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The economics of cardiac biomarker testing in suspected myocardial infarction

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ABSTRACT

Suspected myocardial infarction (MI) is a common reason for emergency hospital attendance and admission. Cardiac biomarker measurement is an essential element of diagnostic assessment of suspected MI. Although the cost of a routinely available biomarker may be small, the large patient population and consequences in terms of hospital admission and investigation mean that the economic impact of cardiac biomarker testing is substantial.

Economic evaluation involves comparing the estimated costs and effectiveness (outcomes) of two or more interventions or care alternatives. This process creates some difficulties with respect to cardiac biomarkers. Estimating the effectiveness of cardiac biomarkers involves identifying how they help to improve health and how we can measure this improvement. Comparison to an appropriate alternative is also problematic. New biomarkers may be promoted on the basis of reducing hospital admission or length of stay, but hospital admission for low risk patients may incur significant costs while providing very little benefit, making it an inappropriate comparator. Finally, economic evaluation may conclude that a more sensitive biomarker strategy is more effective but, by detecting and treating more cases, is also more expensive. In these circumstances it is unclear whether we should use the more effective or the cheaper option.

This article provides an introduction to health economics and addresses the specific issues relevant to cardiac biomarkers. It describes the key concepts relevant to economic evaluation of cardiac biomarkers in suspected MI and highlights key areas of uncertainty and controversy.

The economics of cardiac biomarker testing in suspected myocardial infarction

Suspected myocardial infarction (MI) is a common reason for emergency hospital attendance and admission. Chest pain is responsible for around 700,000 emergency department attendances per year in the UK [1]. Chest pain, angina or MI accounted for 364,206 emergency hospital admissions in England in 2012–13 with an associated 997,028 bed days and an estimated £375 million health service costs [2,3].

Cardiac biomarker measurement is an essential element of diagnostic assessment of suspected MI. Although the cost of a routinely available biomarker may be small, the large patient population and consequences in terms of hospital admission and investigation mean that the economic impact of cardiac biomarker testing is substantial. It is therefore unsurprising that economic considerations play an important role in determining how cardiac biomarkers are used. In particular, the development of new biomarkers or more sensitive assays for existing biomarkers is often driven by the perceived economic value of ruling out MI soon after hospital attendance and reducing hospital length of stay.

An economic evaluation is a study that compares the costs and outcomes of two or more interventions or care alternatives. Few studies of cardiac biomarkers for suspected MI meet this definition of an economic evaluation. The United Kingdom National Health Service Economic Evaluation Database contains economic evaluations of health care interventions. A search of the database identified only 12 economic evaluations of cardiac biomarker testing in suspected acute MI [4–15]. This is perhaps not surprising since formal economic evaluation requires expert health economic input and typically involves the use of concepts and modelling techniques that are unfamiliar to many researchers.

This article will describe the key concepts relevant to economic evaluation of cardiac biomarkers in suspected MI and highlight key areas of uncertainty and controversy.

What is economic evaluation?

As stated above, economic evaluation in healthcare involves comparing two or more alternative interventions or strategies in terms of both costs and outcomes. It should be obvious that cost-

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effectiveness involves measuring effectiveness as well as costs, but it is surprising how often the term is used to describe a comparison of costs alone. If we don't measure effectiveness then we should logically always choose the cheapest option, which usually means doing nothing — hardly a satisfactory approach for both patients and clinicians. Evaluating effectiveness involves measuring how intervention improves patient health (or how lack of intervention reduces patient health). For cardiac biomarkers we need to ask how they help to improve health and how we can measure this improvement. The difficulty of doing this may explain why effectiveness is often overlooked.

Economic evaluation involves comparison of alternatives and identifying appropriate alternatives is crucial in ensuring efficient use of resources. An intervention is likely to appear cost-effective if compared to an ineffective or expensive alternative. This issue is very relevant to cardiac biomarkers. New biomarkers may be promoted on the basis of reducing hospital admission or length of stay, but hospital admission for low risk patients may incur significant costs while providing very little benefit.

Economic evaluation often concludes that the more effective strategy is also the more expensive. In which case how do we decide whether to use the more effective or the cheaper option? Again, this is clearly an important issue for biomarkers as a more sensitive biomarker will detect more cases leading to more patients being treated but higher costs.

These three issues are central to a practical understanding of economic evaluation and form the core of this paper. They will be illustrated using a recent economic analysis of presentation versus delayed troponin testing for suspected acute MI as an example (see Box 1) [5,6].

