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## Deciding on anticoagulating the oldest old with atrial fibrillation: insights from cost-effectiveness 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.

### Health technology

The health intervention examined in the study was anticoagulation treatment with warfarin in patients with nonrheumatic atrial fibrillation (AF).

### Type of intervention

Treatment.

### Economic study type

Cost-utility analysis.

### Study population

The study population comprised patients aged 65 to 100 years with nonrheumatic AF.

### Setting

The setting was a hospital. The economic study was carried out in the USA.

### Dates to which data relate

Data on effectiveness and resource use were derived from studies published between 1994 and 2002. The price year was 2000.

### Source of effectiveness data

Data on effectiveness were derived from previously published studies, supported by the author's assumptions.

### Modelling

A Markov model was constructed to model quality-adjusted survival and the costs of the anticoagulation treatment in comparison with no intervention. Three health states were considered: life without a stroke, life with stroke residuals, and death. Patients were allowed to move across health states: those who were well or had residuals from stroke could remain in their state, suffer a major extracranial bleed (then recovering or dying), have a first or second stroke, or die from other causes. Patients with stroke could be left with residuals after stroke, recover, or die.

### Outcomes assessed in the review

The health outcomes assessed from the published studies were quality of life weights with stroke residuals, and several baseline probabilities: ischemic stroke, haemorrhagic stroke, major non-stroke bleed, death from ischemic stroke, residual after ischemic stroke, death after major nonstroke bleed, death after haemorrhagic stroke, and residual after haemorrhagic stroke.

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

The author stated that one of the primary studies was a systematic review. Age-specific US Life Tables were also used. No information was given for the remaining primary studies.

### **Sources searched to identify primary studies**

Not stated.

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

Not stated.

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

Not carried out.

### **Number of primary studies included**

Five primary studies were used as sources of effectiveness evidence.

### **Methods of combining primary studies**

Narrative methods were used.

### **Investigation of differences between primary studies**

No investigation of differences was carried out.

### **Results of the review**

The quality of life weight was 0.5 with stroke residuals, and 1 in patients without stroke.

The probability values (per person-per year) in patients at the ages 65, 70, 80, 90, and 100 were, as follows:

1.0 (65), 1.2 (70), 1.6 (80), 1.9 (90), and 2.4 (100) for ischemic stroke,

0.3 (65), 0.4 (70), 0.5 (80), 0.6 (90), and 0.7 (100) for ischemic stroke in anticoagulated patient,

0.3 (65), 0.4 (70), 0.9 (80), 2.1 (90), and 5.0 (100) for haemorrhagic stroke,

0.5 (65), 0.8 (70), 1.8 (80), 4.2 (90), and 9.9 (100) for haemorrhagic stroke in an anticoagulated patient,

1.0 (65), 1.2 (70), 1.6 (80), 2.2 (90), and 3.0 (100) for major non-stroke bleed,

3.0 (65), 3.5 (70), 4.8 (80), 6.6 (90), and 9.0 (100) for major non-stroke bleed in an anticoagulated patient, and

0.13 (65), 0.13 (70), 0.34 (80), 0.34 (90), and 0.34 (100) for death from ischemic stroke.

The risk values were 0.78 for residual after ischemic stroke, 0.04 for death after major nonstroke bleed, 0.35 for death after haemorrhagic stroke, 0.7 for death after haemorrhagic stroke in an anticoagulated patient, 0.5 for residual after haemorrhagic stroke, and 1.0 for residual after haemorrhagic stroke in an anticoagulated patient.

### **Methods used to derive estimates of effectiveness**

The author made some assumptions to support the data used in the decision model.

### **Estimates of effectiveness and key assumptions**

The author assumed that a major stroke with residual would have the baseline quality of life at the start of the analysis. Anticoagulated patients were assumed to be at higher risk of major extracranial bleeding, dying from major extracranial bleeding, intracranial bleeding, and having residuals and dying from intracranial bleeding. It was also assumed that patients who had had two major strokes died, that anticoagulation had no effect on nonembolic ischemic strokes, that the efficacy of anticoagulation in preventing ischemic embolic strokes was not related to age and that patients remained anticoagulated or not regardless of their experience with stroke or bleed.

### **Measure of benefits used in the economic analysis**

The benefit measure used in the economic analysis was quality-adjusted life years (QALYs). It was derived from modelling and a 3% discount rate was used.

### **Direct costs**

A 3% discount rate was used as costs were incurred over a period of time longer than 2 years. Unit costs were not reported separately from quantities of resources. The economic evaluation included only the costs of anticoagulation (warfarin administration and acquisition cost) and its complications and strokes related to AF and anticoagulation (hospitalisation due to haemorrhagic stroke, ischemic stroke, and major extracranial bleeding, and nursing home care). The cost/resource boundary was that of society. Hospitalisation charges and nursing home costs were based on actual data derived from the Healthcare Cost and Utilization Project (HCUP) 1997 Nationwide Inpatient Sample and Medicaid average daily rates, respectively. The cost of hospital care was increased by 40%, while ancillary costs were assumed to be 20% higher than hospital costs and both assumptions were accompanied by a justification. All costs were inflated to the year 2000, using the medical proportion of the consumer price index and assuming a 3% increase for the last 2 years. Total costs were modelled.

### **Statistical analysis of costs**

No statistical analysis of costs was carried out.

### **Indirect Costs**

Indirect costs were not included in the analysis, although the author stated that a societal perspective was adopted.

### **Currency**

US dollars (\$).

### **Sensitivity analysis**

One-way sensitivity analyses were performed to assess the robustness of the estimated quality-adjusted life-expectancy by varying all parameters used in the model from 50% below to 50% above the base rates. Baseline quality of life was varied by 1 to 0.5.

