Reviewer's report

Title: Pre-hospital ECG for acute coronary syndrome in urban India: A cost-effectiveness analysis

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Reviewer: Steve Goodacre

Reviewer's report:

This is an original study that addresses an important research question in a part of the world that is often neglected in international cardiology research. The methods used are appropriate and well described and the manuscript mostly adheres to standards for reporting economic evaluations. The conclusions drawn are supported by the analysis presented, although the assumptions behind the analysis may be somewhat limited and the potential uncertainty of estimates has not been fully explored.

I always think it is worthwhile checking that the findings of economic modelling make sense in the light of the way the problem is framed and the data used in the analysis. If the analysis does not pass this test then there is usually something substantially wrong with the model. This analysis seems to pass this test. An ECG is a relatively cheap test and if, as modelled here, it improves either sensitivity (thus increasing the effectiveness of treatment) or specificity (thus reducing unnecessary hospitalisations) or both then it is likely to be cost-effective.

There are two principal limitations to this analysis. Firstly, the derivation of estimates of sensitivity and specificity are somewhat opaque and the possibility that use of an ECG could paradoxically worsen one parameter or the other has not been explored. Although counter-intuitive, it is not beyond the bounds of possibility that using an ECG could reduce diagnostic performance. For example, the initial ECG is often normal in non-ST elevation ACS. If GPs erroneously decided not to refer such cases to hospital then use of an ECG could reduce sensitivity. The estimates of sensitivity and specificity appear to be based upon observational data rather than a randomised comparison of GP diagnostic accuracy with and without ECG, so there must be considerable uncertainty. The effect of diagnostic testing upon decision-making is often unpredictable, so it would be worthwhile exploring a wider range of conceivable values for sensitivity and specificity including the possibility that one or the other is superior when ECG is not used.

The second limitation is that uncertainty has only been explored through one-way sensitivity analysis. Best current practice in economic analysis would involve undertaking probabilistic sensitivity analysis based upon distributions around each of the parameters in the model. This would allow calculation of confidence intervals around ICERs and estimation of the probability of prehospital ECG
being cost-effective at varying thresholds of willingness to pay for health gain. This is a sophisticated technique and would require analysis by someone with expertise in mathematical modelling, but if the authors can undertake such an analysis then it would be a valuable addition to the study. If not then the failure to explore stochastic uncertainty should be acknowledged as a limitation.

Major Compulsory Revisions

The one way sensitivity analysis should be repeated to include the possibility that sensitivity or specificity with the ECG could be worse than without the ECG.

If probabilistic sensitivity analysis is not undertaken then failure to explore stochastic uncertainty should be acknowledged as a limitation.

The limitations in the data used to estimate sensitivity and specificity should also be acknowledged. The ideal data source would be a randomised trial comparing decision-making in GPs with and without ECGs.

Minor Essential Revisions

Background: Is primary angioplasty feasible in the Indian health care system? If so, what percentage of Indian STEMI receive primary angioplasty?

Background, 2nd paragraph: Is the average cited here a mean or median?

Background: What sort of emergency ambulance service is available in urban India? Is there any equivalent of the 999 or 911 emergency call system?

Background and methods: It would be helpful to have more details of the data from reference 8 that are used to justify this study and are a source for sensitivity and specificity estimates. I assume they are observational data. Could the association between use of the ECG and reduced delay be confounded other factors? For example, is it possible that patients with characteristic clinical features of MI and a short time from symptom onset to presentation could have been more likely to have an ECG and a more rapid referral? Would the decision to use an ECG be determined by patient characteristics or availability of ECG equipment?

Methods: It is not entirely clear where the Markov modelling comes in. The model appears to be a simple decision tree. My understanding is that Markov modelling involves assuming that patients move repeatedly between states in cycles of modelling.

Methods: Was sensitivity modelled separately for STEMI and NST-ACS or was it assumed that sensitivity was the same the two conditions?

Discretionary Revisions

If possible, probabilistic sensitivity analysis should be undertaken as outlined above.
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests