Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.
eAppendix. Additional Model Methods and Expanded Results

Decision Tree Parameters

The overall prevalence of pathogenic HBOC variant carriers (0.5%) was based on data from the Geisinger MyCode Community Health Initiative, a Geisinger system-wide DNA biobank with more than 190,000 patient-participants in Pennsylvania and New Jersey.\(^1\)\(^2\) We used test sensitivity (99%) and specificity (99%) to calculate the likelihood that tested individuals are correctly identified.\(^3\) False positives were not considered other than our assumption that a confirmation test (with associated cost) would correct the screening error. The proportion of HBOC variants identified with family history testing was 17.4%, based on a prior cost-effectiveness analysis of HBOC population screening versus family history testing alone.\(^4\) We then used a recent database analysis of 95,561 women who were tested for HBOC using a next generation sequencing panel to calculate the proportions of HBOC variants that were BRCA1, BRCA2, ATM, CHEK2, MSH6, PALB2, RAD51C, and TP53.\(^5\)

Markov Model Transitions

A proportion of pre-cancer, known carriers who opted to undergo intensive screening entered the Markov model in starting state 1, in which they received mammography plus MRI according to age-based guidelines for high risk individuals.\(^6\)\(^7\) Pre-cancer (1) noncarriers, (2) known carriers who opted out of intensive screening, and (3) unknown
carriers entered the Markov model in starting state 2, in which they received mammography only according to age-based guidelines for average risk individuals.\(^8\), \(^9\) Known carriers could opt for prophylactic RRM or RRSO based on age-based cumulative uptake among BRCA1/2 positive women (Figure 2 in main text).\(^10\) We modeled a 1-year health state for the year of the procedure, wherein we applied procedure costs and disutilities (Table 1 in main text). Women who underwent RRM or RRSO then transitioned to post-RRM or post-RRSO procedure health states with reduced risks of cancer incidence.\(^11\) Individuals with one procedure could transition to another 1-year state for a second procedure using a weighted probability of RRM and RRSO, with weighted procedure costs and disutilities; these patients then transitioned to a post-2nd procedure health state where we assumed their breast cancer risk was zero, but the age-based, RRSO-adjusted probability of ovarian cancer remained.\(^11\) We assumed the small number of individuals who receive RRM and/or RRSO and nonetheless go on to develop cancer transition to earlier stage cancers due to continued intensive screening.

All individuals were at risk for breast or ovarian cancer according to age-based cancer incidence among carriers and non-carriers (Figure 2 in main text).\(^12\)-\(^14\) We assumed women undergoing intensive mammography plus MRI would be diagnosed at an earlier stage, on average, than those undergoing standard mammography based on a study showing there were significantly fewer patients with positive lymph nodes at the time of cancer removal surgery in the MRI-screened group compared to the mammography-only screened group.\(^15\) We assumed equivalent incidence of earlier versus later stage...
breast or ovarian cancer, however we applied a mortality risk reduction to earlier stage breast cancer health states over the individual’s remaining lifetime. In both the earlier and later stage cancer states, we modeled first year-specific treatment costs and utility values. Patients who survived the first year of breast or ovarian cancer then transitioned to post-breast or post-ovarian cancer health states with long-term/continuing treatment costs and utility values.

We also derived age-based estimates of non-BRCA variant (ATM, CHEK2, MSH6, PALB2, RAD51C, TP53) cancer incidence from Lu et al., who conducted whole-exome sequencing and gene-phenotype associations on a sample of 11,416 patients with clinical features of breast cancer, ovarian cancer, or both from 1200 hospitals and clinics across the United States, plus 3988 controls who were referred for genetic testing for noncancer conditions. Odds ratios from Lu et al. of breast and/or ovarian cancer risk were converted to relative risk estimates and applied to the cancer incidence data derived for the noncarrier population. Non-BRCA mutations were modeled in the Markov model as an HBOC variant prevalence-weighted pooled group. Annual age-based cancer incidence among noncarriers was derived from the Surveillance, Epidemiology, and End Results (SEER) Program.

**Breast Screening Uptake**

We based uptake of mammography and MRI on current guidelines. Noncarriers and unknown carriers were assumed to undergo routine mammography according to
guidelines for average risk women; starting at age 40, we modeled that 50% chose to receive optional annual mammography, increasing to the recommended 100% from ages 45-54, then all women received recommended biannual mammography from age 55 until death. Known carriers were assumed to undergo routine mammography according to guidelines for increased risk women, which recommend annual mammography alternated with annual breast MRI every 6 months. We assumed 75% of women with known increased risk opted for intensive screening with MRI in addition to mammography. We further assumed the remainder of known increased risk women received mammography only at the recommended frequency.

