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Improved Web-Based Calculators for Predicting Breast Carcinoma Outcomes

Running title: Improved Breast Cancer Outcome Calculators

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ABSTRACT

Purpose: Produce an improved web-based calculator by using published mathematical models of cancer lethality to accurately predict the risk of breast carcinoma death in each of 15 years after diagnosis and the impact of various treatment choices.

Materials and Methods: The *SNAP* method of the published *binary biological model of cancer metastasis* uses information on tumor size, nodal status, and other prognostic factors to accurately estimate of breast cancer lethality at 15 years after diagnosis. By combining these 15-year-lethality estimates with data on the breast cancer hazard function, breast cancer lethality was estimated at each of the 15 years after diagnosis. A web-based calculator was then created to visualize the estimated lethality with and without a range of adjuvant therapy options at any of the 15 years after diagnosis, and incorporate conditional survival information for any years survived since diagnosis. NIH population data was used to estimate non-breast-cancer chance of death. The accuracy of the calculators was tested against two large breast carcinoma datasets: 12,327 patients seen at two academic hospitals and 435,694 patients from the SEER national dataset.

Results: The calculators were found to be highly accurate and specific, with ability to stratify patients into groups differing by as little as a 2% risk of death and to account for tumor size, nodal status, histology, grade, age, and hormone receptor status.

Conclusion: Our calculators, available at www.cancermath.net, improve on existing calculators by more finely and accurately stratifying patients according to risk of death, and displaying more detailed mortality forecasts.

INTRODUCTION

Weighing the risk versus the benefit of various therapy options in breast cancer requires knowledge of the natural history of the disease, especially disease specific death rate and overall survival information. Physicians regularly make such estimates for breast cancer by staging, experience, and intuition. Survival estimates can also be made by the online case-matching tool of the FinProg Study[1].

The most widely used web-tool for estimating the risk of breast carcinoma recurrence and death is Adjuvant!Online[2,3], which sorts patients into risk groups, using data from the SEER national dataset, together with data from the metaanalyses of adjuvant therapy[4,5], to make empirically-based estimates of the risk of relapse and mortality. Adjuvant!Online was the pioneer in the field of cancer web-calculators, and its widespread use among practitioners demonstrated the demand for such information[6]. As such, it provided us with the starting point from which we could consider what additional information should be available in a second generation of breast carcinoma calculators. For example, Adjuvant!Online provides its measure of lethality only at a single time point (10 years). Additionally, Adjuvant!Online uses relatively coarse groupings, such as treating cancers with 1, 2, or 3 positive nodes as all having the same impact on lethality. Doctors and patients may benefit from information on finer stratifications of risk level, as well as data on the risk of death for each and every of the first 15-years after diagnosis, the time point necessary to capture the full risk of breast carcinoma death (see Karrison et al.[12]).

A previously developed mathematical framework, the *binary biological model of cancer metastasis*, captures the features of the lethal and non-lethal spread of cancer cells[8,9,10,11,7] This framework includes a series of linked expressions, the *SNAP* (*Size* + *Nodes* + *Prognostic markers*) method, which can be used to integrate information on tumor size, nodal status, and other prognostic factors into an estimate of the risk of cancer death for each patient.[8,9,10] The *SNAP* method has proven to be remarkably accurate in estimating the risk of breast carcinoma death, as confirmed in multiple populations of patients.[10,7]

Here we describe a set of web-based calculators, available at http://www.cancermath.net, which use the *SNAP* method to estimate the risk of breast carcinoma death, the reduction in life expectancy, and the impact that various adjuvant treatment choices can be expected to have on these measures of outcome.

METHODS

Patient data

The CancerMath calculators were tested on data from two datasets: patients in the SEER national dataset diagnosed from 1973-2007 (the SEER dataset); and patients diagnosed at the Massachusetts General and Brigham and Women's Hospitals from 1968-2007 (the Partners dataset). For analysis, we excluded cases with incomplete nodal or tumor size information, cases diagnosed at autopsy, benign or in situ cases, second or subsequent malignancies, cases with tumors larger than 5cm, and cases with metastases present at diagnosis. After exclusions, 435,694 patients remained in the SEER dataset, and 12,327 patients remained in the Partners dataset. The Mathematical Methods section below contains details on how year of diagnosis was handled, and complete details are in reference 22.

Mathematical methods

The mathematics driving the calculators, the *binary biological model of cancer metastasis*, includes a series of linked equations, the *SNAP* method, used to integrate information on tumor size, nodal status, and other prognostic factors into an estimate of the risk of cancer death for each patient (TABLE I), as well as the *NodalSizeOnly* Equation, for relating tumor size to node positivity.

