Model study of AREDS antioxidant supplementation of AMD compared to Visudyne: a dominant strategy?

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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
The use of the Age-Related Eye Disease Study (AREDS) antioxidant supplementation to prevent neovascular age-related macular degeneration (AMD). This intervention was compared with a strategy of no AREDS supplementation, where patients with neovascular AMD were treated with photodynamic therapy (PT) using Visudyne.

Type of intervention
Primary prevention and treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of 788,000 persons aged 50 to 55 years in the Province of Ontario, Canada, during 2001.

Setting
The study setting would appear to have been primary care. The economic study was carried out in Canada.

Dates to which data relate
The effectiveness data were derived from studies published between 1997 and 2001. The dates to which the resource use data related were not reported. The price year was 2001.

Source of effectiveness data
The effectiveness data were derived from published studies, personal communication and authors’ assumptions.

Modelling
A model was developed to determine the cost-effectiveness of AREDS, but no details of the model were provided. The time horizon was 5 years.

Outcomes assessed in the review
The outcomes assessed were:

Canadian population projections to the year 2026;

the prevalence and incidence of AMD;
the relative risk reduction of progression from Stages 3 and 4 AMD to neovascular AMD when using AREDS antioxidant supplementation; and

the quality decrements associated with macular degeneration.

**Study designs and other criteria for inclusion in the review**

The authors stated that the benefits of AREDS were estimated from a randomised controlled trial, while the reduction in AMD risks was supported by a case-control study. AMD incidence was obtained from the Framingham Eye Study and the prevalence of Stages 3 and 4 from the Beaver Dam Eye study.

**Sources searched to identify primary studies**

Not reported.

**Criteria used to ensure the validity of primary studies**

Not reported.

**Methods used to judge relevance and validity, and for extracting data**

Not reported.

**Number of primary studies included**

The effectiveness data were derived from approximately 6 studies.

**Methods of combining primary studies**

It appears that the primary studies have not been combined.

**Investigation of differences between primary studies**

The authors do not appear to have investigated differences between the primary studies.

**Results of the review**

The authors only reported the relative risk reduction of progression when using AREDS supplementation and the quality of life decrements due to macular degeneration.

The relative risk reduction of progression from Stages 3 and 4 AMD to neovascular AMD when using AREDS antioxidant supplementation was 38% (95% confidence interval, CI: 10 - 57).

The decrease in quality of life for people as a result of blindness because of macular degeneration was 30%.

**Methods used to derive estimates of effectiveness**

The authors supplemented the results from the review of the literature with their own assumptions.

**Estimates of effectiveness and key assumptions**

The authors assumed that Stage 3 and 4 AMD patients were treated with AREDS antioxidant cocktail for 25 years and that compliance was complete. The authors also assumed that for AREDS, the first 5 years' outcomes were reduced by 50%.
Measure of benefits used in the economic analysis
The measure of benefits used was the quality-adjusted life-years (QALYs). The authors derived estimates for the decrements in quality of life due to blindness from a published study. The health benefits were discounted at a rate of 3%.

Direct costs
The direct costs included in the analysis were those to the health care system. These were for PT of AMD with Visudyne and those of AREDS treatment. The authors did not report the source used to derive these costs. Since the costs were incurred during 25 years, discounting was necessary and was appropriately performed at an annual rate of 3%. The study reported the total costs. The costs were adjusted to 2001 prices using the Canadian Consumer Price Index (CPI).

Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
The indirect costs were not included.

Currency
Canadian dollars (Can$).

Sensitivity analysis
In the base-case, the authors used Beaver Dam prevalence data to estimate the numbers of Stage 3 and 4 AMD cases. To test the sensitivity of the model to input data, Framingham incidence data were also tested to see if the results obtained were similar.

The authors undertook sensitivity analyses by varying the discount rate (0 to 5%), cost of AREDS supplementation for AMD, cost of Visudyne treatment for neovascular AMD, and compliance.

To investigate whether AREDS would continue to be more economically attractive than Visudyne, the authors included the lower 95% CIs in their model.

Estimated benefits used in the economic analysis
The cohort receiving no AREDS supplementation lost 1.74 million QALYs, while the cohort receiving AREDS lost 1.41 million QALYs. Therefore, the QALYs saved by AREDS were 330,279 when using the Beaver Dam prevalence data. This represented a saving of 0.42 QALYs for each initial member of the cohort.

When using Framingham incidence data, 51,962 QALYs were saved when patients were given AREDS antioxidant supplementation.