Cascade Testing Module
We used a decision tree to organize key elements of cascade testing including (a) the probability a newly identified carrier will inform their family members, (b) the number of living first degree female relatives, (c) the probability that informed relatives will opt to undergo testing, (d) carrier/noncarrier status, and (e) testing and/or family history testing result. The probabilities for (a) and (c) were informed by a review of family communication of genetic results studies;\textsuperscript{16, 17} based on our findings, we assumed that 70% of population screening identified carriers go on to inform their family members, and 20% of family members go on to receive cascade testing. Probability (b) was informed by the Panel Study of Income Dynamics (PSID), a longitudinal household survey\textsuperscript{18}; from this we extracted the average number of surviving mothers, sisters, and
daughters by age per woman screened. Probabilities for (d) and (e) were equivalent to those used in the primary population screening model.

**eFigure 1. Cascade Testing Module Decision Tree**

The cascade testing module utilized age-based results from the primary screening model, combined with publicly available data on the number of first-degree female relatives of each identified carrier, to calculate the incremental cost and benefits and their impact on the overall model ICER. We estimated age-based incremental outcomes from ages 20 to 100, and estimated a weighted (by number and ages of mother, sisters, and daughters) sum of incremental cost and QALYs over all newly identified family members. These weighted incremental estimates were then “fed back” into the primary population screening model, such that the incremental outcomes from the cascade model are tied to the age of the patient entering the primary model. The process of using the primary model to inform cascade testing incremental outcomes, and then

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adding back to the primary model for the cascade screening scenario, is depicted below.

**eFigure 2. Calculation of Cascade Testing Outcomes**

| Population Screening Model | Age of Screened Individual | Known Carrier Outcomes | Unknown Carrier Outcomes | Incremental Outcomes |
|----------------------------|-----------------------------|------------------------|--------------------------|----------------------|
| 25                         | \(a_{25}\)                  | \(b_{25}\)             | \(a_{25} - b_{25}\)     |                      |
| 26                         | \(a_{26}\)                  | \(b_{26}\)             | \(a_{26} - b_{26}\)     |                      |
| 27                         | \(a_{27}\)                  | \(b_{27}\)             | \(a_{27} - b_{27}\)     |                      |
| ...100                     | \(a_{100}\)                 | \(b_{100}\)            | \(a_{100} - b_{100}\)   |                      |

| Cascade Testing Model | Age of 1st Degree Relative | # Newly ID’d Carrier’s Parents (x) | # Newly ID’d Carrier’s Siblings (y) | # Newly ID’d Carrier’s Children (z) |
|-----------------------|-----------------------------|-----------------------------------|------------------------------------|-----------------------------------|
| 25                    | \(x_{25} \cdot (a_{25} - b_{25})\) | \(y_{25} \cdot (a_{25} - b_{25})\) | \(z_{25} \cdot (a_{25} - b_{25})\) |                      |
| 26                    | \(x_{26} \cdot (a_{26} - b_{26})\) | \(y_{26} \cdot (a_{26} - b_{26})\) | \(z_{26} \cdot (a_{26} - b_{26})\) |                      |
| 27                    | \(x_{27} \cdot (a_{27} - b_{27})\) | \(y_{27} \cdot (a_{27} - b_{27})\) | \(z_{27} \cdot (a_{27} - b_{27})\) |                      |
| ...100                | \(x_{100} \cdot (a_{100} - b_{100})\) | \(y_{100} \cdot (a_{100} - b_{100})\) | \(z_{100} \cdot (a_{100} - b_{100})\) |                      |

Sum of sums:

\[
\sum_{x} x \cdot (a - b\cdot x) = \sum_{y} y \cdot (a - b\cdot y) = \sum_{z} z \cdot (a - b\cdot z)
\]

**Population Screening Model Results** + **Cascade Testing Model Results** = **Population Screening + Cascade Testing Results**

