Reviewer's report

Title: Cost-effectiveness of MRI compared to mammography for breast cancer screening in a high risk population

Version: 1 Date: 14 April 2008

Reviewer: Jeremy Goldhaber-Fiebert

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Major Compulsory Revisions

1. The use of “average” cost-effectiveness ratios can be misleading and should be removed from both the Abstract and the main body of the text. This is particularly the case because the comparator used is $0 cost and 0 QALY life expectancy. Such a comparator does not correspond to the status quo nor does it correspond to no treatment.

2. The authors report the “net benefit” of MRI in the abstract and then whether MRI is cost-effective at a $50,000 QALY threshold. It would seem more appropriate to report net health benefit? Reporting the Net health benefit and its 95% CI for a given WTP or thresholds will provide a more accurate and standard representation of the uncertainty analysis performed. This also impacts how the conclusions of the abstract are reported.

3. Please detail how the model developed in this analysis differs from the breast models developed by others previously such as those from the CISNET collaboration. Please discuss the features of this model that make it more appropriate than using a previous model and specifically how the output of the model developed for this analysis was compared and validated against data not used in its construction (i.e., how does its out compare to SEER to observation or clinical trial data?).

4. Please note the discount rate used in the methods section (page 7) and also note whether it was applied to costs and to quality adjusted life expectancy.

5. While the paper states that the published literature was used to parameterize the model, neither the body of the paper nor Table 1 provides citations for sources of the model parameters. Are any of the probabilities mentioned (death from other causes for example) age-specific? Complete citations should be made in the body of the paper. Also, the probabilities and age-specific probabilities should be further documented in the appendix.

6. The utilities used in the model are not specifically cited. This should be corrected in the body of the paper. Particular attention should be paid to not only citing but also explaining the utility value (0.89) for the temporary state of “False Positive” – is this due to factors other than anxiety? There are methodological discussions of temporary health states and their elicitation which may be useful to cite here.

7. In reporting the results of the probabilistic sensitivity analysis, the following
sentence appears problematic: “From the probabilistic sensitivity analysis, the ICER for the MRI was $151,890/QALY (95% confidence range: $130,233/QALY to $456,633/QALY).” From Figure 3, MRI sometimes costs more and provides less benefit which means that it is dominated (Quadrant II) which changes the interpretation of its incremental cost-effectiveness ratio. Computing an incremental cost-effectiveness ratio only for those times when a strategy is non-dominated can introduce bias. It would also be helpful for the authors to comment on the orientation of the confidence oval – what are the main factors that cause it to go from the upper left to the lower right (when MRI is less effective it is more costly)?

8. Table 1 notes probabilities that exceed 1.0 (for example, True Negative and Live Node Negative). It is unclear how to properly interpret a probability >1.0 and hence it is unclear what this means for the analysis and its results. Is this a function of the normal distributions imposed for probabilistic sensitivity analysis? If so, beta distributions may be more appropriate as they bound the probability between 0 and 1.

9. It is concerning that False Positive (0.89) has a utility that is lower than Breast Cancer (0.95). Please provide the citation for how this value is arrived at and also please comment in the text about how sensitive results are to assumptions about utility of false positive. It would appear that this is likely an uncertain and highly influential parameter.

10. The model schematic appears incomplete as there are utilities for health states not shown in the model schematic – (utilities for health states such as False Positive and False Negative Node Positive). Furthermore, unilateral and bilateral mastectomies are mentioned; does the model then track the remaining breast for further cancer? Please provide a more detailed model description, list of assumptions, and a diagram that shows all transitions and states.

11. It appears from Table 1 that the probability of having a positive result is fixed in the model. Probability of positivity is not a test characteristic (like sensitivity and specificity) that does not depend on prevalence of underlying disease. Since the tests are used repeatedly on a population that develops cancer and dies, the remaining population may have a lower prevalence of disease and thus the probability of positivity may be lower over time. Please comment on this both to clarify what is meant by probability of positivity and how the tests are operationalized in the model.

Minor Essential Revisions

1. Please provide a citation for the following sentence: “Medicare reimbursement data for hospital, physician, and laboratory services according to the methodology described in recently published work.” (page 8)

2. Please comment on whether for the probabilistic sensitivity analysis, any correlation structure was assumed for the normal distributions. For example, when sensitivities are higher are specificities lower in studies of these screening technologies? If so, should such correlation be reflected in the analysis? This could be noted as a limitation in the discussion section if data on the relationship between uncertainty in parameters do not exist.
3. Given that the authors note differences of their results from other CEAs of MRI vs. Mammography, it might be appropriate to comment about differences in their model from the studies/models that provide divergent results.

4. Please provide the results for all univariate analyses in the appendix in table form for all model parameters.

Discretionary Revisions

1. Please make the labels of probabilities in the figures and the tables less abbreviated (for example, “Birad03”) to facilitate easy reading

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests