# Supplementary Online Content

Plevritis SK, Munoz D, Kurian A, et al. Association of screening and treatment with breast cancer mortality by molecular subtype in US women, 2000-2012. *JAMA*. doi:10.1001/jama.2017.19130



This supplementary material has been provided by the authors to give readers additional information about their work.

## eMethods

### *Computing the Relative Contributions Associated with Screening and Treatment*

In the main text, the relative contribution associated with screening versus treatment to the combination was computed as the ratio of the screening alone mortality reduction divided by the sum of the screening alone mortality reduction and treatment alone mortality reduction; similarly for the relative contribution associated with treatment. Herein, we refer to this approach as "Method A." Two alternative approaches for computing the relative contributions associated with screening and treatment were also considered. In "Method B," we evaluated the relative contributions associated with screening and treatment by first quantifying the contributions associated with screening alone and assigning the remainder of the combined effect to treatment. In "Method C", we evaluated the relative contributions associated with screening and treatment by first quantifying the contributions associated with treatment alone and assigning the remainder of the combined effect to screening. A comparison of all three approaches to compute the relative contributions associated with screening and treatment on overall breast cancer mortality is provided in Supplemental eTable 3. All three approaches provide the same ranking of relative contributions, but results differ because the combination associated with screening and treatment is less than the sum of the contributions associated with screening alone and treatment alone. If the combination was equal to the sum of screening alone and treatment alone, all three methods would give the same result. Because Method A provided a result that was "in-between" Methods B and C, we choose it for the primary analysis.

***Computing the Relative Contributions Associated with Screening and Treatment to the Difference in the Reduction Between 2000 and 2012***

In Table 3 of the main text, the relative contribution associated with screening and treatment advances to the different in the mortality reduction between 2000 and 2012 are provided. The results in Table 3 are based on the difference in breast cancer mortality reduction in 2012 and breast cancer mortality reduction 2000. Note that the mortality reduction in 2012 is computed relative to the estimated baseline breast cancer mortality in 2012, where the estimate baseline mortality rate in a given calendar year is defined as the estimate mortality rate in that calendar year had there never been screening or adjuvant therapy. Similarly, the mortality reduction in 2000 is computed relative to the estimated baseline breast cancer mortality in 2000. By computing the difference between 2000 and 2012, the baseline effect is removed and the difference estimates the effect of screening and treatment only (not the baseline effect) over this time period. If we did not remove the effect of baseline then the difference in the mortality rate between 2012 and 2000 could be associated with changes in the baseline as well as changes in screening and treatment. Removing the estimated baseline trend provides more robust results for the relative contributions associated with screening and treatment.

To understand how the relative contributions associated with screening and treatment to the difference in the mortality reduction between 2000 and 2012 is computed, we describe the calculations based on overall mortality using the mean results in Table 3. The overall mortality reduction associated with combined screening and treatment was estimated as 37% in 2000 and 49% in 2012, yielding a difference of 12% between 2000 and 2012. In 2000, the relative contribution associated with screening to

the overall mortality reduction was 44% (based on Method A in Supplemental eTable 3), so the mortality reduction associated with screening (vs. baseline) was 44% of 37% = 16% in 2000. In 2012, the relative contribution associated with screening to the overall mortality reduction was 37% (based on Method A in Supplemental Table 3), so the mortality reduction associated with screening (vs. baseline) was 37% of 49% = 18%. The difference in the mortality reduction associated with screening between 2012 and 2000 was 18%- 16% = 2%. This was associated with screening advances (in this case the conversion to digital mammography because the dissemination of screening had not significantly changed). Hence the relative contribution of screening advances to the difference in the mortality reduction associated with combined screening and treatment was estimated as 2% divided by 12%, giving 17%. This leaves 83% associated with treatment advances. **Supplemental eTable 5** provides the results of these calculations for each model, and the mean across the models.

**eTable 1.** Model Parameters

| Parameters | Data | Data Source* |
|---|---|---|
| **Common Model Parameters** | | |
| Incidence in the absence of screening | An age-period-cohort model is used as a starting point for most models (except Model M) | Ref. [1,2] |
| Mammography dissemination | Screening dissemination is based on the age at first screening and frequency by birth cohort derived from BCSC and NHIS data through 2012 | Ref.[3,4] |
| Proportion of plain film vs. digital mammograms by year | Estimated percent of mammograms in the US that are digital by year from FDA MQSA and BCSC data | Ref.[5,6] BCSC (unpublished data) |
| Mammography performance | By age, type of screen (initial vs. subsequent), screen interval, and plain film vs. digital | BCSC (unpublished data) |
| Distribution of ER/ERBB2-status by age and stage | The probability of ER/ERBB2 conditional on age and stage at diagnosis | BCSC (unpublished data) |
| Survival in the absence of screening and treatment, Overall and by ER/ERBB2 | 26-year breast cancer survival before adjuvant treatment by joint ER/ERBB2 status, age group, and AJCC/SEER stage or tumor size | Ref.[18] |
| ER/ERBB2 specific treatment dissemination by year | Based on observed dissemination in the population over time from SEER and the NCCN Outcomes Database (1997-2012) | Ref. [5,7,8] NCCN Outcomes Database (unpublished data) |
| ER/ERBB2-specific treatment efficacy | Meta-analyses of clinical trial results | Ref.[9] |
| Non-cancer competing causes of death | Age- and cohort-specific all-cause mortality rates by year | Ref. [10] |
| **Model-specific Parameters** | | |
| Tumor sojourn time (or mean tumor doubling time) | Sojourn time by joint ER/ERBB2 status and age group | Ref.[18] |
| Proportion of DCIS that progresses to invasive cancer | Varies by model | Ref.[5,11-16] |
| Mean stage dwell time** or tumor growth rates or both | Varies by models based on model structure; can vary by age and/or ER/ERBB2 status | Ref.[11-17] |
| Screening effects | Stage-shift or change in tumor size between screened and unscreened populations | Ref.[11-16] |

* All reference citations refer to those in the main text.
** The mean stage well time is defined as the average time a tumor spends in each stage before progressing to the next.

**eTable 2.** Computation of the Percent Mortality Reduction, Relative to the Baseline Rate

| | Mortality Rate, per 100,000 Women | | | | Mortality Reduction, Relative to Baseline Rate, % | | |
|---|---|---|---|---|---|---|---|
| | No Screening, No Treatment ("Baseline") | Screening Alone | Treatment Alone | Combined Screening and Treatment | Screening Alone | Treatment Alone | Combined Screening and Treatment |
| Column ID | A | B | C | D | E | F | G |
| Operation | A | B | C | D | (A-B)/A | (A-C)/A | (A-D)/A |
| Model | Calendar Year 2000 | | | | | | |
| Dana Farber | 61 | 44 | 50 | 37 | 27 | 18 | 39 |
| Erasmus | 65 | 56 | 51 | 44 | 14 | 22 | 32 |
| Georgetown-Einstein | 73 | 58 | 56 | 45 | 21 | 23 | 39 |
| MD Anderson | 56 | 48 | 46 | 41 | 13 | 17 | 27 |
| Stanford | 65 | 54 | 47 | 39 | 17 | 28 | 40 |
| Wisconsin | 65 | 54 | 45 | 38 | 17 | 30 | 42 |
| Mean | 64 | 52 | 49 | 40 | **18** | **23** | **37** |
| | Calendar Year 2012 | | | | | | |
| Dana Farber | 59 | 42 | 43 | 30 | 29 | 28 | 49 |
| Erasmus | 67 | 56 | 47 | 39 | 18 | 30 | 43 |
| Georgetown-Einstein | 73 | 55 | 46 | 34 | 25 | 37 | 53 |
| MD Anderson | 54 | 45 | 39 | 33 | 17 | 29 | 39 |
| Stanford | 63 | 51 | 39 | 31 | 18 | 37 | 50 |
| Wisconsin | 63 | 52 | 32 | 27 | 17 | 49 | 58 |
| Mean | 63 | 50 | 41 | 32 | **21** | **35** | **49** |

**eTable 3.** Comparison of three alternative methods to compute the relative contributions associated with screening and treatment on overall breast cancer mortality reduction in 2012*

| | | | | Method A (Main text) | | Method B | | Method C | |
|---|---|---|---|---|---|---|---|---|---|
| | Mortality reduction in 2012 relative to the estimated baseline mortality rate in 2012, % | | | Relative contribution associated with screening, % | Relative contribution associated with treatment, % | Relative contribution associated with screening, % | Relative contribution associated with treatment, % | Relative contribution associated with screening, % | Relative contribution associated with treatment, % |
| | Screening alone | Treatment alone | Combined screening and treatment | | | | | | |
| Column ID | A | B | C | D | E | F | G | H | I |
| Operation | A | B | C | A/(A+B) | B/(A+B) | A/C | 1-A/C | 1-B/C | B/C |
| **Model** | **Overall Breast Cancer Mortality** | | | | | | | | |
| Dana-Farber | 29 | 28 | 49 | 51 | 49 | 59 | 41 | 43 | 57 |
| Erasmus | 18 | 30 | 43 | 37 | 63 | 41 | 59 | 30 | 70 |
| Georgetown -Einstein | 25 | 37 | 53 | 40 | 60 | 47 | 53 | 31 | 69 |
| MD Anderson | 17 | 29 | 39 | 38 | 62 | 44 | 56 | 27 | 73 |
| Stanford | 18 | 37 | 50 | 33 | 67 | 36 | 64 | 26 | 74 |
| Wisconsin-Harvard | 17 | 49 | 58 | 26 | 74 | 30 | 70 | 16 | 84 |
| **Mean** | **21** | **35** | **49** | **37** | **63** | **43** | **57** | **29** | **71** |

* See Supplemental Methods subsection "*Computing the Relative Contributions Associated with Screening and Treatment*" for description of these calculations.

**eTable 4.** Comparison of breast cancer mortality reduction, overall and by ER/ERBB2-subtype, across models, in 2000 vs 2012

| | Mortality reduction in 2000 relative to the estimated baseline mortality rate in 2000, % | | | Mortality reduction in 2012 relative to the estimated baseline mortality rate in 2012, % | | | Difference in the mortality reduction between 2012 and 2000, % | | | Relative contribution associated with screening in 2000, % | Relative contribution associated with treatment in 2000, % | Relative contribution associated with screening in 2012, % | Relative contribution associated with treatment in 2012, % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Screening alone | Treatment alone | Combined screening and treatment | Screening alone | Treatment alone | Combined screening and treatment | Screening alone | Treatment alone | Combined screening and treatment | | | | |
| Column ID | A | B | C | D | E | F | G | H | I | J | K | L | M |
| Operation | A | B | C | D | E | F | D-A | E-B | F-C | A/(A+B) | B/(A+B) | D/(D+E) | E/(D+E) |
| **Model** | **Overall** | | | | | | | | | | | | |
| Dana-Farber | 27 | 18 | 39 | 29 | 28 | 49 | 2 | 11 | 10 | 60 | 40 | 51 | 49 |
| Erasmus | 14 | 22 | 32 | 18 | 30 | 43 | 4 | 8 | 10 | 39 | 61 | 37 | 63 |
| Georgetown-Einstein | 21 | 23 | 39 | 25 | 37 | 53 | 4 | 14 | 14 | 48 | 52 | 40 | 60 |
| MD Anderson | 13 | 17 | 27 | 17 | 29 | 39 | 4 | 12 | 13 | 44 | 56 | 38 | 62 |
| Stanford | 17 | 28 | 40 | 18 | 37 | 50 | 1 | 9 | 10 | 38 | 62 | 33 | 67 |
| Wisconsin-Harvard | 17 | 30 | 42 | 17 | 49 | 58 | 1 | 18 | 16 | 35 | 65 | 26 | 74 |
| **Mean** | **18** | **23** | **37** | **21** | **35** | **49** | **3** | **12** | **12** | **44** | **56** | **37** | **63** |

**eTable 4 (Continued).** Comparison of breast cancer mortality reduction, overall and by ER/ERBB2-subtype, across models, in 2000 vs 2012

| | Mortality reduction in 2000 relative to the estimated baseline mortality rate in 2000, % | | | Mortality reduction in 2012 relative to the estimated baseline mortality rate in 2012, % | | | Difference in the mortality reduction between 2012 and 2000, % | | | Relative contribution associated with screening in 2000, % | Relative contribution associated with treatment in 2000, % | Relative contribution associated with screening in 2012, % | Relative contribution associated with treatment in 2012, % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Screening alone | Treatment alone | Combined screening and treatment | Screening alone | Treatment alone | Combined screening and treatment | Screening alone | Screening alone | Treatment alone | | | | |
| Column ID | A | B | C | D | E | F | G | H | I | J | K | L | M |
| Operation | A | B | C | D | E | F | D-A | E-B | F-C | A/(A+B) | B/(A+B) | D/(D+E) | E/(D+E) |
| **Model** | **ER+, ERBB2- Subtype** | | | | | | | | | | | | |
| Dana-Farber | 28 | 21 | 43 | 30 | 30 | 52 | 2 | 9 | 9 | 57 | 43 | 50 | 50 |
| Erasmus | 15 | 22 | 34 | 18 | 34 | 46 | 4 | 12 | 13 | 40 | 60 | 35 | 65 |
| Georgetown-Einstein | 21 | 25 | 41 | 26 | 39 | 54 | 5 | 13 | 13 | 45 | 55 | 40 | 60 |
| MD Anderson | 13 | 19 | 29 | 17 | 31 | 42 | 4 | 12 | 13 | 41 | 59 | 36 | 64 |
| Stanford | 17 | 34 | 45 | 19 | 41 | 53 | 1 | 7 | 8 | 34 | 66 | 31 | 69 |
| Wisconsin-Harvard | 15 | 35 | 45 | 16 | 51 | 59 | 1 | 16 | 14 | 30 | 70 | 24 | 76 |
| **Mean** | **18** | **26** | **39** | **21** | **38** | **51** | **3** | **11** | **12** | **41** | **59** | **36** | **64** |

**eTable 4 (Continued).** Comparison of breast cancer mortality reduction, overall and by ER/ERBB2-subtype, across models, in 2000 vs 2012

| | Mortality reduction in 2000 relative to the estimated baseline mortality rate in 2000, % | | | Mortality reduction in 2012 relative to the estimated baseline mortality rate in 2012, % | | | Difference in the mortality reduction between 2012 and 2000, % | | | Relative contribution associated with screening in 2000, % | Relative contribution associated with treatment in 2000, % | Relative contribution associated with screening in 2012, % | Relative contribution associated with treatment in 2012, % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Screening alone | Treatment alone | Combined screening and treatment | Screening alone | Treatment alone | Combined screening and treatment | Screening alone | Screening alone | Treatment alone | | | | |
| Column ID | A | B | C | D | E | F | G | H | I | J | K | L | M |
| Operation | A | B | C | D | E | F | D-A | E-B | F-C | A/(A+B) | B/(A+B) | D/(D+E) | E/(D+E) |
| **Model** | **ER+, ERBB2+ Subtype** | | | | | | | | | | | | |
| Dana-Farber | 25 | 21 | 41 | 27 | 38 | 57 | 2 | 17 | 17 | 54 | 46 | 41 | 59 |
| Erasmus | 14 | 24 | 33 | 20 | 42 | 52 | 6 | 18 | 19 | 36 | 64 | 32 | 68 |
| Georgetown-Einstein | 22 | 27 | 41 | 24 | 43 | 58 | 2 | 16 | 17 | 45 | 55 | 36 | 64 |
| MD Anderson | 13 | 18 | 28 | 18 | 38 | 46 | 5 | 20 | 18 | 41 | 59 | 32 | 68 |
| Stanford | 16 | 37 | 47 | 17 | 58 | 66 | 1 | 21 | 19 | 31 | 69 | 23 | 77 |
| Wisconsin-Harvard | 18 | 31 | 46 | 19 | 62 | 71 | 0 | 31 | 25 | 37 | 63 | 23 | 77 |
| **Mean** | **18** | **26** | **39** | **21** | **47** | **58** | **3** | **21** | **19** | **41** | **59** | **31** | **69** |