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### eTable. Expanded Model Results

| Screened Age | Earlier Stage Cases/100K | Later Stage Cases/100K | Total Cancer Cases/100K | Cost/Woman Screened | QALYs/Woman Screened | Life Years/Woman Screened | ICER |
|--------------|--------------------------|------------------------|-------------------------|---------------------|----------------------|---------------------------|------|
| 20           | 125                      | -215                   | -90                     | $245                | 0.0027               | 0.0022                    | $90,600 |
| 21           | 126                      | -215                   | -89                     | $245                | 0.0028               | 0.0023                    | $89,100 |
| 22           | 127                      | -215                   | -88                     | $245                | 0.0028               | 0.0023                    | $87,600 |
| 23           | 128                      | -215                   | -87                     | $245                | 0.0028               | 0.0023                    | $86,200 |
| 24           | 128                      | -215                   | -86                     | $245                | 0.0029               | 0.0024                    | $84,900 |
| 25           | 131                      | -216                   | -86                     | $246                | 0.0029               | 0.0024                    | $83,800 |
| 26           | 132                      | -216                   | -83                     | $247                | 0.0029               | 0.0024                    | $84,200 |
| 27           | 134                      | -215                   | -81                     | $248                | 0.0029               | 0.0024                    | $84,700 |
| 28           | 135                      | -214                   | -79                     | $249                | 0.0029               | 0.0024                    | $85,400 |
| 29           | 137                      | -214                   | -77                     | $251                | 0.0029               | 0.0024                    | $86,500 |
| 30           | 138                      | -214                   | -75                     | $252                | 0.0029               | 0.0024                    | $87,700 |
| 31           | 140                      | -212                   | -72                     | $252                | 0.0028               | 0.0023                    | $90,700 |
| 32           | 143                      | -211                   | -68                     | $253                | 0.0027               | 0.0022                    | $94,400 |
| 33           | 145                      | -209                   | -64                     | $253                | 0.0026               | 0.0021                    | $99,200 |
| 34           | 147                      | -207                   | -60                     | $254                | 0.0024               | 0.0020                    | $105,300 |
| 35           | 150                      | -206                   | -56                     | $255                | 0.0023               | 0.0019                    | $112,500 |
| 36           | 152                      | -204                   | -52                     | $255                | 0.0022               | 0.0019                    | $118,100 |
| 37           | 154                      | -203                   | -49                     | $255                | 0.0020               | 0.0018                    | $125,200 |
| 38           | 155                      | -201                   | -46                     | $256                | 0.0019               | 0.0017                    | $134,300 |
| 39           | 157                      | -199                   | -42                     | $256                | 0.0017               | 0.0016                    | $146,900 |
| 40           | 157                      | -194                   | -37                     | $257                | 0.0016               | 0.0014                    | $164,100 |
| 41           | 157                      | -192                   | -35                     | $258                | 0.0015               | 0.0014                    | $175,800 |
| 42           | 158                      | -190                   | -32                     | $258                | 0.0014               | 0.0013                    | $190,400 |
| 43           | 158                      | -188                   | -30                     | $258                | 0.0012               | 0.0012                    | $209,200 |
| 44           | 159                      | -185                   | -27                     | $259                | 0.0011               | 0.0011                    | $234,500 |
| 45           | 159                      | -183                   | -24                     | $261                | 0.0010               | 0.0010                    | $268,200 |
| 46           | 159                      | -181                   | -22                     | $261                | 0.0009               | 0.0009                    | $291,300 |
| 47           | 159                      | -179                   | -20                     | $262                | 0.0008               | 0.0009                    | $320,800 |
| 48           | 159                      | -177                   | -18                     | $262                | 0.0007               | 0.0008                    | $359,800 |
| 49           | 159                      | -175                   | -16                     | $263                | 0.0006               | 0.0008                    | $415,100 |
| 50           | 159                      | -173                   | -14                     | $265                | 0.0005               | 0.0007                    | $482,100 |
| 51           | 157                      | -171                   | -13                     | $265                | 0.0005               | 0.0007                    | $512,600 |
| 52           | 156                      | -168                   | -13                     | $264                | 0.0005               | 0.0006                    | $549,200 |
| 53           | 154                      | -166                   | -12                     | $264                | 0.0004               | 0.0006                    | $593,900 |
| 54           | 153                      | -164                   | -11                     | $264                | 0.0004               | 0.0006                    | $649,700 |
| 55           | 148                      | -157                   | -9                      | $263                | 0.0003               | 0.0005                    | $831,500 |
| 56           | 146                      | -155                   | -8                      | $262                | 0.0003               | 0.0005                    | $889,700 |
| 57           | 144                      | -152                   | -8                      | $261                | 0.0003               | 0.0005                    | $961,100 |
| 58           | 143                      | -150                   | -7                      | $260                | 0.0002               | 0.0004                    | $1,051,100 |

