Breast Cancer Screening: Technical Report Prepared for the National Commission on Prevention Priorities

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A. USPSTF Recommendation

The U.S. Preventive Services Task Force (USPSTF) recommends screening mammography, with or without clinical breast examination (CBE), every 1-2 years for women aged 40 and older. B Reccomendation. [1;2]The USPSTF found fair evidence that mammography screening every 12-33 months significantly reduces mortality from breast cancer. Evidence is strongest for women aged 50-69, the age group generally included in screening trials. For women aged 40-49, the evidence that screening mammography reduces mortality from breast cancer is weaker, and the absolute benefit of mammography is smaller, than it is for older women. Most, but not all, studies indicate a mortality benefit for women undergoing mammography at ages 40-49, but the delay in observed benefit in women younger than 50 makes it difficult to determine the incremental benefit of beginning screening at age 40 rather than at age 50. The absolute benefit is smaller because the incidence of breast cancer is lower among women in their 40s than it is among older women. The USPSTF concluded that the evidence is also generalizable to women aged 70 and older (who face a higher absolute risk for breast cancer) if their life expectancy is not compromised by comorbid disease. The absolute probability of benefits of regular mammography increase along a continuum with age, whereas the likelihood of harms from screening (false-positive results and unnecessary anxiety, biopsies, and cost) diminish from ages 40-70. The balance of benefits and potential harms, therefore, grows more favorable as women age. The precise age at which the potential benefits of mammography justify the possible harms is a subjective choice. The USPSTF did not find sufficient evidence to specify the optimal screening interval for women aged 40-49.[2]

B. Choice of Screening Tools and Intervals

The USPSTF recommends screening for breast cancer using mammography with or without clinical breast examination, but found insufficient evidence to conclude that clinical breast exam has an incremental benefit when added to mammography. Therefore, we based our estimates on mammography alone. The included effectiveness studies had screening intervals of 12 to 36 months, most between 12 and 24 months.

C. Literature Search and Abstraction

SEER (surveillance, Epidemiology and End Results) cancer statistics are a will-known, highly regarded source of cacner mortality data.[3] Therefore, an extensive search for cancer mortality data was not necessary.

C1. Effectiveness Literature:

We conducted a Level 1 literature search[4;5] to identify articles that examined the effectiveness of breast cancer screening in reducing mortality. This literature search identified 590 articles between January 1992 and October 2003 in PubMed. As a result of this search and the review of references in identified articles, we identified a total of 85 articles for potential abstraction.[6-90] Several articles were excluded for more than one reason. The reasons for exclusion prior to abstraction included the availability of more recent or more complete reports for the same study populations, lack of breast cancer mortality as an endpoint, and modeled mortality endpoints. In addition we excluded meta-analysis and review articles. We used results of our own literature abstraction rather

than those of carefully conducted systematic reviews in order utilize each study's adherence data to better estimate effectiveness in current practice. For the same reason, we did not limit our abstraction to randomized controlled trials. After these exclusions we abstracted 17 articles:[8-10;15;18;27;33;42-44;48;54;58;62;65;66;81] each examined the relationship between breast cancer screening and breast cancer mortality.

C2. Cost Effectiveness Literature:

We conducted a Level 1 literature search[4;5] to identify cost effectiveness literature on breast cancer screening. This literature search identified 92 articles between January 1992 and October 2003 from PubMed. As a result of this search and review of references in identified articles, we identified a total of 27 articles for potential abstraction.[91-117] Twenty three of these articles were not abstracted because they assessed resource use of health care systems outside the United States, analyzed screening in settings outside of primary care, examined strategies to increase mammography use rather than mammography itself, analyzed only costs rather than cost-effectiveness, or were older results from models with recent updates. After these exclusions, four of the articles were abstracted.[101;105;108;109]

D. Clinically Preventable Burden (CPB) Estimate

Conceptually, CPB is the burden addressed by the service multiplied by the effectiveness of the service. Table 1 shows the summary calculations for CPB. Some of the data points in Table 1 are estimates from the literature and others are calculated based upon other data in the table. The "Data Source" column in Table 1 shows either the reference numbers for estimates in parenthesis or the formula used to calculate the variable. The letters in the formulas refer to the row labels (left most column) for the data on which the calculation is based. The "Base Case" column shows the best available estimate for each variable that is used in our calculation of CPB, and the "Range" column shows the range over which the point estimates arre varied in our sensitivity analysis.[5;118] We created additional tables (not shown) to summarize the evidence and perform supporting calculations. Their contents are described below.