Cost results
The cost of Visudyne treatment for AMD, assuming the prevalence in the Beaver Dam study, was Can$2,678 million for those not given AREDS supplementation and Can$1,733 million for those receiving AREDS antioxidant supplementation.

The total savings incurred by giving AREDS supplementation to patients with Stage 3 to 4 AMD was Can$431 million, once the costs of AREDS supplementation had been taken into consideration (Can$513 million). This represented savings of Can$547 per person.
Using Framingham incidence data, Can$70.3 million were saved by giving AREDS supplementation to patients with Stage 3 to 4 AMD.

**Synthesis of costs and benefits**
The costs and benefits were not combined as AREDS antioxidant supplementation was found to be both more effective and cheaper than conventional care.

The authors reported that economic analyses of the costs of AMD to the Ontario Ministry of Health indicated that savings were predicted for AREDS of up to approximately twice the yearly cost of AREDS (Can$182.50) when using the Beaver Dam prevalence. Reduced compliance rates in the sensitivity analyses simply reduced the savings by the percentage of the cohort failing to comply. If the costs of AREDS supplementation were to double, savings would no longer be accrued.

The results of the worst-case scenario showed that when assuming a 10% risk reduction for progression to neovascular AMD requiring PT, and after subtracting the costs of AREDS treatment, the net cost was Can$265 million; the Framingham incidence-based model showed savings of Can$10 million. The results of the worst-case scenario also showed that a total of 86,915 QALYs were saved with AREDS supplementation (Beaver Dam data), while 13,674 were saved when using Framingham data.

**Authors’ conclusions**
If the case progresses to wet age-related macular degeneration (AMD), then Age-Related Eye Disease Study (AREDS) antioxidant supplementation with Visudyne is less expensive than Visudyne alone; AREDS with Visudyne yields more QALYs than Visudyne alone; and under all but the most extreme assumptions, the conclusions reached are robust. Hence, AREDS antioxidant supplementation would appear to be a cost-effective way of averting costly photodynamic therapy (PT) for a significant portion of people who become affected with macular degeneration.

**CRD COMMENTARY - Selection of comparators**
A justification was given for the comparator used. It represented current practice in the authors' settings. However, despite the justification, the authors should have reported explicitly and at the beginning of their study what both the intervention and comparator therapies involved, and the sample to be treated.

**Validity of estimate of measure of effectiveness**
The authors did not state whether a systematic review of the literature was undertaken to identify relevant research and minimise biases. The authors used data from the available studies selectively. Uncertainty remains around the literature search and the possible omission of relevant studies, as no details of any search strategy were reported in the paper. The authors supplemented the results of the literature with their own assumptions. It is important to note that a key input into the model was not drawn from published evidence but was based on an authors' assumption. More specifically, for AREDS the first 5 years’ outcomes were reduced by 50%. The assumptions, however, were appropriately varied in the sensitivity analysis using worst-case scenarios and one-way sensitivity analyses (e.g. compliance rates).

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled. However, the authors did not provide any details of the model used.

**Validity of estimate of costs**
The perspective of a third-party payer was adopted in the economic analysis. The only costs included in the review were the costs of PT using Visudyne and the costs of AREDS supplementation. Other relevant costs, such as those associated with blindness or other adverse consequences, were not included in the analysis. It is unclear if such an omission would have affected the authors' results. The costs and the quantities were not reported separately, which will limit the generalisability of the authors' results. The authors did not report where the unit costs were derived from. The authors...
undertook appropriate sensitivity analyses of the costs, but these were difficult to understand. Discounting was necessary, as the costs were incurred during a long time, and was appropriately undertaken. The authors used the CPI to inflate the costs to 2001 prices, although the health component of the CPI would have provided a better approximation as it is generally the case that health care prices rise faster than overall prices.

Other issues
The authors did not compare their findings with those from other studies. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively, but they should have reported the interventions being compared and the methods used more clearly. The authors' conclusions would appear to reflect the scope of the analysis. The authors reported a limitation of their study in that the risk reductions found for AREDS might not have been stable. However, this parameter was tested in a sensitivity analysis and a worst-case scenario.

Implications of the study
The authors reported that antioxidant supplementation would appear to be a relatively inexpensive and cost-effective way of averting costly PT for a significant portion of people who become affected with macular degeneration. As such, subsidising its cost would be a cost-effective strategy for the Ontario Health Insurance Plan to introduce.

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Other publications of related interest


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