**eTable 4** (Continued)**.** Comparison of breast cancer mortality reduction, overall and by ER/ERBB2-subtype, across models, in 2000 versus 2012

| | Mortality reduction in 2000 relative to the estimated baseline mortality rate in 2000, % | | | Mortality reduction in 2012 relative to the estimated baseline mortality rate in 2012, % | | | Difference in the mortality reduction between 2012 and 2000, % | | | Relative contribution associated with screening in 2000, % | Relative contribution associated with treatment in 2000, % | Relative contribution associated with screening in 2012, % | Relative contribution associated with treatment in 2012, % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Screening alone | Treatment alone | Combined screening and treatment | Screening alone | Treatment alone | Combined screening and treatment | Screening alone | Screening alone | Treatment alone | | | | |
| Column ID | A | B | C | D | E | F | G | H | I | J | K | L | M |
| Operation | A | B | C | D | E | F | D-A | E-B | F-C | A/(A+B) | B/(A+B) | D/(D+E) | E/(D+E) |
| **Model** | **ER-, ERBB2+ Subtype** | | | | | | | | | | | | |
| Dana-Farber | 24 | 14 | 33 | 25 | 28 | 49 | 1 | 15 | 16 | 64 | 36 | 47 | 53 |
| Erasmus | 14 | 14 | 26 | 17 | 28 | 41 | 3 | 15 | 15 | 51 | 49 | 37 | 63 |
| Georgetown-Einstein | 21 | 16 | 33 | 25 | 32 | 52 | 3 | 17 | 19 | 58 | 42 | 43 | 57 |
| MD Anderson | 13 | 11 | 20 | 15 | 23 | 33 | 2 | 12 | 13 | 53 | 47 | 39 | 61 |
| Stanford | 17 | 10 | 26 | 17 | 25 | 40 | 0 | 15 | 14 | 63 | 37 | 40 | 60 |
| Wisconsin-Harvard | 22 | 16 | 33 | 23 | 43 | 55 | 1 | 27 | 22 | 58 | 42 | 34 | 66 |
| **Mean** | **19** | **13** | **29** | **20** | **30** | **45** | **2** | **17** | **16** | **58** | **42** | **40** | **60** |

**eTable 4** (Continued)**.** Comparison of breast cancer mortality reduction, overall and by ER/ERBB2-subtype, across models, in 2000 versus 2012

| | Mortality reduction in 2000 relative to the estimated baseline mortality rate in 2000, % | | | Mortality reduction in 2012 relative to the estimated baseline mortality rate in 2012, % | | | Difference in the mortality reduction between 2012 and 2000, % | | | Relative contribution associated with screening in 2000, % | Relative contribution associated with treatment in 2000, % | Relative contribution associated with screening in 2012, % | Relative contribution associated with treatment in 2012, % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Screening alone | Treatment alone | Combined screening and treatment | Screening alone | Treatment alone | Combined screening and treatment | Screening alone | Screening alone | Treatment alone | | | | |
| Column ID | A | B | C | D | E | F | G | H | I | J | K | L | M |
| Operation | A | B | C | D | E | F | D-A | E-B | F-C | A/(A+B) | B/(A+B) | D/(D+E) | E/(D+E) |
| **Model** | **ER-, ERBB2- Subtype** | | | | | | | | | | | | |
| Dana-Farber | 25 | 13 | 34 | 26 | 20 | 40 | 1 | 6 | 6 | 65 | 35 | 57 | 43 |
| Erasmus | 13 | 15 | 26 | 17 | 22 | 35 | 4 | 7 | 10 | 46 | 54 | 43 | 57 |
| Georgetown-Einstein | 22 | 17 | 35 | 24 | 29 | 46 | 2 | 12 | 11 | 56 | 44 | 45 | 55 |
| MD Anderson | 14 | 11 | 22 | 18 | 14 | 27 | 4 | 3 | 5 | 57 | 43 | 56 | 44 |
| Stanford | 17 | 12 | 27 | 18 | 17 | 33 | 1 | 5 | 7 | 59 | 41 | 52 | 48 |
| Wisconsin-Harvard | 16 | 18 | 32 | 18 | 30 | 42 | 2 | 12 | 8 | 48 | 52 | 38 | 62 |
| **Mean** | **18** | **14** | **29** | **20** | **22** | **37** | **2** | **8** | **8** | **55** | **45** | **48** | **52** |

**eTable 5.** Relative contributions associated with screening and treatment advances on the difference in the breast cancer mortality reduction between 2000 and 2012*

| | | | | Model** | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Year | Metric | Row ID | Operation | D | E | G-E | M | S | W-H | Mean |
| 2000 | Mortality Reduction in 2000 Relative to Baseline in 2000, Screening Alone, % | A | A | 27 | 14 | 21 | 13 | 17 | 17 | **17** |
| | Mortality Reduction in 2000 Relative to Baseline in 2000, Treatment Alone, % | B | B | 18 | 22 | 23 | 17 | 28 | 30 | **23** |
| | Mortality Reduction in 2000 Relative to Baseline in 2000, Combined Screening and Treatment, % | C | C | 39 | 32 | 39 | 27 | 40 | 42 | **37** |
| | Relative Contribution Associated with Screening, % | D | A/(A+B) | 60 | 39 | 48 | 44 | 38 | 35 | **44** |
| | Relative Contribution Associated with Treatment, % | E | B/(A+B) | 40 | 61 | 52 | 56 | 62 | 65 | **56** |
| | Mortality Reduction Associated with Screening given Combination, % | F | D*C | 24 | 13 | 19 | 12 | 15 | 15 | **16** |
| | Mortality Reduction Associated with treatment given combination, % | G | E*C | 16 | 20 | 21 | 15 | 25 | 27 | **21** |
| 2012 | Mortality Reduction Relative to Baseline, Screening Alone, % | H | H | 29 | 18 | 25 | 17 | 18 | 17 | **21** |
| | Mortality Reduction Relative to Baseline, Treatment Alone, % | I | I | 28 | 30 | 37 | 29 | 37 | 49 | **35** |
| | Mortality Reduction Baseline, Combined Screening and Treatment, % | J | J | 49 | 43 | 53 | 39 | 50 | 58 | **49** |
| | Relative Contribution Associated with Screening, % | K | H/(H+I) | 51 | 37 | 40 | 38 | 33 | 26 | **37** |
| | Relative Contribution Associated Treatment, % | L | I/(H+I) | 49 | 63 | 60 | 62 | 67 | 74 | **63** |
| | Mortality Reduction Associated with Screening given Combination, % | M | K*J | 25 | 16 | 22 | 15 | 16 | 15 | **18** |
| | Mortality Reduction associated with Treatment given Combination, % | N | L*J | 24 | 27 | 32 | 24 | 34 | 43 | **31** |
| 2000 vs 2012 | Difference in Mortality Reduction Between 2000 and 2012, % | Q | J-C | 10 | 10 | 14 | 13 | 10 | 16 | **12** |
| | Difference in the Mortality Reduction Associated with Screening Advances Between 2000 and 2012, % | O | M-F | 1 | 3 | 3 | 3 | 1 | 0 | **2** |
| | Difference in the Mortality Reduction Associated with Treatment Advances Between 2000 and 2012, % | P | N-G | 9 | 7 | 11 | 10 | 9 | 15 | **10** |
| | Relative Contribution Associated with Screening Advances Between 2000 and 2012, % | R | O/Q | 13 | 31 | 21 | 24 | 14 | 2 | **17** |
| | Relative Contribution Associated with Treatment Advances Between 2000 and 2012, % | S | P/Q | 87 | 69 | 79 | 76 | 86 | 98 | **83** |

* See Supplemental Methods subsection "*Computing the Relative Contributions of Screening and Treatment to the Difference in the Reduction Between Two Calendar Years*" for description of these calculations.
** *Abbreviations*: Model D is Dana Farber; Model E is Erasmus; Model G-E is Georgetown-Einstein; Model M is MD Anderson; Model S is Stanford; Model W-H is Wisconsin-Harvard.

**eTable 6.** Relative contributions associated with screening, chemotherapy, hormone therapy and trastuzumab to breast cancer mortality reduction in 2012, broken down by advances before and after 2000*

| Relative Contributions Associated with Mortality Reduction in 2012, Percent | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Screening Advances before 2000 | Screening Advances after 2000 | Chemo-therapy Advances before 2000 | Chemo-therapy Advances after 2000 | Hormone Therapy Advances before 2000 | Hormone Therapy Advances after 2000 | Trast-uzumab |
| Model | **Overall** | | | | | | |
| Dana-Farber | 48 | 3 | 16 | 7 | 15 | 9 | 2 |
| Erasmus | 29 | 8 | 30 | 8 | 17 | 8 | 1 |
| Georgetown-Einstein | 35 | 5 | 23 | 14 | 16 | 2 | 4 |
| MD Anderson | 30 | 8 | 15 | 7 | 22 | 12 | 6 |
| Stanford | 30 | 3 | 26 | 8 | 24 | 4 | 5 |
| Wisconsin-Harvard | 26 | 1 | 20 | 13 | 27 | 9 | 5 |
| **Mean** | 33 | 4 | 22 | 9 | 20 | 7 | 4 |
| | **ER+, ERBB2- Subtype** | | | | | | |
| Dana-Farber | 48 | 2 | 19 | 6 | 17 | 8 | 0 |
| Erasmus | 29 | 6 | 26 | 4 | 17 | 18 | 0 |
| Georgetown-Einstein | 35 | 6 | 21 | 13 | 22 | 2 | 0 |
| MD Anderson | 29 | 8 | 13 | 8 | 27 | 16 | 0 |
| Stanford | 28 | 3 | 26 | 7 | 30 | 5 | 0 |
| Wisconsin-Harvard | 23 | 1 | 17 | 12 | 35 | 11 | 0 |
| **Mean** | 32 | 4 | 20 | 8 | 25 | 10 | 0 |
| | **ER+, ERBB2+ Subtype** | | | | | | |
| Dana-Farber | 38 | 3 | 18 | 6 | 15 | 8 | 12 |
| Erasmus | 23 | 9 | 25 | 3 | 15 | 15 | 10 |
| Georgetown-Einstein | 32 | 4 | 19 | 14 | 19 | 5 | 7 |
| MD Anderson | 25 | 7 | 12 | 2 | 23 | 13 | 18 |
| Stanford | 22 | 1 | 24 | 7 | 26 | 4 | 17 |
| Wisconsin-Harvard | 23 | 0 | 14 | 10 | 27 | 7 | 18 |
| **Mean** | 27 | 4 | 19 | 7 | 21 | 9 | 14 |
| | **ER-, ERBB2+ Subtype** | | | | | | |
| Dana-Farber | 44 | 4 | 25 | 12 | 0 | 0 | 16 |
| Erasmus | 32 | 5 | 31 | 13 | 0 | 0 | 18 |
| Georgetown-Einstein | 38 | 7 | 30 | 14 | 0 | 0 | 11 |
| MD Anderson | 34 | 8 | 25 | 1 | 0 | 0 | 32 |
| Stanford | 40 | 0 | 24 | 11 | 0 | 0 | 25 |
| Wisconsin-Harvard | 34 | 0 | 25 | 17 | 0 | 0 | 24 |
| **Mean** | 37 | 4 | 27 | 11 | 0 | 0 | 21 |

**eTable 6** (Continued)**.** Relative contributions associated with screening, chemotherapy, hormone therapy and trastuzumab to breast cancer mortality reduction in 2012, broken down by advances before and after 2000*

| Relative Contributions Associated with Mortality Reduction in 2012, Percent | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Screening Advances before 2000 | Screening Advances after 2000 | Chemo-therapy Advances before 2000 | Chemo-therapy Advances after 2000 | Hormone Therapy Advances before 2000 | Hormone Therapy Advances after 2000 | Trast-uzumab |
| | **ER-, ERBB2- Subtype** | | | | | | |
| Dana-Farber | 55 | 2 | 30 | 13 | 0 | 0 | 0 |
| Erasmus | 34 | 9 | 40 | 18 | 0 | 0 | 0 |
| Georgetown-Einstein | 43 | 3 | 35 | 19 | 0 | 0 | 0 |
| MD Anderson | 46 | 10 | 28 | 15 | 0 | 0 | 0 |
| Stanford | 47 | 5 | 33 | 15 | 0 | 0 | 0 |
| Wisconsin-Harvard | 36 | 2 | 39 | 23 | 0 | 0 | 0 |
| **Mean** | 44 | 5 | 34 | 17 | 0 | 0 | 0 |

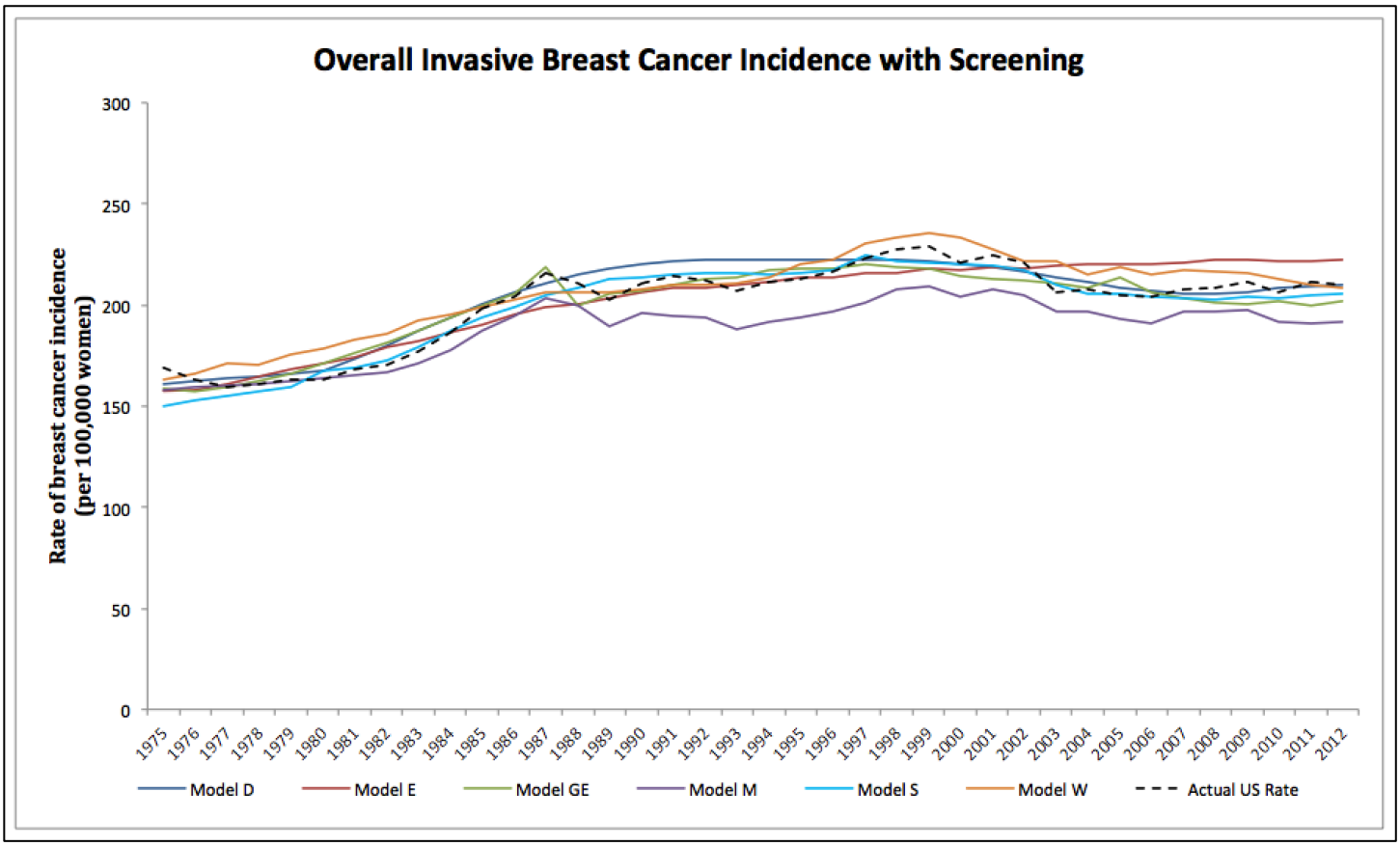
*Row sum is 100%, within rounding error.

**eTable 7.** Breakdown of overall breast cancer mortality reduction in 2012 by molecular subtype*

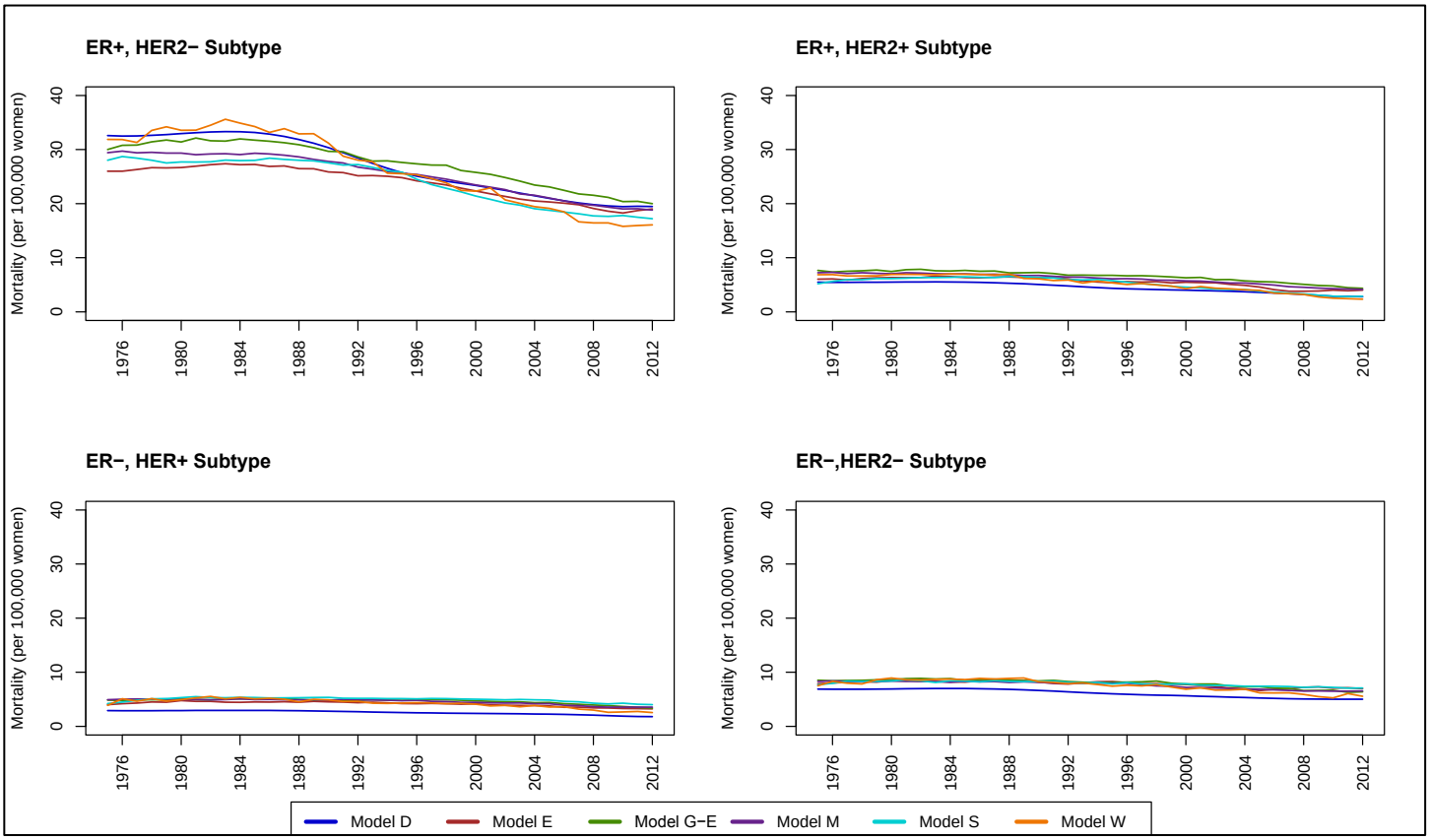
| Model | ER+/ERBB2- Subtype | ER+/ERBB2+ Subtype | ER-/ERBB2+ Subtype | ER-/ERBB2- Subtype |
|---|---|---|---|---|
| Dana-Farber | 70 | 13 | 6 | 11 |
| Erasmus | 62 | 17 | 10 | 12 |
| Georgetown-Einstein | 62 | 15 | 9 | 14 |
| MD Anderson | 61 | 17 | 9 | 13 |
| Stanford | 65 | 16 | 8 | 11 |
| Wisconsin-Harvard | 66 | 15 | 8 | 11 |
| **Mean** | **64** | **16** | **8** | **12** |

*Row sum is 100%.

**eFigure 1.** Comparison of model projections to actual US breast cancer incidence, for women ages 30-79, invasive cancer only

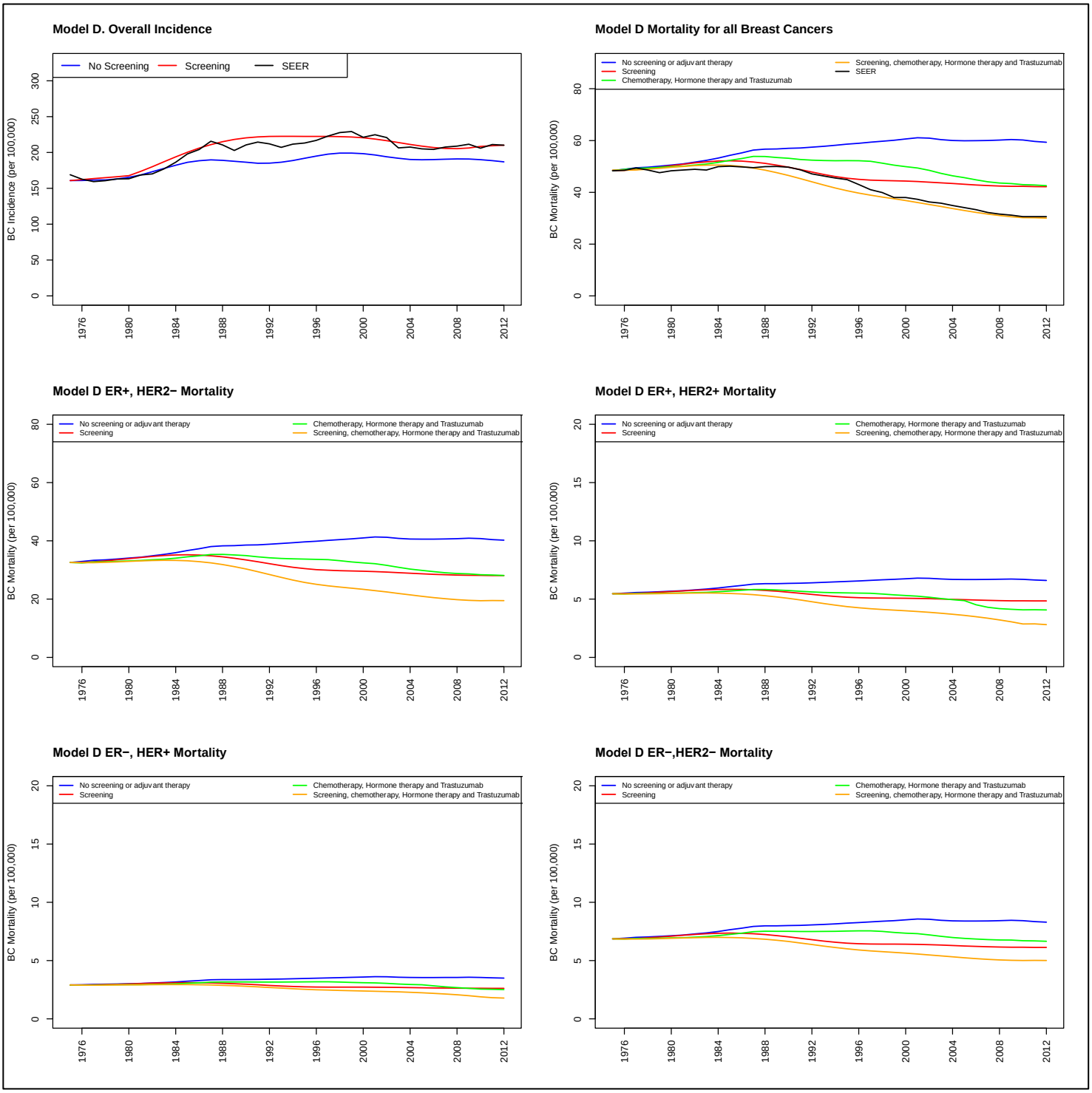


**eFigure 2.** Comparison of model projections for ER-/ ERBB2-specific breast cancer mortality trends between 1975-2012, for women ages 30-79, by molecular subtype. (Upper left) ER+/ERBB2-, (upper right) ER+/ERBB2+, (lower left) ER-/ERBB2+, (lower right) ER-/ERBB2- subtypes**.**

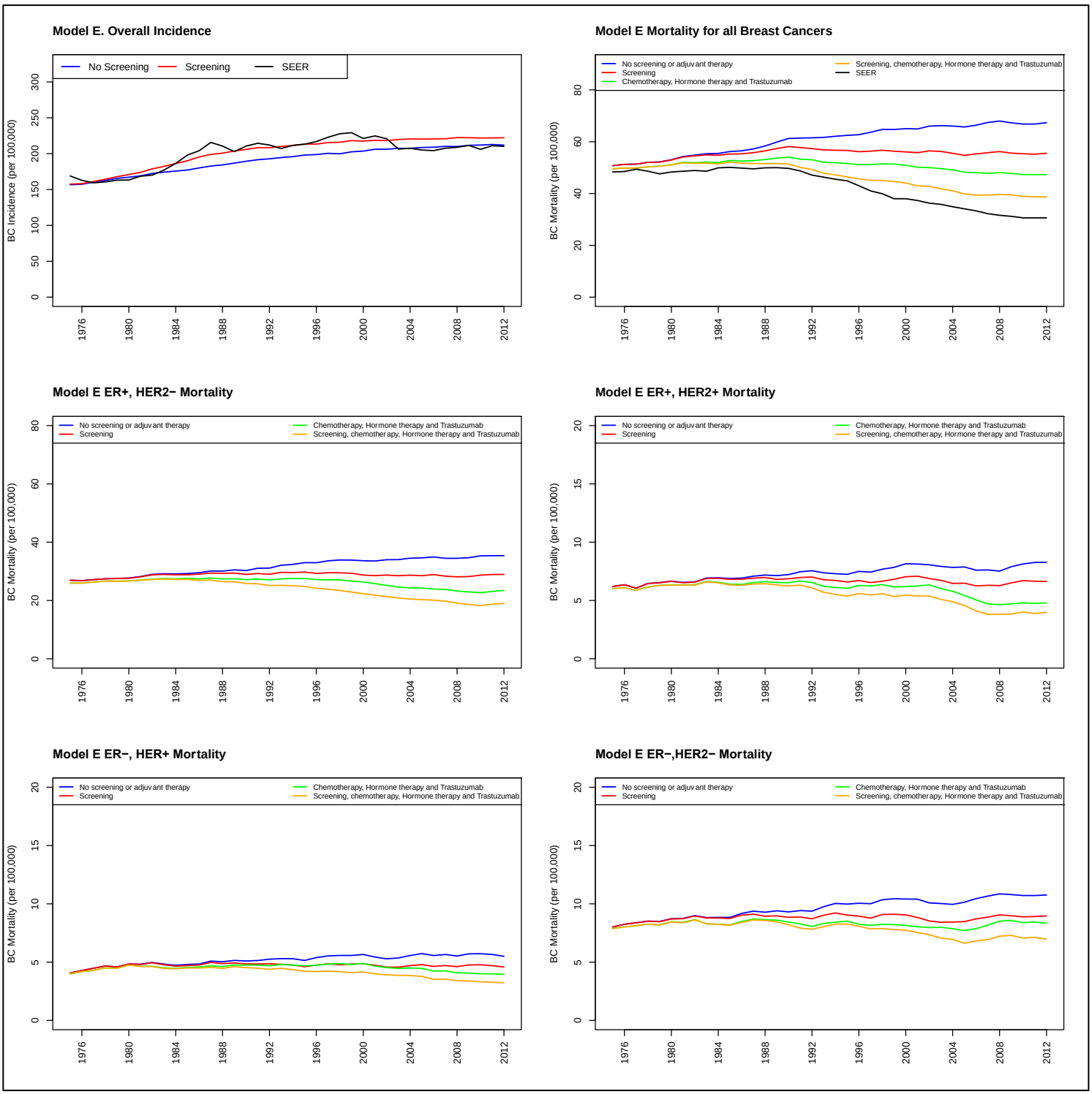


**eFigure 3.** Individual model projections for overall US breast cancer incidence and mortality (vs. SEER) and ER/ERBB2-subtype-specific mortality from 1975-2012, for women ages 30-79*