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| Screened Age | Earlier Stage Cases/100K | Later Stage Cases/100K | Total Cancer Cases/100K | Cost/ Woman Screened | QALYs/ Woman Screened | Life Years/ Woman Screened | ICER          |
|--------------|--------------------------|------------------------|-------------------------|----------------------|------------------------|---------------------------|---------------|
| 59           | 141                      | -148                   | -7                      | $259                 | 0.0002                 | 0.0004                    | $1,169,200    |
| 60           | 136                      | -141                   | -5                      | $257                 | 0.0002                 | 0.0004                    | $1,166,100    |
| 61           | 133                      | -138                   | -5                      | $256                 | 0.0001                 | 0.0004                    | $1,773,100    |
| 62           | 130                      | -136                   | -5                      | $255                 | 0.0001                 | 0.0003                    | $1,897,200    |
| 63           | 128                      | -133                   | -5                      | $254                 | 0.0001                 | 0.0003                    | $2,043,600    |
| 64           | 125                      | -130                   | -5                      | $253                 | 0.0001                 | 0.0003                    | $2,219,700    |
| 65           | 119                      | -123                   | -4                      | $250                 | 0.0001                 | 0.0003                    | $4,424,400    |
| 66           | 116                      | -120                   | -4                      | $249                 | 0.0000                 | 0.0003                    | $5,360,300    |
| 67           | 113                      | -116                   | -3                      | $248                 | 0.0000                 | 0.0003                    | $6,856,400    |
| 68           | 110                      | -113                   | -3                      | $246                 | 0.0000                 | 0.0002                    | $9,655,100    |
| 69           | 106                      | -110                   | -3                      | $245                 | 0.0000                 | 0.0002                    | $16,930,700   |
| 70           | 100                      | -102                   | -2                      | $243                 | -0.0001                | 0.0002                    | $-4,391,900   |
| 71           | 96                       | -98                    | -2                      | $242                 | -0.0001                | 0.0002                    | $-3,910,000   |
| 72           | 92                       | -94                    | -2                      | $241                 | -0.0001                | 0.0002                    | $-3,522,000   |
| 73           | 88                       | -90                    | -2                      | $239                 | -0.0001                | 0.0002                    | $-3,200,900   |
| 74           | 84                       | -85                    | -2                      | $238                 | -0.0001                | 0.0002                    | $-2,929,200   |
| 75           | 83                       | -84                    | -1                      | $239                 | -0.0001                | 0.0001                    | $-2,448,000   |
| 76           | 78                       | -79                    | -1                      | $237                 | -0.0001                | 0.0001                    | $-2,309,600   |
| 77           | 73                       | -75                    | -1                      | $236                 | -0.0001                | 0.0001                    | $-2,185,700   |
| 78           | 68                       | -70                    | -1                      | $235                 | -0.0001                | 0.0001                    | $-2,073,400   |
| 79           | 63                       | -64                    | -1                      | $234                 | -0.0001                | 0.0001                    | $-1,970,500   |
| 80           | 57                       | -58                    | -1                      | $231                 | -0.0002                | 0.0001                    | $-1,492,500   |
| 81           | 54                       | -55                    | -1                      | $230                 | -0.0002                | 0.0001                    | $-1,448,000   |
| 82           | 51                       | -52                    | -1                      | $228                 | -0.0002                | 0.0001                    | $-1,406,500   |
| 83           | 48                       | -49                    | -1                      | $227                 | -0.0002                | 0.0001                    | $-1,367,500   |
| 84           | 45                       | -46                    | -1                      | $225                 | -0.0002                | 0.0001                    | $-1,330,200   |
| 85           | 43                       | -44                    | -1                      | $224                 | -0.0002                | 0.0001                    | $-1,314,100   |
| 86           | 40                       | -41                    | -1                      | $223                 | -0.0002                | 0.0001                    | $-1,283,200   |
| 87           | 37                       | -37                    | -1                      | $221                 | -0.0002                | 0.0001                    | $-1,253,800   |
| 88           | 33                       | -34                    | -1                      | $220                 | -0.0002                | 0.0001                    | $-1,225,300   |
| 89           | 30                       | -30                    | -1                      | $219                 | -0.0002                | 0.0001                    | $-1,196,600   |
| 90           | 24                       | -25                    | 0                       | $216                 | -0.0002                | 0.0000                    | $-1,037,300   |
| 91           | 23                       | -23                    | 0                       | $214                 | -0.0002                | 0.0000                    | $-1,025,400   |
| 92           | 22                       | -22                    | 0                       | $213                 | -0.0002                | 0.0000                    | $-1,014,100   |
| 93           | 21                       | -21                    | 0                       | $212                 | -0.0002                | 0.0000                    | $-1,003,100   |
| 94           | 20                       | -20                    | 0                       | $211                 | -0.0002                | 0.0000                    | $-991,800     |
| 95           | 15                       | -15                    | 0                       | $208                 | -0.0002                | 0.0000                    | $-940,100     |
| 96           | 14                       | -14                    | 0                       | $206                 | -0.0002                | 0.0000                    | $-930,000     |
| 97           | 12                       | -13                    | 0                       | $205                 | -0.0002                | 0.0000                    | $-919,700     |
| 98           | 10                       | -10                    | 0                       | $202                 | -0.0002                | 0.0000                    | $-908,500     |
| 99           | 7                        | -8                     | 0                       | $199                 | -0.0002                | 0.0000                    | $-894,900     |