D.1 Burden of Disease:

Breast Cancer Mortality: Rows a and b.

CPB is based on delivery of the service to a one-year U.S. birth cohort (the size of which is defined consistently in this study as 4 million) over the age range the service is recommended by the USPSTF. Breast cancer mortality (rows a and b) is estimated from 2000 death rates data using the SEER database.[3] US population estimates used to calculate incidence rates are taken from the 2000 census.[119] The number of breast cancer deaths in a birth cohort of 4 million individuals is estimated and stratified by 5-year age groups, using women only for ages 40 years and older. In order to take into account the potential difference in the effectiveness of screening before and after age 50, we separate mortality into two age groups. An exact age cut-off for mortalities that are preventable by screening up to age 49 cannot be defined. We made the simplifying assumption that half of breast cancer mortalities in ages 50-54 are potentially preventable by screening during ages 40-49 and the other half are potentially preventable by screening after age 50. An estimate of 5,947 breast cancer deaths among women 40-49 yrs and 50% of the women

ages 50-54 yrs in a birth cohort is obtained by multiplying the incidence rate by the number of years of life lived in the birth cohort (row a). Similarly an estimate of 52,569 breast cancer deaths among women 55 yrs and older, and 50% of the women ages 50-54 yrs (row b).

Delivery Rates: Rows c and d.

These estimates reflect cumulative (lifetime risk) breast cancer deaths among women in a birth cohort given current breast cancer screening and treatment practices. To estimate the total value of screening and treatment, we first predict what the burden would be in the absence of screening by adjusting for current screening and treatment rates. We use the 1995 United States breast cancer screening rate using mammography for screening purposes in the last 2 years for women 40-49 yrs of 57% (row c) and 63% (row d) for those ages 55 yrs and older, estimated from the Behavioral Risk Factor Surveillance Survey (BRFSS) as the delivery rate of screening to the service population.[120] These rates reflect self-reported receipt of mammography within the last two years, adjusted by self-report as to whether or not the mammography was for screening purposes.

Predicted Deaths in the Absence of Screening: Rows e and f.

The efficacy estimates in the calculations shown for rows e and f are explained below in the discussion of efficacy and effectiveness. Using the calculations shown for row e, we estimate that 7,138 breast cancer deaths would occur among women 40-49 yrs (row e) and 50% of the women between ages 50-54 years in the birth cohort in the absence of screening and treatment. For women 55 years and older and 50% of the women 50-54 years, we estimate that 69,390 breast cancer deaths would occur in the birth cohort (row f).

D.2 Effectiveness of Screening:

The primary distinction we make between efficacy and effectiveness is that effectiveness reflects the level of patient adherence that can be expected in every-day practice, while efficacy reflects 100% patient adherence.[5;118] CPB is based on effectiveness, where patient adherence is defined as the percent who accept the service once offered and adhere with follow-up treatment or advice to change behavior.

D.2.1 Effectiveness Literature:

Of the 17 articles that were abstracted for effectiveness of breast cancer screening in reducing mortality,[8-10;15;18;27;33;42-44;48;54;58;62;65;66;81] one time-series study was excluded due lack of data on adherence with the studied screening programs;[33] one retrospective cohort study was excluded due to low adherence with the evaluated screening program combined the potential for contamination of the comparison group;[66] and one case-control study was excluded because it compared responders to non-responders without control for potential confounders.[65] In addition, the case-control estimates from one study were excluded for the same reason, but time-series estimates from the same study were included.[18]

D.2.2 Efficacy of Screening: Rows g and h.

We summarize effectiveness estimates for women 39-49 years of age separately from those for women 50 or years of age. Age is usually defined as age at diagnosis in measuring breast cancer mortality by age group. For ages 39-49 we include estimates from seven RCTs[8;9;15;27;43;54;58] and one case-control study.[48] We use adherence with invitations for screening in the RCTs to estimate what the impact of screening would be with 100% adherence (i.e. efficacy = effectiveness ÷ adherence), and for the case-control study we treat the results as an approximation of efficacy as all individuals identified as having received screening received at least one screen. Our adjustment for compliance is, in effect, a simplification of the adjustment proposed by Newcombe,[121] but does not incorporate contamination of the comparison group which is infrequently reported. The range of the resulting estimates is -8% to +46% with a mean of 24.3% and median of 29.3%. The estimate from the single case-control study is 20%. Due to the wide variation in estimates, we chose the median as our base-case estimate (row g).

For women 50 or more years of age we include estimates from seven RCTs,[8;15;27;42;54;58;81] one case-cohort study,[62] two case-control studies,[44;48] one retrospective cohort study,[10] and one time-series study.[18] After adjustments to obtain estimates of efficacy adjusting for non-adherence the range of the resulting estimates is -2% to +52% with a mean of 35.9% and median of 38.2%. If only RCTs were included, the mean and median would be virtually unchanged (34.0% and 38.5%). Due to the wide variation in estimates, we chose the median as our base-case estimate (row h).

In sensitivity analysis, we include zero in the plausible range of estimates for the effectiveness of screening during ages 40-49+ because two studies included in our summary effect found no effect for this age group and others were not statistically significant. In the age group 50+, only one of nine RCTs found no effect of screening on mortality, and therefore for this age group we use the next lowest estimate, 20%, as our lower bound for plausible estimates.

D.2.3 Patient Adherence: Row i.

The mean adherence in the randomized control trials, measured as percent of scheduled screens attended is about 75% (range 55% to 90%). All but one of these trials occurred outside the United States and all trials started before the benefits of mammography were well documented. Therefore the current adherence with clinician advice to receive breast cancer screening in the US may be different. In 2003, approximately 85% of women ages 40+ who responded to the BRFSS questionnaire received a mammogram with in the last two years, and 80% of women had received a mammogram for screening purposes.[120]

We reviewed the literature on the effectiveness of invitations among women who are not up-to-date with screening. We excluded studies in non-US populations, studies in which some who were targeted were up-to-date (unless we could separately calculate results for those not up-to-date), studies in which 100% of participants received a prior screen, studies limited to women who had a prior screen, studies of systems to increase screening that did not focus on invitations for screening, and studies among women who may have been self-selected due to their agreement to participate in an RCT on adherence.[111;122-155] Among the included studies,[156-166] on average 55% of women who are not up to date with screening were up-to-date within 3 to 12 months following face-to-face, mail, or telephone recommendations to receive screening.

If we were to apply this estimate to the 15% of women who have not had a mammogram in the last 2 years, we calculate that approximately 88% of women would adhere with offers of screening (80% up-to-date with screening plus 15%x55% = 8% additional screened with invitations). However, this calculation is approximate because it relies on:

- accurate recollection of time since last screen among BRFSS participants;
- an assumption that frequency of prior screening offers to women who are not up-to-date in the US population is similar to frequency in participants of studies of the effectiveness of invitations; and
- an assumption that adherence with the various types of screening invitations in the included studies (such as mailed invitations and reminders) is similar to adherence with in-person recommendations by primary care clinicians.

Similar issues and similar overall adherence estimates are found in estimating adherence with cervical cancer screening. We use the same adherence estimate for both services (85% row i) so that their relative ranking does not reflect differences in adherence that are not supported by good evidence.

D.3 CPB Estimate: Rows j-p.

The total number of deaths prevented is equal to predicted breast cancer deaths among women multiplied by effectiveness of screening and treatment. The prevention service of screening for breast cancer prevents 1,780 deaths (row j) if periodic screening is offered to all women 40-49 years in a birth cohort of 4 million. And for women 50 years and older, periodic breast cancer screening prevents 22,520 deaths (row k). For each death prevented, we tabulate the years of life saved as the life expectancy for the age at which the breast cancer death would have occurred.[3;167] We show the average life-expectancy weighted by the number of deaths per age group in rows l and m. Multiplying this average by the number of deaths prevented for women ages 40-49 years yields 59,415 life years saved (row n). Similarly, for women ages 50 years and older yields 296,499 life years saved (row o). CPB is the total of quality adjusted life years saved from mortality prevented by offering periodic screening for breast cancer and treatment over the lifetimes of women starting at age 40 in a birth cohort of 4 million individuals: 355,914 life years saved (row p).

D.4 Sensitivity Analysis for CPB

In single variable sensitivity analysis we vary the efficacy of breast cancer in reducing mortality for ages 40-49 and ages 50+ together with the presumption that if either the literature or our adjustments for compliance in the studies causes us to misestimate the efficacy in one age group it has the same effect for the other. Because screening in ages 40-49 addresses relatively few breast cancer mortalities, changing the estimate of effectiveness for this age group alone does not substantially impact the CPB estimate.

We find CPB to be most sensitivity to changes in the efficacy of screening at reducing breast cancer deaths (rows g and h of Table 1) and, secondarily, to the estimates of deaths in a birth cohort given current screening practices (rows a and b), and the years of life saved per death prevented (rows l and m). Over the ranges specified in Table 1 for the efficacy of breast cancer screening, CPB decreases and increases 50% from the base-

case estimate of 356,000 years of life saved. CPB is moderately sensitive to the estimate of cancers in a birth cohort given current screening rates (row a), current screening rates (row b), and the years of life gained for each death prevented (row j). Changing the frequency of screening in the current population (rows c and d) or adherence with screening (row i) changes CPB by less than 15%.

Following our methods,[5;118] we conduct multivariate sensitivity analysis to determine the three variables which, when changed together produces the highest and lowest estimates of CPB. Simultaneously changing the three variables noted above over the ranges specified in Table 1 produces a CPB range of 110,00 to 770,000 years of life saved.

Our estimate of CPB is expressed in years of life saved because it does not include net quality of life improvements. The CE literature on breast cancer screening also expresses results in terms of years of life saved rather than QALYs. This may be because data for estimating quality of life adjustments are scarce. Salzmann et al. provided an cost-effectiveness estimate in terms of $/QALY saved only as secondary analysis due to insufficient data on quality of life effects.[109] To explore the potential importance of excluding net QALYs lost from morbidity, we estimate the potential QALYs saved from fewer late-stage cancers and the potential QALYs lost to screening and biopsies resulting from screening.

Although treatment choices vary from person-to-person, we assume that early stage cancers would, on average, have a smaller quality of life decrement than late stage cancers due to reduced probability of chemotherapy and fewer occurrences of non-localized cancer. Based on staging in the Malmo trial,[81] we estimate the number of stage II-IV cancers with and without screening in a birth cohort of 4,000,000 and we assume that, on average, each stage of late stage cancer prevented by early detection would bring a marginal improvement of quality of life (early stage compared to late stage) of 0.1 QALYs for 6 months. The result is a gain of 18,000 QALYs.

To estimate the quality of life decrement from screening and biopsy, we assume that each screen brought a quality of life decrement of 0.05 QALYs for a duration of one day, and that each positive screen resulted in a biopsy and anxiety equivalent to 0.1 QALYs lost for a period of 2 weeks. The result is a loss of 8,000 QALYs. Therefore, this rough approximation yields a net gain of 10,000 QALYs, or an increase in CPB of 2%. With different assumptions, net loss of QALYs can also be obtained. It is not clear whether quality of life adjustment will increase or decrease CPB and it seems unlikely that the net impact will substantially change our CPB estimate in either direction. Therefore, the estimate of years of life saved in Table 1 is also a reasonable estimate of number of quality adjusted years of life saved and is comparable to the CPB measures for other services in this study.

The estimate of CPB may be overstated due to the inclusion of a mortality benefit for all women above the age of 70. The USPSTF does not specify an upper age limit for screening and notes that the risk of breast cancer mortality increases with age and false positive screens decrease. The USPSTF does note that screening may be discontinued for women with shortened life-expectancy. In including all breast cancer mortality of older women, we assume that that breast cancer is rarely listed as the cause of death for women for whom screening was not recommended by the physician due to shortened life-expectancy.

E. Cost-Effectiveness Estimate

We use the same methods for producing estimated of CE across preventive services.[5;118] These methods are consistent with the 'reference case' of the Panel of Cost-Effectiveness in Health and Medicine.[168] Our methods include the use of a 3% discount rate for both cost and health benefits, the exclusion of productivity losses from disease costs, and the exclusion of medical costs that are not related to the conditions prevented by the service. We use year 2000 dollars of all cost data.

E.1 Cost-effectiveness Literature.

We abstracted four studies of the cost-effectiveness of screening for women 40 or more years of age.[101;105;108;109] Three studies examined CE of screening up to the age of 70. Of these, the study by Salzmann et al.[109] provided superior reporting of model parameters and results, allowing us to base our CE estimate on this study rather than developing a new CE model. In addition, the same authors extended their model to estimate the marginal benefits of screening after the age of 69,[101] allowing us to reasonably estimate the CE of screening from age 40-79 using the results from a single model. Therefore, we chose these two studies[101;109] as the basis of our CE estimate.

E.2 Adjusted CE Ratio.

In the study of screening at younger ages Salzmann et al.[109] provided base-case estimates in terms of years of life saved, and a secondary analysis with roughly estimated quality of life adjustments. This was not repeated by Kerlikowske et al.[101] in the study of screening at older ages. As discussed above for CPB, the direction of the effect of quality of life adjustments for CPB is uncertain. The rough quality of life adjustments by Salzmann et al. found a differences of only 3% in life years saved compared to QALYs saved (with years of life saved being greater).

Table 2 shows the results of Salzmann et al. and Kerlikowske et al., with adjustments to ensure consistency with other CE estimates in this study. Rows a-e show our calculation of the average CE of screening (screening compared to no screening) from ages 40-69 using the results reported in Table 3 of Salzmann et al.[109] and Table 5 of Kerlikowske et al.[101] These estimates reflect screening every 18 months from ages 40-49 followed by biennial screening from ages 50-69 and ages 70-79. Row g shows the same estimates adjusted to year 2000 dollars using the MCPI. Kerlikowske et al. used similar costs as Salzmann et al., and assumed that screening was equally effective for ages 70-79 as ages 50-69. Therefore, the difference in the CE ratios appears to be driven primarily by fewer years of life saved for each death prevented by screening in during ages 70-79.

E.2.1 Adjustment of Screening Costs.

Rows g-j of Table 2 show an adjustment made to screening costs to account for incomplete adherence. The effectiveness of screening in reducing mortality in the Salzmann and Kerlikowske model is similar to the effectiveness estimates resulting from our literature review. However, in estimating the costs of screening, it appears that both Salzmann et al. and Kerlikowske et al. did not account for incomplete adherence that is reflected in the literature-based estimates of effectiveness. Therefore, in rows g-j we reduce the costs of screening by average non-adherence from our literature review (25%),

and recalculate the CE ratios. The result, after inflation adjustment and this adjustment to screening costs are shown in row j.

E.2.2 Adjustment of Patient Time Costs.

Finally, we make an adjustment to account for patient time costs for screening and follow-up. Rows k-q show the calculation of the discounted time costs of travel and attendance of screening visits, where the time costs for a visit are based upon 2 hours valued at average annual earnings plus benefits.[169] We calculate the total number of screening and follow-up diagnostic visits based on the modeled frequency for each age group, the annual survival rate from life tables,[167] and the estimate of 25% non-adherence used to adjust screening costs (row h). The time costs of follow-up visits are based on the probability of abnormal screening results used by Salzmann et al. We assume 50% of evaluations would eventually occur in the absence of screening and thus did not attribute time costs for these visits to screening. We use life tables[167] to estimate the median year of the screening from the beginning of each model and present value tables to approximate the effect of discounting time costs at a 3% annual rate (rows n-p). Because the two models start at different ages (age 40 in Salzmann et al.; age 65 in Kerlikowske et al.), the time costs for the older age group are not discounted over a longer time period as might be expected.

