Quality of anticoagulation control and costs of monitoring warfarin therapy among patients with atrial fibrillation in clinic settings: a multi-site managed-care study

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 study compared the costs and outcomes from anticoagulation clinics in three geographically diverse US managed care organisations (MCOs).

Site A had one pharmacist-managed clinic that used computerised tracking software.

Site B had two nurse-managed clinics with paper records, one in a primary care centre and one in a cardiology centre.

Site C clinics used computerised tracking software. Eight were nurse-managed and one was pharmacist-managed.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with chronic non-valvular atrial fibrillation who were receiving warfarin. The eligibility criteria for the patients were:

18 years of age or older;

treated with warfarin at an anticoagulation clinic for at least 30 days;

evidence of atrial fibrillation in the medical chart, but no evidence of mitral stenosis, severe mitral insufficiency, or severe tricuspid regurgitation noted in echocardiography reports; and

no participation in prospective clinical studies involving anticoagulation care during the study period.

Setting
The study setting was primary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were collected between 1996 and 1998. The price year was 2003.

Source of effectiveness data
The effectiveness data were derived from a single study.
Link between effectiveness and cost data
The costing was undertaken retrospectively on the same patient sample as that used in the effectiveness study.

Study sample
No sample size was determined in the planning phase of the study. Each of the three health plans generated a list of potential study candidates by screening records from all anticoagulation clinics. At each of the three sites, a random sample of 200 patients was drawn from those who met the entry criteria, for a total of 600 patients. At Sites A and B, patients were selected if they were seen at the clinics between 1 January 1996 and 31 December 1998. At Site C, only patients seen in 1998 were selected. Of the 200 patients in Site A, 54.5% were males and the mean age in this group was 73.9 (+/- 9.3) years. Of the 200 patients in Site B, 60.5% were males and the mean age in this group was 72.0 (+/- 10.6) years. Of the 200 patients in Site C, 54.0% were males and the mean age in this group was 70.8 (+/- 9.0) years.

Study design
The study had a retrospective cohort design and was based on data from anticoagulation clinics affiliated to three MCOs. The patients were followed up for a maximum of 12 months, or until discontinuation of clinic services. The mean duration of follow-up was 10.1 (+/- 3.5) months for patients in Site A, 10.4 (+/- 3.3) months for patients in Site B, and 11.0 (+/- 2.5) months for patients in Site C. The authors reported that 15 (2.5%) patients across all sites died during the 1-year observation period, and an additional 123 (20%) discontinued anticoagulation clinic care during the follow-up period. The authors reported that, for most cases, the specific reasons for death or discontinuation were unknown.

Analysis of effectiveness
All of the patients included in the study were accounted for in the analysis. The quality of anticoagulation therapy was assessed by evaluating all observed values for international normalised ratio (INR) tests performed for each patient during the 1-year follow-up period. The authors also estimated the number of patients who discontinued anticoagulation clinic care within this 1-year follow-up period and the proportion of time patient spent within, above, or below the target INR range (i.e. 2.0 - 3.0), which was calculated using the Rosendaal linear trend method. The complications of warfarin therapy were also estimated but as complications were rare, the authors reported the rates of adverse outcomes as a risk per 100 patient-years, assuming a Poisson distribution. The outcomes were extracted from software systems, medical records systems and/or anticoagulation cards. An independent reviewer at each site re-abstracted a 10% random sample of completed case report forms to assess the accuracy and completeness of the data.

Logistic regressions were used to evaluate predictors of anticoagulation control. The independent predictors included patient characteristics (e.g. age, gender, race, prior myocardial infarction, stroke or transient ischaemic attack, congestive heart failure, diabetes, and warfarin treatment at time of clinical referral), as well as binary variables representing site location.

The patients in the study were mostly elderly, male and white, with racial diversity being different according to the site.

Effectiveness results
The mean percentage of time patients spent within the target INR range (i.e. 2.0 - 3.0) was 62% overall (interquartile range: 49 - 73). There was little variation observed by site: 60% in Site A, 61% in Site B and 65% in Site C, (p=0.18).

The predictors of good anticoagulation control (at least 75% of days in target INR range) included older age, white race and lack of co-morbidity.

The rate of embolic stroke in the overall sample was 1.00 per 100 patient-years (95% confidence interval, CI: 0.31 - 2.22). By site, the rate of embolic stroke was 0 in Site A, 0.6 (95% CI: 0 - 3.20) in Site B and 2.2 (95% CI: 0.60 - 5.60) in Site C.

The rate of major bleeding in the overall sample was 3.60 per 100 patient years (95% CI: 2.03 - 5.42). By site, the rate
of major bleeding was 4.2 (95% CI: 1.67 - 8.58) in Site A, 2.3 (95% CI: 0.63 - 5.89) in Site B and 3.8 (95% CI: 1.54 - 7.88) in Site C. The authors did not report if these differences were statistically significant.