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In one-way sensitivity analysis, one parameter at a time is varied to its low and high value while keeping all other parameters constant. Parameters with the greatest impact on results have the largest bars in the “tornado” diagram and are located on top.

### eFigure 3. Results of One-Way Sensitivity Analysis

| Parameter Description | Low Input | High Input | Low Result | High Result | Spread |
|------------------------|-----------|------------|------------|-------------|--------|
| **Population: 30-Year-Old Women** |
| Breast Cancer 5-Year Survival | -20% | +20% | $86,291 | $117,098 | $48,807 |
| Screening Test Sensitivity | $160 | $240 | $74,348 | $100,806 | $26,458 |
| Breast Cancer HR Post-Oophorectomy: BRCA2 | 0.16 | 0.82 | $75,879 | $106,015 | $26,136 |
| Breast Cancer HR Post-Oophorectomy: BRCA1 | 0.41 | 0.96 | $79,098 | $99,216 | $19,218 |
| BRCA2 Oophorectomy Annual Uptake | -50% | +50% | $99,787 | $80,068 | $19,711 |
| Ovarian Cancer HR Post-Oophorectomy: BRCA1 | 0.12 | 0.82 | $83,332 | $99,657 | $16,325 |
| BRCA1 Oophorectomy Annual Uptake | -50% | +50% | $97,705 | $81,649 | $16,056 |
| Proportion of Carriers: BRCA2 | 0.232 | 0.348 | $96,186 | $60,563 | $15,023 |
| BRCA2 Mastectomy Annual Uptake | -50% | +50% | $95,302 | $81,659 | $13,643 |
| Annual Interval Screening (MRI) Cost | $1,172 | $1,683 | $91,519 | $93,785 | $12,266 |
| BRCA1 Mastectomy Annual Uptake | -50% | +50% | $94,348 | $82,126 | $12,219 |
| HBOC Carrier Prevalence (Overall) | 0.452% | 0.538% | $94,014 | $82,318 | $11,696 |
| Proportion of Carriers: BRCA1 | 0.221 | 0.332 | $93,929 | $82,250 | $11,671 |
| Breast Cancer HR Post-Oophorectomy: Non-BRCA | 0.16 | 0.82 | $84,192 | $95,711 | $11,519 |
| BRCA2 Breast Cancer Annual Incidence | -20% | +20% | $93,476 | $83,091 | $10,385 |
| Utility: Well | 0.950 | 1.00 | $97,388 | $87,652 | $9,737 |
| Utility: Post Breast Cancer | 0.770 | 0.851 | $83,988 | $91,686 | $7,729 |
| Mammography-MRI Uptake, Increased Risk, 30-74 | 0.900 | 1.00 | $80,598 | $87,652 | $6,955 |
| Proportion of Known Carriers Who Get MRI | 0.600 | 0.900 | $84,401 | $90,867 | $6,466 |
| Breast Cancer Mortality Relative Reduction: Early Stage | 0.900 | 1.00 | $85,025 | $91,227 | $6,202 |
| Proportion ID1 Mutations with FH Testing | 0.139 | 0.209 | $84,842 | $90,709 | $5,867 |
| BRCA1 Breast Cancer Annual Incidence | -20% | +20% | $90,651 | $85,283 | $5,388 |
| Breast Cancer Odds Ratio: PALB2 | 2.24 | 17.65 | $90,249 | $84,892 | $5,357 |
| General Population Breast Cancer Annual Incidence | -20% | +20% | $90,142 | $85,553 | $4,859 |
| Screening Test Sensitivity | 0.992 | 1.00 | $91,405 | $86,917 | $4,488 |