E.2.3 Weighted Adjusted CE Ratio

The discounted time costs are added to the costs of screening (row q) and used to calculate our base-case CE estimate for each age group: 40,700 $/LY saved for ages 40-69 and 77,400 $/LY saved for ages 70-79 (row r). Ideally, we would have added the screening costs, net treatment costs, and LY saved though screening across both age groups and then calculated an overall CE of screening for ages 40-79. However the costs and LY saved reported in the two studies were discounted to different ages and therefore cannot be added. Although discounted to different ages, the CE ratios are still comparable because, within each model, all costs and benefits are discounted to the same age. Therefore we estimate an overall CE ratio by weighting the CE ratio for each age group according to the number of screens in each age group. The result is our base-case estimate of 47,900 $/LY saved.

E.3 Sensitivity Analysis for CE.

In sensitivity analysis, we change variables as shown in the range column of Table 2. In addition, we vary the net-costs of treatment and the years of life saved simultaneously to approximate the impact of over- and understating the effectiveness of screening. We still change LYs saved (row d) separately in order to assess the impact of changes to the underlying mortality risk. Because changes to net savings have very little impact on the CE ratio, the changing effectiveness and changing years of life saved have nearly identical impact on the CE ratio (range: 38,500 to 63,600 $/LY saved). Changing screening costs produces a CE range of 38,800 to 57,000 $/LY saved, and changing the time costs of screening produces a CE range of 42,500 to 53,300 $/LY saved.

In multivariate sensitivity analysis, we follow our standard methods rather than our methods for sensitivity analysis with aggregate variables[5;118] because costs and treatment savings are reported separately and we are able to assess the impact of

changing effectiveness. Therefore we change three variables simultaneously to determine which combination produces the widest range. Changing effectiveness, screening costs, and the LY years (to assess changes to breast cancer mortality risk) produces a range of 25,000 to 101,000 $/LY saved.

F. Scoring

We ranked services in the Prevention Priorities Project based upon scores for CPB and CE rather than point estimates.[4;5] For each measure, we assigned scores according to the quintile in which the service's CPB and CE estimates fall among all services included in the study scope. Services having the highest CPB or best-cost-effectiveness received a score of 5.

The base case estimate of 356,000 QALYs saved resulted in a CPB score of 4. The base-case is highest among the services that received a score of 4. Therefore it is not surprising that sensitivity analysis revealed several scenarios in which CPB would have received a score of 5. At the same time, sensitivity analysis also revealed scenarios in which CPB would have received a score of 3. No scenarios produced CPB estimates that were consistent with scores of 2 or 1.

The base case CE estimate of $48,000/QALY saved resulted in a CE score of 2. The base case estimate was near the midpoint of all services that received a CE score of 2. Multivariate sensitivity analysis found several scenarios that generated CE estimates consistent with a CE score of 3, but none consistent with CE scores of 1, 4, or 5.

The base case estimates for CPB and CE produced a total score of 6, and the multivariate sensitivity analysis indicated that a total score as high as 8 and as low as 5 are possible.

G. Limitations

There are several data points that were uncertain in the analysis. The uncertainty of the benefit of screening from ages 40-49 on breast cancer mortality after age 50 had a minimal effect on CPB and CE because the portion of breast cancer deaths that occur in the years immediately following age 49 was small. Potentially more importantly, there were few data directly demonstrating the effectiveness of screening past the age of 69. Following Kerlikowske et al.,[101] we assumed the mortality reduction with screening after age 69 was equal in percentage terms to the mortality reduction of screening from age 50 to 69. Finally, our estimate of the CE of screening excluded ages 80+. It is likely that screening was less cost-effective in this age group due to fewer years of life saved per death prevented. However, based on life tables, we estimated that only 12% of all screens would occur after age 80.

There were no direct estimates of adherence with clinician recommendations to receive screening, but sensitivity analysis revealed that changes to adherence within a reasonable range had little impact on CPB.

Data on quality of life impact of screening (including the frequency of some events, the magnitude of quality of life reduction or improvement, and the duration of quality of life change) were so sparse as to make quality of life adjustments impractical. However, it does not appear that quality of life adjustment would substantially impact either CPB or CE because years of life saved were likely to dominate small changes to

quality of life. When using assumed values to modeling quality of life reductions following treatment and living with metastatic cancer, Salzmann et al. found changes of CE ratios of less than 5% compared to CE based upon un-adjusted year of life saved.[109] Positive improvements to quality of life from earlier, less demanding treatments would be offset by reductions due discomfort of screening and anxiety of false-positive results.

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Table 1. Summary of CPB Estimate for Breast Cancer				
Row	**Variable**	**Base Case**	**Data Source**	**Range for Sensitivity Analysis**
a	Deaths in birth cohort between ages 40-49, and 50% ages 50-54	5,947	[3]	+/- 20%
b	Deaths in birth cohort 50% of ages 50-54, and ages 55+	52,569	[3]	+/- 20%
c	Frequency of screening in last two years ages 40-49	57%	[120]	65% to 75%
d	Frequency of screening in last two years ages 55+	63%	[120]	70% to 80%
e	Predicted deaths in the absence of screening ages 40-49, and 50% ages 50-54	7,138	a/(1-c*g)	
f	Predicted deaths in the absence of screening 50% of ages 50-54, and ages 55+	69,390	b/(1-d*h)	
g	Efficacy of mammography screening in preventing mortality ages 40-49	29.3%	[8;9;15;27;43;48;54;58]	0% to 40%
h	Efficacy of mammography screening in preventing mortality ages 50+	38.2%	[8;10;15;18;27;42;44;48;54;58;62;81]	20% to 50%
i	Adherence all ages	85%	[120;156-166]	75% to 95%
j	Deaths prevented by screening ages 40-49	1,780	e*g*i	
k	Deaths prevented by screening ages 50+	22,520	f*h*i	
l	LE at average age of breast cancer death ages 40-49, and 50% ages 50-54	33.4	[166]	+/- 20%
m	LE at average age of breast cancer death 50% of ages 50-54, and ages 55+	13.2	[166]	+/- 20%
n	LYs saved from screening ages 40-49	59,415	j*l	
o	LYs saved from screening ages 50+	296,499	k*m	
p	Total LY saved (CPB)	355,914	n+o	

Table 2. Summary of CE Estimate for Breast Cancer

Row	Variable	Base Case Ages 40-69	Base Case Ages 70-79	Data Source	Range
a	Net treatment costs	(1,050,000)	1,040,000	[109]	+/- 25%
b	Screening costs	14,850,000	3,950,000	[109]	+/- 25%
c	Net costs	13,800,000	4,990,000	[109]	
d	LYs saved	393	67.7	[109]	+/- 25%
e	$/LY saved	35,115	73,708	= c/d	
f	Price index to $2000	0.845475	0.92830		
g	$/LY saved in $2000	$41,532	$79,401	= (c/f)/d	
h	Compliance adjustment	25%	25%		
i	Adjusted screening costs	13,173,061	3,191,317	= (b/f)*(1-h)	
j	Adjusted CE ratio in $2000	30,847	62,501	= (i+a)/d	
k	Time cost per trip	$42	$42	[169]	+/- 50%
l	Screening and follow-up visits during age range per 10,000	126,203	30,999	see text	
m	Time costs for screening	$5,340,918	$1,311,898	= k*l	
n	Median years to discount additional screening costs (from beginning age of respective models)	11	9	[167]	
o	Discount factor for time costs	0.722	0.766	present value tables	+/-10%
p	Time costs discounted 3%	$3,858,279	$1,005,439	= m*o	
q	Costs of screening including patient time costs	$17,031,340	$4,196,756	= i+p	
r	Final CE ratio ($/LY saved)	40,665	77,352	= (q+a)/d	
s	Weighted CE ratio	47,900			