Clinical conclusions
The authors concluded that anticoagulation clinics from three geographically diverse health plans were all found to provide a high quality of anticoagulation control with low complication rates. The levels of anticoagulation control were similar across the sites, despite differences in clinic organisation and patient characteristics.

Measure of benefits used in the economic analysis
The authors did not derive a summary measure of health benefit. The study was, in effect, a cost-consequences analysis.

Direct costs
The direct costs of the health care provider were included in the analysis. These were for the anticoagulation clinic service (i.e. staff labour expenses, laboratory costs, and overheads such as office space and equipment). The labour costs were estimated from actual time spent by clinic staff on individual patient encounters, which was determined using a time study conducted at every study site. The estimated time was multiplied by published national sources of data on salaries and benefits for clinic staff. The cost of laboratory work was measured using Medicare payments for a prothrombin time/INR test and a venous blood draw. In addition, the authors also evaluated staff costs using budgeted time, which was based on full-time equivalent staff time assigned to the clinics. Since the costs were incurred during one year, discounting was not relevant and was not performed. The study reported the average costs. Two costing studies were performed, one which included all patients and another which included only those patients with a full 12-month follow-up period. The price year was 2003.

Statistical analysis of costs
The costs were treated stochastically. An ordinary least-squares regression was used to evaluate predictors of costs using the same independent predictors as used in the multivariate regressions for anticoagulation control.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analyses were performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The average cost per patient during follow-up was $261 (+/- 107) in Site A, $305 (+/- 141) in Site B and $205 (+/- 75) in Site C. The costs were found to vary across sites, (p<0.01).

The full-year average cost per patient was approximately 10 to 15% higher, with $288 (+/- 95) in Site A, $339 (+/- 134) in Site B and $216 (+/- 68) in Site C. The costs were found to vary across sites, (p<0.01).
The mean costs of warfarin monitoring, based on budgeted (rather than observed) staff time, were $349 per patient at Site A, $411 at Site B and $311 at Site C.

**Synthesis of costs and benefits**
The costs and benefits were not combined.

**Authors' conclusions**
Based on data from three geographically diverse health plans, anticoagulation clinics provided a high quality of control which would require a substantial commitment for services. The mean cost of warfarin monitoring per patient varied from $205 to $305 across sites.

**CRD COMMENTARY - Selection of comparators**
The authors compared the costs and outcomes of anticoagulation clinics affiliated with three geographically diverse health plans. No reason was given as to why clinics in these three health plans were chosen.

**Validity of estimate of measure of effectiveness**
This was a retrospective cohort study, which was appropriate for the study question. However, a prospective cohort study would have been more desirable as it is less prone to bias than retrospective studies. The study sample was representative of the study population. The patients’ baseline characteristics (e.g. age, race, gender and prior co-morbidities) were reported for the three patient groups and the overall sample. Appropriate multivariate regressions were undertaken using baseline patient characteristics, as well as site location, as predictors.

**Validity of estimate of measure of benefit**
The authors did not derive a summary measure of health benefit. The analysis was, therefore, categorised as a cost-consequences analysis.

**Validity of estimate of costs**
All the categories of cost relevant to the health care provider perspective adopted were included in the analysis. It would appear that all the major relevant costs have also been included in the analysis. The costs and the quantities were not reported separately, which will limit the generalisability of the authors' results. However, the authors stratified costs by three different cost categories, that is, staff, laboratory tests and overhead costs. The costs were derived from the authors' settings and published sources. An appropriate statistical analysis was performed to test whether differences in costs between the sites were statistically significant. Since all the costs were incurred during one year, discounting was unnecessary and was not performed. For some cost categories, Medicare charges were used to proxy prices and this might not reflect the true cost of providing the service. The price year was reported, which will aid any possible inflationary exercises.

**Other issues**
The authors reported that data on the quality of anticoagulation control across multiple clinic sites was limited and, to their knowledge, the costs of providing clinic services in the USA had not been assessed. The issue of generalisability to other settings was addressed since the authors compared the costs and outcomes of anticoagulation clinics across geographically diverse sites. However, the reader is referred to the limitations already highlighted above in relation to the issue of generalisability. The authors do not appear to have presented their results selectively. In their conclusions, the authors did not report that significant differences in costs between the three sites were observed. However, in their discussion, the authors reported several reasons (e.g. regional differences in labour and non-labour costs, staffing mix and levels, and efficiency) why costs might differ from site to site.

The authors reported a number of further limitations to their study. First, the quality of anticoagulation therapy might
have been higher in the study anticoagulation clinics than that achievable in other clinic settings, as these had been established for many years. Second, the study did not include patients undergoing warfarin therapy using other treatment modalities, such as point-of-care testing or home monitoring. Finally, fewer patients had education visits recorded on study forms than anticipated. Hence, if these education services were in fact provided but not adequately captured, monitoring costs could be as much as 10% higher than those reported in the study.

**Implications of the study**
At the end of the study, the authors appear to imply that more substantial financial commitment for anticoagulation clinics should be made so as to provide the high quality of anticoagulation control reported in this study.

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