Measuring costs and outcomes

Although measuring costs may be unfamiliar to clinical researchers, this is often the easy bit of an economic evaluation. Some issues may need to be considered, such as analysis of skewed cost data, handling of infrequent high cost events, estimation of lifetime costs, litigation costs and productivity losses (i.e. time taken off work), but established guidance exists for most of these issues. It is helpful to understand these issues but they can often be left to the health economists. The same cannot be said for estimating effectiveness. This involves clinical understanding of the intervention and how it is expected to benefit patients. Failure of engagement on this issue between clinicians and economists can lead to a fundamentally flawed analysis.

Estimating the effectiveness of using a diagnostic technology, such as a cardiac biomarker, is clearly going to be challenging. Diagnostic tests are usually evaluated in terms of accuracy (sensitivity and specificity). The benefit of diagnostic testing lies in detecting and treating true positive cases, which must be balanced against the potential harm associated with detecting and treating false positives. It may be tempting to postulate a benefit in terms of reassurance from a true negative test but this is controversial. Reassurance may be short-lived or may only be required because of iatrogenic anxiety. If we scare patients by telling them they may be having a heart attack can we really claim there is a benefit when negative tests provide reassurance?

Estimating the benefit of treating true positives would ideally involve a randomised trial comparing patients with detected and treated disease (true positives) to those with undetected and untreated disease (false negatives). Few such trials exist and as a result economic evaluations of diagnostic tests often have to rely upon other methods to estimate benefit. Non-randomised or observational comparisons may be used as alternatives to randomised trials, but the potential impact of confounding needs to be considered [16]. The use of historical controls in particular will tend to overestimate the effect of diagnosis [17]. If no appropriate empirical data exist then expert opinion can be used to estimate a treatment effect. However, this is a very weak form of evidence and may be based on the preconceived notions that analysis needs to challenge. If we have no empirical evidence that diagnosis improves outcome then why should expert opinion assume that it does? As a general rule we should always seek empirical data, even if this requires extrapolation from one setting to another.

Box 2 illustrates how we estimated the benefit of detecting additional cases of MI using delayed troponin testing.

Estimating the harm from detecting false positives is even more difficult and depends upon our assumptions regarding the system of care and subsequent management of false positives. If it is assumed that false positives are quickly and decisively identified by a subsequent "gold standard" test then an impact on outcome is unlikely and the only consequence is a modest increase in costs. If it is assumed that false

Box 1

Cost-effectiveness of presentation versus delayed troponin testing for MI.

The appropriate timing of troponin testing in suspected acute MI depends upon cost-effectiveness. Troponin sensitivity is time-dependent and increases over the hours after presentation. The effectiveness of testing is therefore improved by delayed testing, compared to testing only at presentation. However, delayed testing prolongs hospital stay and thus incurs additional costs. So the question is — do the improved outcomes associated with delayed testing justify the additional costs?

To answer this question we undertook decision-analysis modelling to compare the costs and outcomes associated with delayed troponin testing compared to troponin testing at presentation only, and estimate the cost-effectiveness of delayed troponin testing compared to presentation testing for patients presenting to hospital with suspected acute MI. We also explored the cost-effectiveness of measuring a high sensitivity troponin at presentation. Use of a high sensitivity assay at presentation may increase effectiveness but by generating more positive results it will increase costs.

Box 2

Estimating the benefit of detecting cases of MI.

MI refers to non-ST elevation MI in the context of evaluating biomarkers in suspected acute MI. There are no randomised trials comparing treatment to no treatment for non-ST elevation MI but good non-randomised data are available from a study by Mills et al. [18]. They collected data from patients who were admitted to their hospital with suspected AMI and investigated with troponin testing. The same troponin assay was used throughout the two year study period but the threshold at which positive results were reported was changed after one year. As a consequence patients with troponin levels between the two thresholds could be identified and compared between the two study phases. The results showed that revealing these true positive results to clinicians led to greater use of invasive investigation and treatment, greater use of antithrombotic therapy and reduced subsequent mortality and non-fatal MI. Overall, detecting and treating these cases of MI appears to be associated with an approximate halving of the subsequent risk of death and non-fatal MI.

A previous economic analysis [14], undertaken before the Mills study was published, used a more complex approach involving extrapolation of various data sources (including randomised trials of interventions for non-ST elevation MI and historical data) but resulted in a similar estimate that treatment approximately halved the risk of adverse outcome.