uncertainty was investigated, using both deterministic and probabilistic approaches, and the findings were clearly illustrated and discussed. The authors compared their results with those of other published studies, highlighting the relevance of including future costs. The authors did not discuss the transferability of their results to other settings and these findings should be considered specific to the Netherlands.

Concluding remarks:
The methods were valid, the sources were robust, and the uncertainty was considered. The authors’ conclusions appear to be valid.

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