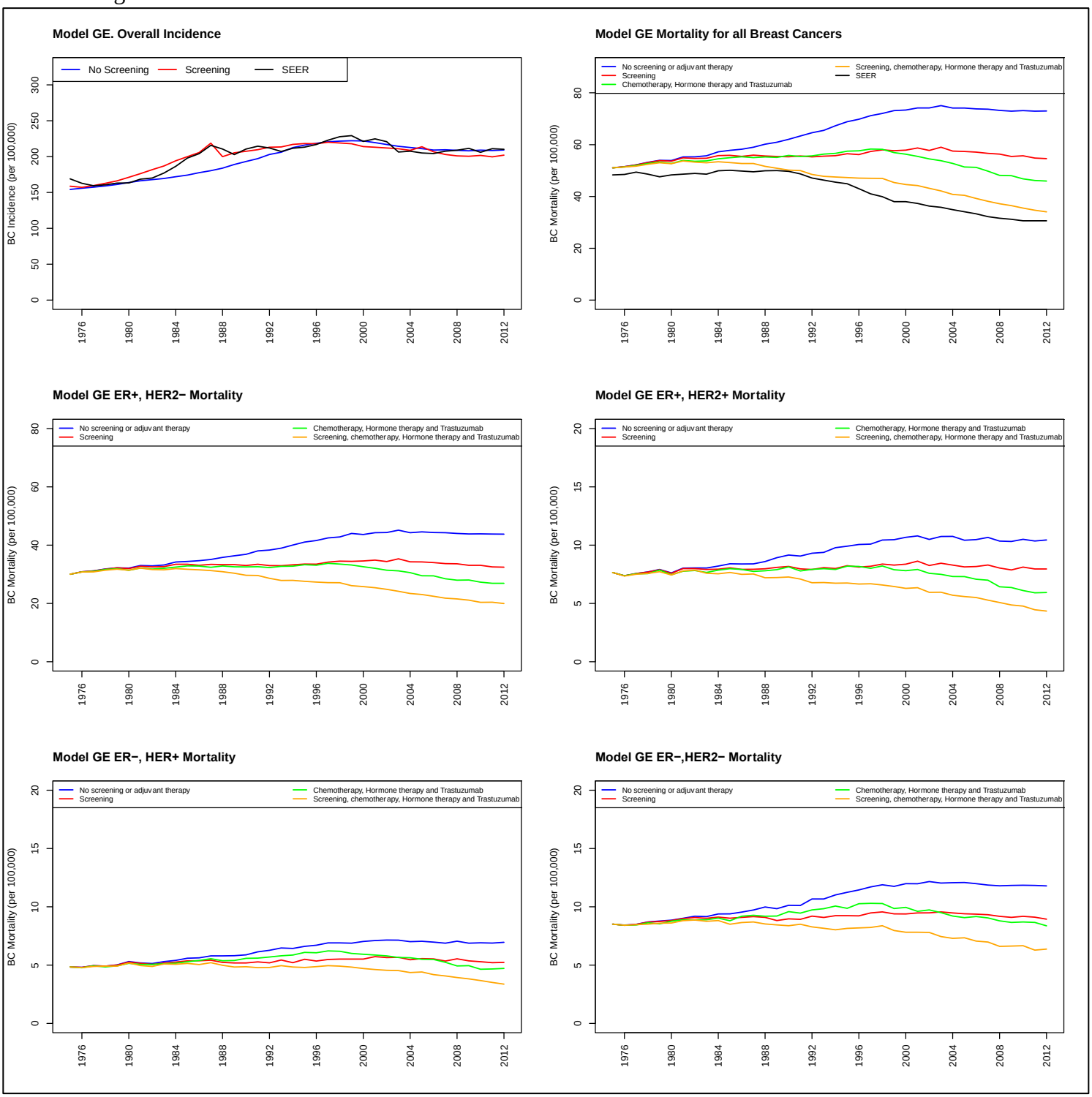
Model Dana-Farber



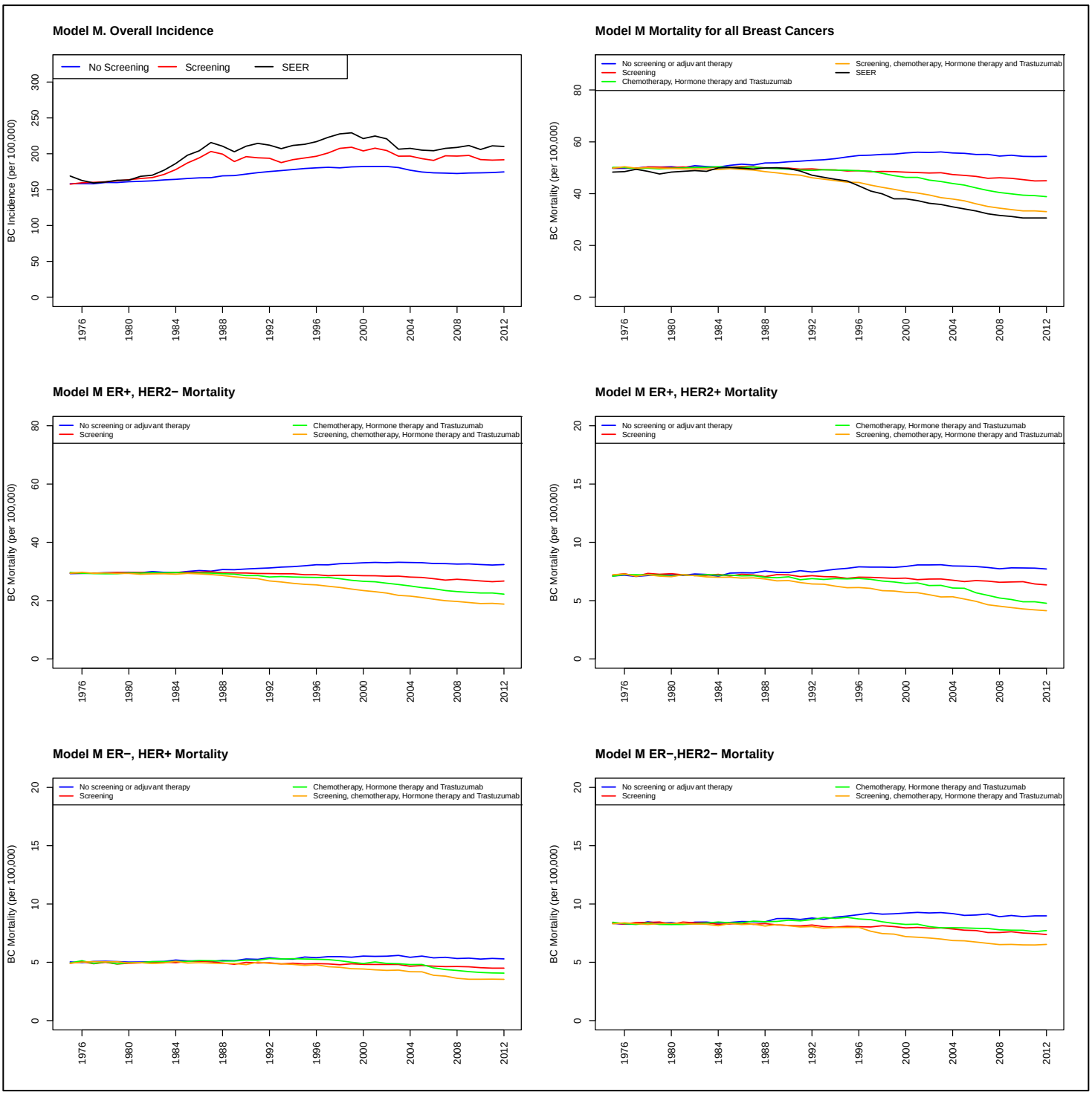
Model Erasmus



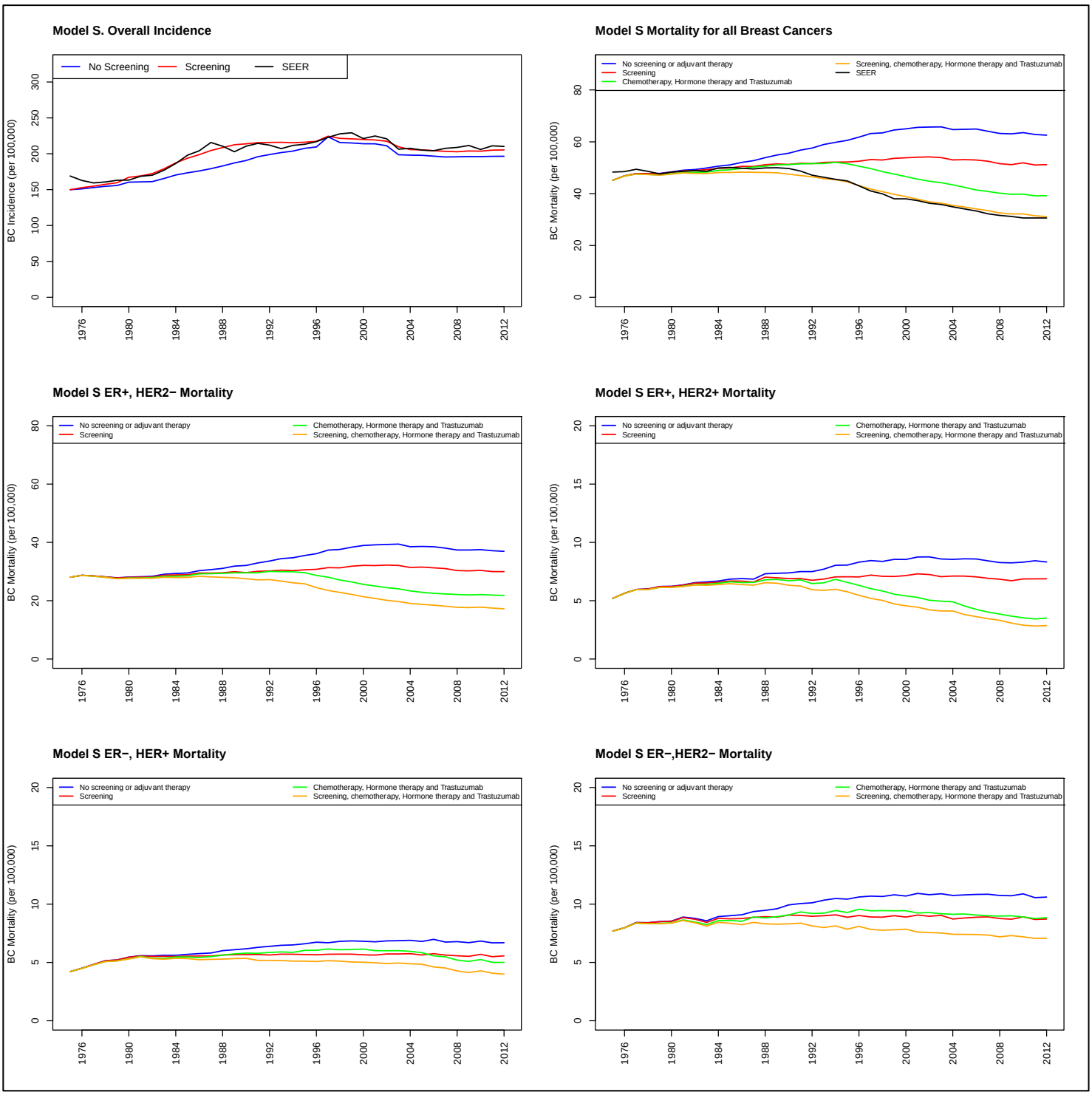
Model Georgetown-Einstein



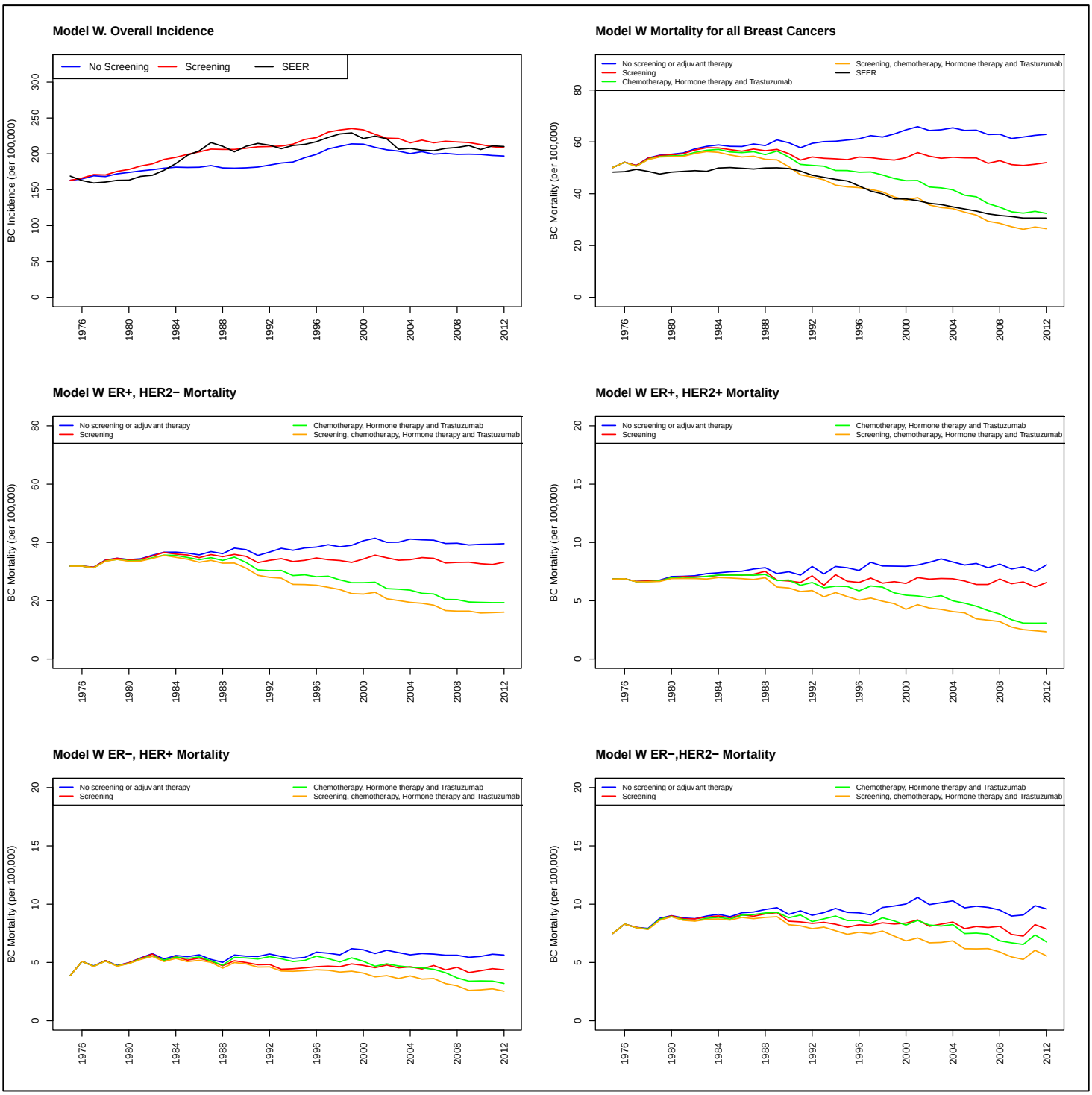
Model MD Anderson



Model Stanford



Model Wisconsin-Harvard




*** Legend for Supplemental Figure 3**: (upper two panels) Individual model projections of breast cancer incidence and mortality rates vs. SEER rates to 2012, with modeled incidence reported in the presence and absence of screening; (lower four panels) Individual model projections by ER/ERBB2 under 4 scenarios: (i) no screening and treatment, (ii) screening alone, (iii) treatment alone, (iv) screening and treatment combined. Subtype-specific comparison to SEER is not possible because ER and ERBB2 status were not jointly reported over this period.

**eReferences.**


1. Gangnon RE, Sprague BL, Stout NK, et al. The contribution of mammography screening to breast cancer incidence trends in the United States: an updated age-period-cohort model. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology.* 2015;24(6):905-912.
2. Holford TR, Cronin KA, Mariotto AB, Feuer EJ. Changing patterns in breast cancer incidence trends. *Journal of the National Cancer Institute Monographs.* 2006(36):19-25.
3. Cronin KA, Mariotto AB, Clarke LD, Feuer EJ. Additional common inputs for analyzing impact of adjuvant therapy and mammography on U.S. mortality. *Journal of the National Cancer Institute Monographs.* 2006(36):26-29.
4. Cronin KA, Yu B, Krapcho M, et al. Modeling the dissemination of mammography in the United States. *Cancer causes & control : CCC.* 2005;16(6):701-712.
5. Mandelblatt JS, Near AM, Miglioretti DL, Munoz D, Sprague BK, Trentham-Dietz A, Gangnon R, Kurian AW, Weedon-Fekjaer H, Cronin KA, Plevritis SK. Common model inputs used in CISNET collaborative breast cancer modeling. Medical Decision Making. In Press 2017.
6. US Food and Drug Administration. http://www.fda.gov/Radiation-EmittingProducts/MammographyQualityStandardsActandProgram/default.htm. June 2013. Silver Spring, Maryland US Dep Health and Human Services. Accessed January 2015.
7. Mariotto A, Feuer EJ, Harlan LC, Wun LM, Johnson KA, Abrams J. Trends in use of adjuvant multi-agent chemotherapy and tamoxifen for breast cancer in the United States: 1975-1999. *Journal of the National Cancer Institute.* 2002;94(21):1626-1634.
8. Mariotto AB, Feuer EJ, Harlan LC, Abrams J. Dissemination of adjuvant multiagent chemotherapy and tamoxifen for breast cancer in the United States using estrogen receptor information: 1975-1999. *Journal of the National Cancer Institute Monographs.* 2006(36):7-15.
9. Peto R, Davies C, Godwin J, et al. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials. *Lancet (London, England).* 2012;379(9814):432-444.
10. Gangnon RE, Stout NK, Alagoz O, Hampton JM, Sprague BL, Trentham-Dietz A. Contribution of Breast Cancer to Overall Mortality for U.S. Women. Medical Decision Making. In Press. 2017.
11. Lee SJ, Li X, Huang H, Zelen M. Models for breast cancer screening strategies updated for ductal carcinoma in situ and subgroups. Medical Decision Making. In Press. 2017.
12. van den Broek JJ, van Ravesteyn NT, Heijnsdijk EA, de Koning H. Estimating the effects of risk based screening and adjuvant treatment using the miscan-fadia continuous tumor growth model for breast cancer. Medical Decision Making. In Press. 2017.
13. Schechter CB, Near AM, Jayasekera J, Chang Y, Mandelblatt JS. structure, function, and applications of the Georgetown-Einstein (GE) breast cancer simulation model. Medical Decision Making. In Press. 2017.
14. Huang X, Li Y, Song J, Berry D. The MD Anderson CISNET model for estimating benefits of adjuvant therapy and screening mammography for breast cancer: an update. Medical Decision Making. In Press. 2017.
15. Munoz D, Xu C, Plevritis SK. A molecular subtype-specific stochastic simulation model of US breast cancer incidence and mortality trends from 1975 to 2000. Medical Decision Making. In Press. 2017.
16. Alagoz O, Ergun MA, Cevik M, et al. The University Of Wisconsin breast cancer epidemiology simulation model: An update. Medical Decision Making, In Press. 2017.
17. Munoz D, Near AM, van Ravesteyn NT, et al. Effects of screening and systemic adjuvant therapy on ER-specific US breast cancer mortality. *Journal of the National Cancer Institute.* 2014;106(11).
18. Munoz D, Plevritis SK. Estimating breast cancer progression features and survival by molecular subtype in the absence of screening and treatment. Medical Decision Making. In Press. 2017.