### **Estimated benefits used in the economic analysis**

The QALYs gained were as follows:

in patients with no risk factors: 11.5 with anticoagulation and 11.8 with no anticoagulation at aged 65, and 2.0 with anticoagulation and 2.1 with no anticoagulation at aged 100;

in patients with a history of diabetes mellitus: 11.5 with anticoagulation and 11.4 with no anticoagulation at aged 65, and 2.0 with anticoagulation and 2.0 with no anticoagulation at aged 100;

in patients with history of high blood pressure: 11.5 with anticoagulation and 11.5 with no anticoagulation at aged 65, and 2.0 with anticoagulation and 2.1 with no anticoagulation at aged 100;

in patients with history of stroke or transient ischemic attack (TIA): 11.5 with anticoagulation and 11.1 with no anticoagulation at age 65, and 2.0 with anticoagulation and 2.0 with no anticoagulation at age 100;

in patients with diabetes mellitus and high blood pressure: 11.6 with anticoagulation and 10.9 with no anticoagulation at age 65, and 2.0 with anticoagulation and 2.0 with no anticoagulation at age 100;

in patients with diabetes mellitus and stroke or TIA: 11.6 with anticoagulation and 10.4 with no anticoagulation at age 65, and 2.0 with anticoagulation and 2.2 with no anticoagulation at age 100;

in patients with high blood pressure and stroke or TIA: 11.6 with anticoagulation and 10.5 with no anticoagulation at age 65, and 2.0 with anticoagulation and 1.2 with no anticoagulation at age 100; and

in patients with diabetes mellitus, high blood pressure and stroke or TIA: 11.7 with anticoagulation and 9.5 with no anticoagulation at age 65, and 2.0 with anticoagulation and 1.9 with no anticoagulation at age 100.

### **Cost results**

Total costs were not reported.

### **Synthesis of costs and benefits**

An incremental cost-utility analysis was performed to combine costs and benefits of the interventions. The author reported that in patients with AF who had histories of previous stroke or TIA, diabetes mellitus, and hypertension, anticoagulation was cost-saving and extended life. It was dominant over no treatment. For example, in a 65-year-old, the cost-savings were \$1,434 and the increase in life-expectancy was 2.2 QALYs; in an 85-year-old, the cost-savings were \$1,767 and the improvement in QALYs was 0.5. For a 95-year-old, with hypertension and previous stroke or TIA, the incremental cost-effectiveness ratio was \$30,000 per QALY saved. Sensitivity analyses showed that the estimated cost-utility ratios were sensitive to almost all variables used in the decision model. The most limiting factor was the competing risk of death from other illnesses in the oldest old.

### **Authors' conclusions**

The author concluded that the anticoagulation treatment was not effective in significantly improving life expectancy in patients with AF and without other risk factors at any age, and proved to be effective only for specific subgroups of patients with other risk factors for stroke. As a result, "even for the oldest old who are at the greatest risk for embolic stroke ... the decision to anticoagulate is still quite close to that not to anticoagulate, and the results are based on parameters whose values are uncertain".

### **CRD COMMENTARY - Selection of comparators**

The rationale for the choice of the comparator was clear. "No intervention" was selected as this comparison appeared not to have been made with anticoagulation therapy. You, as a user of this database, should decide whether it represents a valid comparator in your own setting.

### **Validity of estimate of measure of effectiveness**

The effectiveness estimates were derived from published studies. However, a formal review of the literature was not reported and assumptions were made. Without knowledge of the source and validity of the estimates used as model inputs it is difficult to have confidence in the results. It is useful that sensitivity analyses were performed with apparently wide variation in their values. However, the sensitivity analyses would have benefited from using the variability by source of estimate.

### Validity of estimate of measure of benefit

QALYs were used as the benefit measure and were obtained from a decision model that appears to have been appropriate to simulate the natural progression of the disease. Discounting was performed. The use of QALYs enhanced the comparability of the cost-effectiveness of the intervention with other procedures used in the health care system. The number of QALYs gained in specific subgroups of patients was clearly reported.

### Validity of estimate of costs

The author stated that the analysis of costs was carried out from the perspective of society, but indirect costs were not included and the author stated that lost wages were usually small in the population of elderly people included in their analysis. The economic evaluation comprised only the costs of the treatment and complications. Total costs were calculated using modelling, but estimated costs were not reported. A specific price year was used. Unit costs were not reported separately from quantities of resources. Costs were treated deterministically in the base-case analysis, but several sensitivity analyses were carried out. The source of cost data was appropriately reported. The author stated that although charges were used, a cost-to-charge ratio was used to convert charges into costs.

### Other issues

The author made several comparisons of the findings of the paper with those from other studies. The issue of the generalisability of the study results to other settings was not explicitly addressed, but several sensitivity analyses were conducted, and appropriate subgroup analyses were performed. A study population of older patients with AF was considered in the study and this was reflected in the author's conclusions. Results were reported selectively, particularly for costs, which were not reported either in a disaggregated or aggregated form. Some limitations of the study were noted, such as the use of assumptions in the decision model and the non-differentiation between different types of intracerebral bleeding. It was also noted that there was no age-adjustment for patients with risk factors and this could have overestimated the benefits of anticoagulation in this group of patients. The author's conclusions were moderate and in keeping with the scope of the analysis.

### Implications of the study

The author suggests that there is no compelling evidence that anticoagulation may extend survival in the oldest old with nonrheumatic AF. Further research should be carried out to help decision makers understand the benefits and costs of the anticoagulation treatment in old patients in different clinical conditions. "Recommendations that all older persons with AF should be anticoagulated are premature."

### Source of funding

None stated.

### Bibliographic details

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