| Parameter Description | Low Input | High Input | Low Result | High Result | Spread |
|------------------------|-----------|------------|------------|-------------|--------|
| **Population: 45-Year-Old Women** |
| Breast Cancer 5-Year Survival | -20% | +20% | $221,245 | $292,244 | $107,999 |
| BRCA2 Oophorectomy Annual Uptake | -50% | +50% | $329,820 | $228,412 | $101,408 |
| Breast Cancer Mortality Relative Reduction: Early Stage | 0.900 | 1.00 | $233,115 | $236,329 | $32,214 |
| Screening Test Sensitivity | $160 | $240 | $242,593 | $333,326 | $90,633 |
| Proportion of Carriers: BRCA2 | 0.232 | 0.348 | $297,360 | $244,849 | $52,711 |
| BRCA1 Oophorectomy Annual Uptake | -50% | +50% | $291,885 | $244,743 | $47,140 |
| HBOC Carrier Prevalence (Overall) | 0.452% | 0.538% | $286,997 | $252,369 | $34,629 |
| Ovarian Cancer HR Post-Oophorectomy: BRCA1 | 0.12 | 0.82 | $259,153 | $292,391 | $33,236 |
| Annual Interval Screening (MRI) Cost | $1,122 | $1,683 | $263,667 | $282,666 | $29,999 |
| Breast Cancer HR Post-Oophorectomy: BRCA1 | 0.41 | 0.96 | $257,221 | $263,770 | $6,549 |
| Proportion of Carriers: BRCA1 | 0.221 | 0.332 | $281,843 | $255,861 | $25,982 |
| Cascade Screening: Proportion, Family Tested | 0.400 | 0.000 | $281,150 | $256,644 | $25,515 |
| Cascade Screening: Proportion, Test Family | 0.560 | 0.840 | $281,441 | $256,257 | $25,184 |
| Cascade Screening: Proportion, Family Tested | 0.160 | 0.240 | $281,441 | $256,257 | $25,184 |
| Cascade Screening: Proportion, Test Family | 0.560 | 0.840 | $281,441 | $256,257 | $25,184 |
| BRCA2 Breast Cancer Annual Incidence | -20% | +20% | $282,360 | $257,215 | $25,145 |
| Hereditary Breast Cancer Risk: Non-BRCA | 0.16 | 0.82 | $280,072 | $264,544 | $23,471 |
| Utility: Well | 0.950 | 1.00 | $291,409 | $268,162 | $23,247 |
| BRCA1 Mastectomy Annual Uptake | -50% | +50% | $279,792 | $257,541 | $22,251 |
| Annual Interval Screening (MRI) Cost | $1,122 | $1,683 | $263,667 | $282,666 | $29,999 |
| Proportion ID1 Mutations with FH Testing | 0.139 | 0.209 | $260,171 | $276,930 | $16,759 |
| Mammography-MRI Uptake, Increased Risk, 30-74 | 0.800 | 1.00 | $252,315 | $268,162 | $15,847 |
| Screening Test Sensitivity | 0.992 | 1.00 | $281,387 | $265,576 | $15,811 |
| Utility: Post Breast Cancer | 0.770 | 0.851 | $261,536 | $275,132 | $13,596 |
| BRCA1 Breast Cancer Annual Incidence | -20% | +20% | $274,061 | $262,817 | $11,844 |

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Probabilistic sensitivity analysis results are presented as cost-effectiveness acceptability curves, which show the Bayesian probability that the results are cost-effective at increasing willingness-to-pay per QALY thresholds (supplementary Figure e4). For 30-year-olds, population screening had a 0%, 78%, and 100% probability of being cost-effective versus family history testing alone at the $50,000, $100,000, and $150,000 per QALY thresholds, respectively. When we added potential harm to noncarriers who avoid recommended mammography, the probability of population screening being cost-effective fell to 0%, 2%, 34% at the $50,000, $100,000, and $150,000 per QALY thresholds, respectively. Population screening was not cost-effective for 45-year-olds in any probabilistic simulations with a willingness-to-pay per QALY threshold below $150,000.

**eFigure 4. Results of Probabilistic Sensitivity Analysis**
eReferences.

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