The essential mathematics used by the calculators for calculating cancer lethality is the *SNAP* method[7,10], which combines information on tumor size, number of positive nodes, and other prognostic factors, to provide an estimate of the 15-Year Kaplan-Meier cancer-specific death rate, *L* (TABLE I).[8,9,10,11] 15 years was chosen as the end point as analysis of the hazard function by Karrison et al[12] and ourselves[8] reveals that while there is a measurable risk of cancer death for at least 15-year after diagnosis, by 15 years ~90% of this risk has occurred.

The central parameter of the *SNAP* method, *Q*, was derived as a measure of the probability of the lethal spread of a cancer cell from a malignant tumor.[9,8] The *SNAP* method uses *g* parameters, which sit next to *Q* and modify its value, to then adjust the risk for cancer subtypes and patient characteristics such as age, ER/PR/Her2 status, histology, and grade on the risk of death (TABLE I).[10]

The *Q* parameter can reflect differences in lethality that have occurred over time, as the result of changes in treatment. For example, using the data reported by Marioto et al[13], we have found that between 1975 and 1983 only 10% of breast carcinoma patients received adjuvant therapy, while since 1987 a relatively constant majority of patients (~80%) received such therapy.[14] Reflecting these changes, before 1983 Q=0.014751, while after 1987 Q=0.010054. Using the pre-1983 value of Q=0.014751 makes it possible to generate an intrinsic underlying risk of death for any given patient in the absence of adjuvant therapy. We can then estimate the risk of death given modern treatments by applying the adjuvant therapy reduction in death reported by the metaanalyses,[4,5] as summarized by Radvin et al.[1,2] For cases in which treatment is unknown or uncertain, the modern value of Q=0.010054 is used to estimate the risk of death given the average standard of care since radiation and chemotherapy became widespread.

After the above methods are used to determine, *L*, the Kaplan-Meier risk of cancer death after 15 years, the risk of death for each year after diagnosis is determined by 15 sequential multiplications of *L* by a 15-part step function derived from the normalized breast cancer hazard function. Since patients with more advanced cancers are more likely to die in the years immediately following diagnosis, ten hazard functions were computed from the breast carcinoma patients in the SEER dataset, one for each decile of predicted 15-year lethality. After computing a patient's predicted 15-year lethality, the appropriate hazard function and step function are then chosen to determine the likelihood of cancer death in each of the 15 years following diagnosis. These values are then combined with the risk of non-cancer death (based on the U.S. National Vital Statistics Reports[15]) to compute the expected cumulative incidence of both cancer and non-cancer death under a competing risks model.[16]

For patients who have survived at least one year since diagnosis, conditional survival is calculated by reducing the 15-year lethality estimate by the expected lethality in each of the years the patient has survived. If the patient has recently been confirmed to have no evidence of distant recurrence,

the chance of death in the following two years is also reduced, with the reduction in death based on the hazard function for breast cancer patients for whom no metastases were present at diagnosis.

After determining the risk of death due to cancer in each of the 15 years after diagnosis, this information is combined with the risk of death due to non-cancer causes in each of the 15 years to produce overall survival estimates, and life expectancy impact.

Technical methods

The calculators were written in JavaScript, PHP, and HTML, using XML/SWF Charts v5.07 package with Adobe Flash to display the graphs. The JavaScript code for the calculators, together with documentation, can be viewed in the browser by selecting "View→Source" in the browser menu. A full narrative description of the code can be found at reference 22. Statistical validation was performed using MATLAB.

The code behind the CancerMath calculators

The JavaScript code for the calculators, together with documentation, can be viewed in the browser by selecting "View→Source" in the browser menu. Here we outline the code for the *breast carcinoma treatment calculator*, but the *outcome* and *conditional survival* calculators have a similar structure. The code begins by loading several lengthy arrays, such as the life expectancy tables, and proceeds through a series of sequential "Steps', which are numbered below, and are also identified in the source code which is visible in the browser:

1. **STEP 1** The program collects information that the user has entered into the web form:
    1. Tumor size (in centimeters, to 1 decimal point)
    2. Whether nodal status is known, and if so, the number of positive nodes (0, 1, 2, etc.)
    3. Age
    4. Tumor prognostic factors: ER/PR/Her2 status, histology, Bloom-Richardson grade
    5. Adjuvant therapy options
2. **STEP 2** The program calculates yearly and cumulative breast cancer, non-breast cancer, and total death rates for each of the 15 years after diagnosis, based on the entered user information:
    1. The program loads information on the value of the parameters Q, Z, $j_{primaty}$ and $L_{per\text{-}node}$ (TABLE I), which are needed to execute the *SNAP* calculation (**STEP 2.b** below) for the probability of cancer death to cancer at 15 years.
    2. The program loads information on whether nodal status is known
    3. **STEP 2.a** The program loads the g parameters determined by the user input, and computes the product of all of them.
    4. **STEP 2.b** The program calculates the 15-year Kaplan-Meier cancer death rate, L, using the *SNAP* method (TABLES 1 and 2) from information on tumor size (**STEP 1** above), number of positive lymph nodes (**STEP 1** above), and other prognostic factors, as captured by the product of the g parameters (**STEP 2.a** above).
    5. **STEP 2.c** The program calculates 15 values for the breast cancer death rate in each of the 15 years after diagnosis. It accomplishes this for each year by multiplying the 15-year Kaplan-Meier cancer death rate, L, (calculated in **STEP 2.b** above) by the fraction of the total lethality which can be expected in each year. The total lethality expected in each year is a pre-computed 15-part step function derived from the breast carcinoma hazard function, which we have derived from data on all 362,491 breast carcinoma patients in the SEER dataset for whom we have complete tumor size and nodal status information[17].
    6. **STEP 2.d** The program calculates 15 values for the non-cancer death rate in each of the 15 years after diagnosis. It accomplishes this for each year by multiplying the fraction of patients not dying of cancer (=1 – (death rate calculated in **STEP 2.b**)) times

the yearly risk of death due to non-cancer causes for the given age. The values for the yearly probability of death due to all non-cancer causes for ages 0 to 100 were taken from the National Vital Statistics Report (herein referred to as "NVSR")[18], while the values for ages 101 to 123 were extrapolated using the methodology described in the NVSR. Before creating the array values (nvsr_death_prob_yearly), we corrected them to account for the ~3% of deaths that can be ascribed to breast cancer. These values were loaded at the top of the program, before **STEP 1** as noted above.

7. **STEP 2.e** The program calculates 15 values for the overall death rate in each of the 15 years after diagnosis. It accomplishes this for each year by summing the cancer death rate (**STEP 2.c**) and the non-cancer death rate (**STEP 2.d**).
8. **STEP 2.f** The program calculates 15 values for cumulative breast cancer, non-breast cancer, and total death rates by summing the respective yearly values computed in the steps above.

3. **STEP 3** The program calculates the mean number of years of life left that can be expected for the cancer patient:
   1. **STEP 3.a** The program loads the value at year 0 for the number of people out of a group of 100,000 who survive to the user-specified age, based on yearly probabilities of death given by the NVSR.
   2. **STEP 3.b** For year 1 through year 15, the program multiplies the number of people out of the group of 100,000 who survive to the appropriate age (age+1 at year 1, age+2 at year 2, etc.) by the corresponding cumulative overall death rate (**STEP 2.f**). This applies the additional risk from cancer.
   3. **STEP 3.c** The program calculates the survival difference at year 15 by subtracting the calculated number of individuals surviving to year 15 from the NVSR-given value for the corresponding age (age+15).
   4. **STEP 3.d** The program then calculates 15 values for the total number of years lived by all surviving individuals in the group of 100,000 between each year, by taking the average of the number of individuals surviving to a given year and the number of individuals surviving to the following year.
   5. **STEP 3.e** The program calculates the total number of years lived by surviving individuals past each year, from year 0 to year 15. It begins at year 15, by taking the remaining years of life expected for the corresponding age (age+15), and subtracting away the total number of years that is expected to be lost because of cancer. The life expectancy in years for each age group is calculated as the number of people out of the group of 100,000 who survive to that age (from NVSR) multiplied by the residual life expectancy at that age (also from NVSR data). That expected number is the survival difference calculated in **STEP 3.c** multiplied by the additional number of years beyond the age at year 15 to reach age 101.
   6. **STEP 3.f** Then, working backwards from year 14 to year 0, the program calculates the total number of years lived by surviving individuals past each year by adding this value for the following year to the total number of years lived between that year and the following year (**STEP 3.d**). For example, the total number of years lived by surviving individuals past year 14 is the total number of years lived by surviving individuals past year 15 plus the total number of years lived between year 14 and year 15.
   7. **STEP 3.g** The program then calculates the mean life expectancy for the cancer patient by dividing the new total number of years lived by individuals of the specified age (the value at year 0 from **STEP 3.f**) by the number of people out of the group of 100,000 who survive to that age (**STEP 3.f**).

8. **STEP 3.h** The program calculates the expected years of life lost due to cancer, by subtracting the calculated life expectancy (**STEP 3.a**) from the NVSR-given life expectancy for the specified age.

4. **STEP 4** The program calculates the yearly and cumulative breast cancer death rates with therapy:
   1. **STEP 4.a** The program calculates the "risk-reduction" value based on the combination of therapies entered by the user and the information collected in **STEP 1.c** and **STEP 1.d**, consistent with the assumptions of Adjuvant! Online[1,2].
   2. **STEP 4.b** The program calculates 15 values for the breast cancer death rate with therapy in each of the 15 years after diagnosis by multiplying the 15-year Kaplan-Meier cancer death rate, *L*, (calculated in **STEP 2.b**) by the "risk-reduction" value computed above, and by the fraction of the total lethality which can be expected in each year (the 15-part step function described in **STEP 2.c** that captures the breast carcinoma hazard function). This step is analogous to that carried out in **STEP 2.c** described above, for the death rate that would occur in the absence of adjuvant therapy.
   3. **STEP 4.c** The program calculates 15 values for the cumulative breast cancer death rate in each of the 15 years after diagnosis by summing the respective yearly risks of cancer death, with therapy, (**STEP 2**) from the time of diagnosis. This step is analogous to that carried out in **STEP 2.f** described above, for the cumulative cancer death rate that would occur in the absence of adjuvant therapy.
   4. **STEP 4d** The program calculates 15 values for the cumulative overall death rate, with therapy, in each of the 15 years after diagnosis by summing the respective yearly risks of the sum of the cancer death rates with therapy (**STEP 4.c)** and non-cancer death (**STEP 2.c**) from the time of diagnosis.

5. **STEP 5** The program calculates life expectancy gained from therapy:
   1. **STEP 5.a** Using the method outlined in the National Vital Statistics Report[18], the program first substitutes the NVSR-given yearly non-cancer probability of death with the yearly overall risk of death with therapy, calculated in **STEP 4** (which includes death due to cancer as well as causes other than cancer).
   2. **STEP 5.b** Next, the program calculates the new total number of years lived by individuals of the specified age group past that age, by using the values from **STEP 3**
   3. **STEP 5.c** The program then calculates the mean life expectancy with therapy by dividing the new total number of years lived by individuals of the specified age (**STEP 2.d**) by the number of people out of the group of 100,000 who survive to that age (**STEP 1.b**).
   4. **STEP 5.d** The program calculates the life expectancy gained from therapy by subtracting the mean life expectancy with therapy (**STEP 2.e**) from the mean life expectancy for the cancer patient (**STEP 3**).

6. **STEP 6** The program graphs the risk curves for cancer (**STEP 2b**), cancer with therapy (**STEP 1.a**), non-cancer (**STEP 1.a**), overall (**STEP 2.d**), and overall with therapy (**STEP 5.b**) in the user-specified mode, either as mortality curves, survival curves, a bar graph, a pie chart, or a pictogram. For the outcome calculator, the program displays the life expectancy (**STEP 3.a**), the life expectancy lost to cancer (**STEP 3.a**), and the 15-year Kaplan-Meier cancer-specific death rate (**STEP 1**). For the treatment calculator, the program displays these values, as well as the risk reduction value from therapy (**STEP 1**) and the life expectancy gained from therapy (**STEP 5.d**).

7. **STEP 7** The program computes grade and stage, according to the AJCC criteria[19]

Validation

To test the accuracy of the *SNAP* calculations used in the *breast carcinoma outcome* calculator (Figure 1b), individuals in the SEER and Partners datasets were sorted into groups of many types and the predicted survival value calculated by the *SNAP* method were compared with the actual cancer specific Kaplan-Meier death rates for each group in each of the 15 years following diagnosis. The calculators were validated against both the SEER dataset, from which the parameters were generated, and the independent Partners dataset. For validation, patients were stratified by tumor size, positive nodes, grade, hormone receptor status, age, histology, and predicted lethality, and combinations thereof. Model bias was assessed using weighted mean error (predicted-empirical); model specificity and accuracy was assessed using mean absolute error, weighted mean absolute error, maximum error, and concordance index.

The information provided by the CancerMath calculators

The CancerMath breast cancer outcome calculator provides a cancer, non-cancer, and overall lethality estimate for each of the 15 years after diagnosis, and how those values are impacted by therapy. The lethality estimates include conditional survival information where appropriate. The estimates can be viewed in a variety of formats: in terms of death curves, survival curves, pie charts, or in terms of "smiley-face" charts, which have been provided to present the information is a fashion that may be more comprehensible to the lay person. The calculator provides the cancer's impact on life expectancy, and how any therapy might impact that life expectancy. The patient's classification (T, N, and M) and stage is also displayed according to AJCC Seventh Edition staging guidelines.[20,21]

Validation of 15-year lethality measures:

. For validation, patients were stratified by tumor size, positive nodes, grade, hormone receptor status, age, histology, and predicted lethality, and combinations thereof. For example, the *SNAP* method was used to sort the patients from the SEER dataset into groups of differing by a 2% predicted risk of death (i.e. those patients expected to have 0-2% risk of death, 2%-4% risk of death, 4%-6%, etc). A cumulative incidence survival analysis for each group revealed that the expected and observed survival values agreed within 4% for all subgroups of patients with up to a 44% risk of death (TABLE 2, FIGURES 2A-2D). Likewise, when the Partners dataset was stratified by predicted lethality, the predicted mortality differed from the observed lethality by less than 4% in all but one subgroup (which differed by 7%, and was still within the confidence bounds of the observed survival). Further, when patients in both the SEER and Partners populations were sorted by tumor size, nodal status, grade, age, histology, ER/PR status, sex, and race, the agreement between the expected and observed survival values also proved to be excellent (TABLE 2, FIGURES 2A-2D). While TABLE 2, FIGURES 2A-2D only show representative results of selected validation tests, full results and exact values for all tests are available at Technical Report #10 available on our website.[22]

Validation of lethality over each of the 15 years

The values shown in TABLE 2 and FIGURE 2 confirm the accuracy of the estimation of the risk of cancer death at 15 years, as calculated by *SNAP* calculations used in the *CancerMath.net* calculators, again revealed a remarkable agreement between the calculations provided by the *breast carcinoma outcome* calculator and the actual survival values.

Validation of conditional survival calculations

DISCUSSION

We present a web based breast carcinoma outcome calculator which physicians can use when making treatment choices for individual patients. The CancerMath calculator is capable of giving estimates of survival that are accurate to within a few percents for most patients, as seen by examining patients in two large populations, sorted by tumor size, nodal status, grade, age, histology, ER/PR status, and race. The specificity and accuracy of the underlying mathematics of the CancerMath calculators is confirmed by its ability to stratify patients into groups differing by as little as 2% risk of death. We believe the CancerMath calculator presents four distinct advantages over currently available outcome calculators.

(1) The CancerMath calculator provides information on the risk values for each of the first 15 years after diagnosis, and adjusts these values based on time survived since diagnosis. With treatment decisions increasingly being made many years after diagnosis due to 5-year and 10-year chemotherapy courses, the additional survival information may be of further use to clinicians. The Adjuvant!Online calculator provides information on the underlying 10-year risk of death based only on information at the time of diagnosis.

(2) The CancerMath calculator provides more individualized assessment of risk—finely stratifying patients based on differences as small as 1mm of tumor size. By contrast, the Adjuvant!Online calculator considers as a single group all patients with tumors 3-5cm and 1-3 positive nodes, and assigns a risk of cancer death of approximately 45% to this group. However, this group contains patients with tumor of 3 cm and 1 positive nodes, which the CancerMath calculators indicate have about a 27% 15-year cancer-specific death rate, while other patients in this Adjuvant!Online group that have tumors of 5 cm and 3 positive nodes, but have a 47% risk of death.

(3) The CancerMath calculator accurately accounts for differing mortality of differing histological subtypes. (see TABLE 2, noting that the CancerMath calculator predicted lethality had an error of less than 4% for all 10 histological subtypes for which data was available). This is unlike Adjuvant!Online, for which Radvin and his colleagues note, "The outcomes of ductal and lobular cancers were accurately predicted, but for other histological subtypes, the predicted outcomes by Adjuvant! are too pessimistic".[23]

(4) The CancerMath Java Script code that drives calculators is completely visible in the browser, together with abundant documentation.[7,22] This not only allows the mathematics to be verified externally, but also allows our methods to be adopted or extended by researchers wishing to compute lethality estimates for large populations of patients.

A limitation of the CancerMath *breast carcinoma* calculator is that, like Adjuvant!Online, it relies on the reductions in death reported by the metaanalyses[4,5] as summarized by Radvin et al[2] for determining adjuvant therapy impact. That is, both calculators estimate the impact of adjuvant therapy by multiplying the reduction in death found in the trials by the underlying risk of death specific to each patient. This is a leap of faith by both CancerMath and Adjuvant!Online, but such a calculation arguably captures the general thinking by oncologists when considering the potential benefit of adjuvant therapy. As we have noted previously[24], the *SizeAssessment* method of the *binary biological model of cancer metastasis* offers a way to quantify the impact of adjuvant therapy from data outside of trials, and we are currently collecting such data for use in future versions of the CancerMath calculators.

A further limitation of our methods is the use of patients from 1988-2007 to validate a survival prediction for patients who will be diagnosed in 2010, despite the significant changes in screening, treatment, population demographics, and lethality all occurring over this time period. However, our methods mitigate this limitation in four ways.

(1) Our calculator computes very finely stratified risks of death—accounting for differences in tumor size as small as 1mm, or single positive nodes. Thus our method will not be invalid simply as a result of improved screening methods leading to tumors being diagnosed smaller or less advanced.

(2) Our calculator uses therapy death reduction values from literature when specific therapies are entered. This allows our calculator to incorporate the most recent data on treatment effectiveness on reducing lethality, and thus account for improvements in adjuvant therapy over time.
(3) Our calculator computes non-cancer death based only on the most recent U.S. government data available on population death rates.[15] Our research has shown that breast cancer patients die of non-breast-cancer causes at roughly the same rate as gender, age, race and region-matched controls.[25]
(4) Both the Partners and SEER datasets have grown substantially since 1988, with over twice as many patients diagnosed per year in the most recent years, weighting survival calculations more heavily towards recent diagnoses.

Providing physicians with the most accurate calculation of survival applicable to each patient, rather relying on estimates based on intuition would seem to be valuable, but it is not unreasonable to ask why? Arguably, the reason for such a goal is to find the way to use the resources available, to achieve the maximal possible extension in life. For example, the CancerMath *breast carcinoma treatment* calculator shows that a 34 year old ER-/PR- patient who has a 1cm mass and 1 positive node can be expected to gain 806 days of life from CMF therapy, while an 82 year old woman with these characteristics will only gain 50 days of life.

The mathematics used by the CancerMath calculators, the *binary-biological model of cancer metastasis*, was built by considering that each cell in a tumor will *either* spread to the periphery and cause death, *or* it will not[8,9,,24]. One the advantages of the *binary biological* framework that drives the CancerMath calculators is that this mathematics can work with as little information as is at hand (the *SNAP* method can generate survival estimates with just tumor size), as well as with as much information as is desired. The methods for measuring the lethal impact of prognostic factors and determining the values of the parameters used to calculate outcome are described in reference 8, and an ongoing effort by our group is to collect such data on additional prognostic factors and add this information to the CancerMath calculators. For example, the *SNAP* method provides a way to measure the impact of local recurrence on survival, thus offering a way to include the impact of adjuvant radiation therapy in subsequent versions of the calculators.[26,27]

In addition to breast carcinoma, we have found that the *binary biological* mathematical framework that drives the CancerMath breast carcinoma calculators also accurately captures many features of melanoma lethality, thus leading to the development of a suite of both melanoma and renal cell carcinoma calculators located at the CancerMath website (Bush et al, in preparation). Thus, we would suggest that the CancerMath breast carcinoma calculators provide an example of the sort of web-based tools that can be created to provide physicians and patients with highly accurate, patient-specific information in many contexts.

TABLE 1: The *SNAP* (*Size+Nodes+PrognosticMarkers*) Method for Estimating the Risk of Breast Carcinoma Death from Information on Tumor Size, Nodal Status, and Other Prognostic Factors

$$L = L_{primary} + L_{nodes} - (L_{primary} * L_{nodes})$$

L *= 15 year* Cancer-specific Kaplan-Meier Death Rate

Source of Lethality	***Method of Estimation***	***Independent Variable***	***Parameters***	***Interpretation***
The lethal contribution from cancer at the primary site	$L_{primary} = 1 - e^{-(Q * j_{primary}) * (g_1 * g_2 * g_3 * \ldots) D^Z}$ (1c)	*D* = Tumor Diameter	*Q* = 0.014751 *treatment calculator* *Q* = 0.010054 *outcome and conditional survival* *Z* = 1 $j_{primary}$=0.8057 *known nodal status* $j_{primary}$ =1 *unknown nodal status* ***g* parameters**: ER+/PR+ 0.9155 ER+/PR- 1.1389 ER-/PR+ 1.0462 ER-/PR- 1.1902 Grade 1 0.4324 Grade 2 0.8570 Grade 3 1.1224 Age 21-30 1.2545 Age 31-40 1.126685 Age 41-50 1.86605 Age 51-60 1.01903 Age 61-70 1.01715 Age 71-80 1.02005 Age 81-90 1.16455 Ductal 1.0573 Lobular 0.9032 Intraductal + LCIS 0.8573 Mucinous 0.4646 Medullary 0.5995 Tubular 0.2752 Comedo 0.8645 Scirrhous 1.6314 Inflammatory 3.3130 Paget's disease 1.4535 Papillary 0.5414 Cribriform 0.9636	*The lethal contribution of the primary mass increases gradually with tumor size, and the amount of that lethal contribution is influenced by prognostic factors, as captured by the g-parameters*
The lethal contribution from cancer in the lymph nodes	$L_{nodes} = 1 - e^{-(M * L_{per-node})}$ eq. (2)	*M* = The Number of Positive Nodes	$L_{per\text{-}node}$ = 0.07581	*The presence of each positive lymph node contributes approximately 8% extra chance of death*

The *SNAP* (*Size+Nodes+PrognosticMarkers*) method reduces to:

- **the *Size+Nodes* method, when only size and nodal status are known.**
- **the *SizeOnly* method, when only size is known.**

TABLE II
Values Used for the Reduction in Death that may be Expected for Various Adjuvant Therapy Regimens

Adjuvant Therapy	**Age**	**ER Unknown**	**ER+**	**ER-**
Hormonal Therapy (Tamoxifen, Aromatase Inhibitor, Tamoxifen to Aromatase Inhibitor, Ovarian Ablation, Ovarian Ablation + Tamoxifen)	age < 50	20%	32%	0%
	age >= 50 and < 60	21%	32%	0%
	age >= 60	23%	32%	0%
Chemotherapy (CMF-like)	age < 50	30%	30%	30%
	age >= 50 and < 60	18%	16%	22%
	age >= 60	10%	8%	15%
Chemotherapy (Anthracyclines)	age < 50	41%	41%	41%
	age >= 50 and < 60	31%	29%	34%
	age >= 60	24%	23%	29%
Chemotherapy (1st generation regimens: CA*4, CMF, FE(50)C*6)	age < 50	30%	30%	30%
	age >= 50 and < 60	18%	16%	22%
	age >= 60	10%	8%	15%
Chemotherapy (2nd generation regimens: CA*4+T*4, DC*4, CEF*6, CAF*6, FAC*6, FE(100)C*6, E*4+CMF*4)	age < 50	44%	44%	44%
	age >= 50 and < 60	34%	33%	38%
	age >= 60	28%	26%	32%
Chemotherapy (3rd generation regimens: TAC*6, FE(100)C*3+D*3, CA*4+T*4)	age < 50	55%	55%	55%
	age >= 50 and < 60	47%	45%	49%
	age >= 60	42%	40%	45%

See Materials and methods sections for the basis of these values.

A

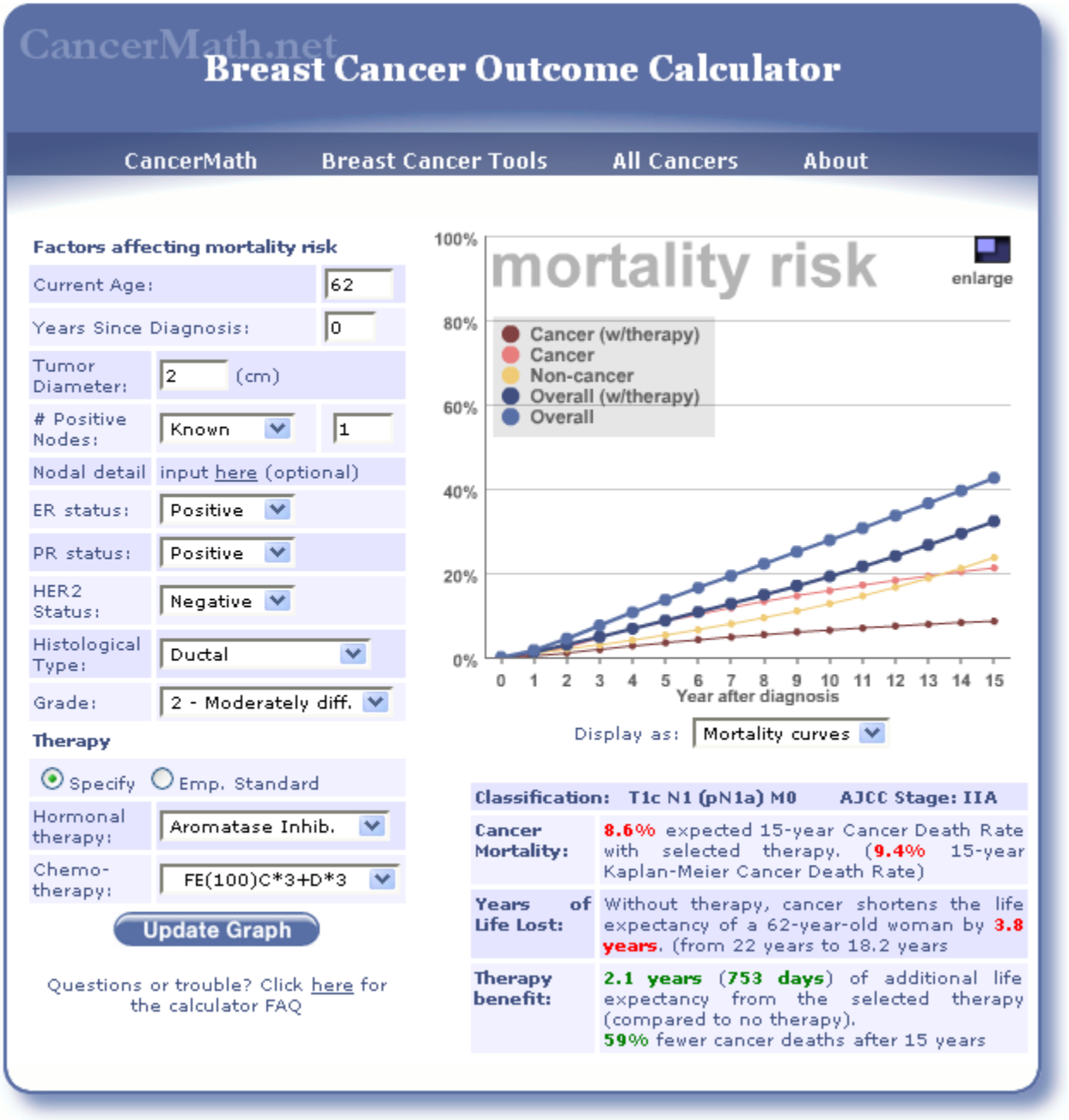

Figure 1. *CancerMath.net* breast carcinoma calculators.

Validation of outcome calculator. LIST OF AL 36 TABLE and Figure 2's shown below:
All patients after 1987, parameters for the outcome calculator, see TABLE I.

TABLE and Figure 2a: Verification on the SEER dataset. Patients grouped by 10% predicted lethality bins
TABLE and Figure 2b: Verification on the SEER dataset. Patients grouped by 5% predicted lethality bins
TABLE and Figure 2c: Verification on the SEER dataset. Patients grouped by 2% predicted lethality bins
TABLE and Figure 2d: Verification on the SEER dataset. Patients grouped by 1% predicted lethality bins
TABLE and Figure 2e: Verification on the SEER dataset. Patients grouped by 10% predicted lethality percentiles
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TABLE and Figure 2cc: Verification on the Partners dataset. Patients grouped by 2% predicted lethality bins
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TABLE and Figure 2ff: Verification on the Partners dataset. Patients grouped by 10 mm tumor size bins
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TABLE and Figure 2mm: Verification on the Partners dataset. Permutations of 10 mm tumor size bins and tumor grade
TABLE and Figure 2mm: Verification on the Partners dataset. Permutations of age
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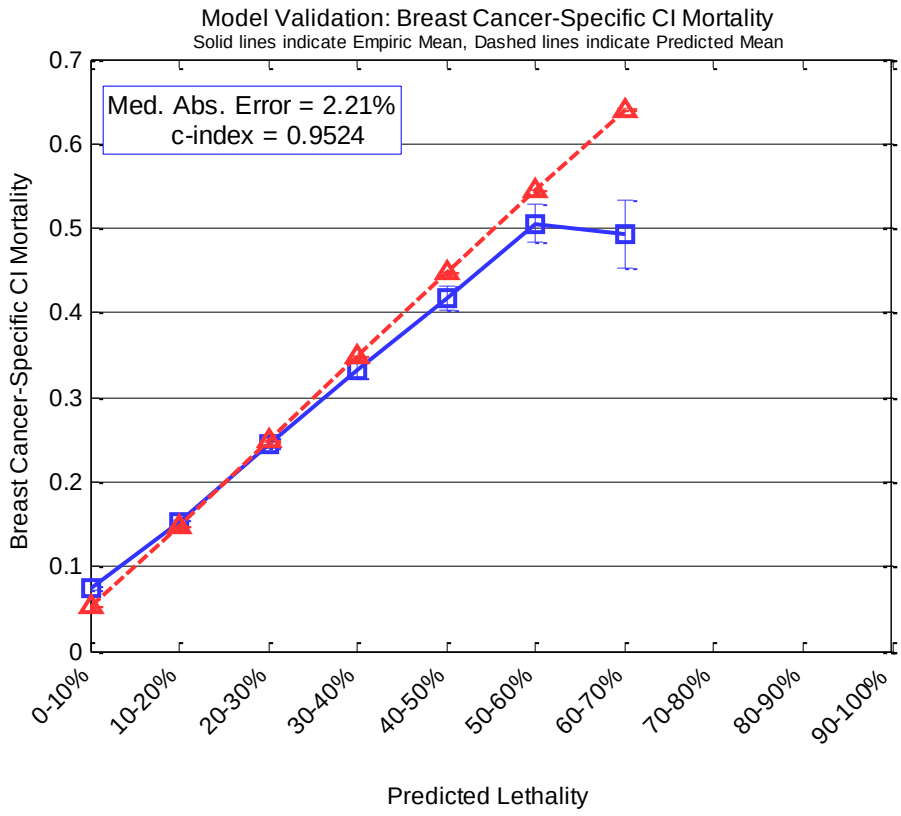
I. VALIDATION WITH SEER DATASETS

Table and Figure 2a: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 10% predicted lethality bins using the Size+Nodes+PrognosticFactors equation

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0-10%'	190878	'7.46% (0.2%)'	'5.25% (0%)'	'-2.21%'
'10-20%'	109183	'15.25% (0.4%)'	'14.7% (0%)'	'-0.55%'
'20-30%'	51064	'24.54% (0.6%)'	'24.84% (0%)'	'0.3%'
'30-40%'	25126	'33.21% (1%)'	'34.91% (0%)'	'1.71%'
'40-50%'	11401	'41.66% (1.4%)'	'44.78% (0.1%)'	'3.11%'
'50-60%'	4685	'50.58% (2.2%)'	'54.54% (0.1%)'	'3.96%'
'60-70%'	1238	'49.3% (4.1%)'	'64.06% (0.1%)'	'14.75%'
'Weighted Mean Error'		'-0.89%'		
'Median Absolute Error'		'2.21%'		
'Weighted Mean Absolute Error'		'1.56%'		
'Maximum Error'		'14.75% (60-70% group)'		
'Concordance Index'		'0.9524'		

'Groups 70-80%, 80-90%, 90-100% excluded due to insufficient follow-up or observed confidence intervals > 20%'

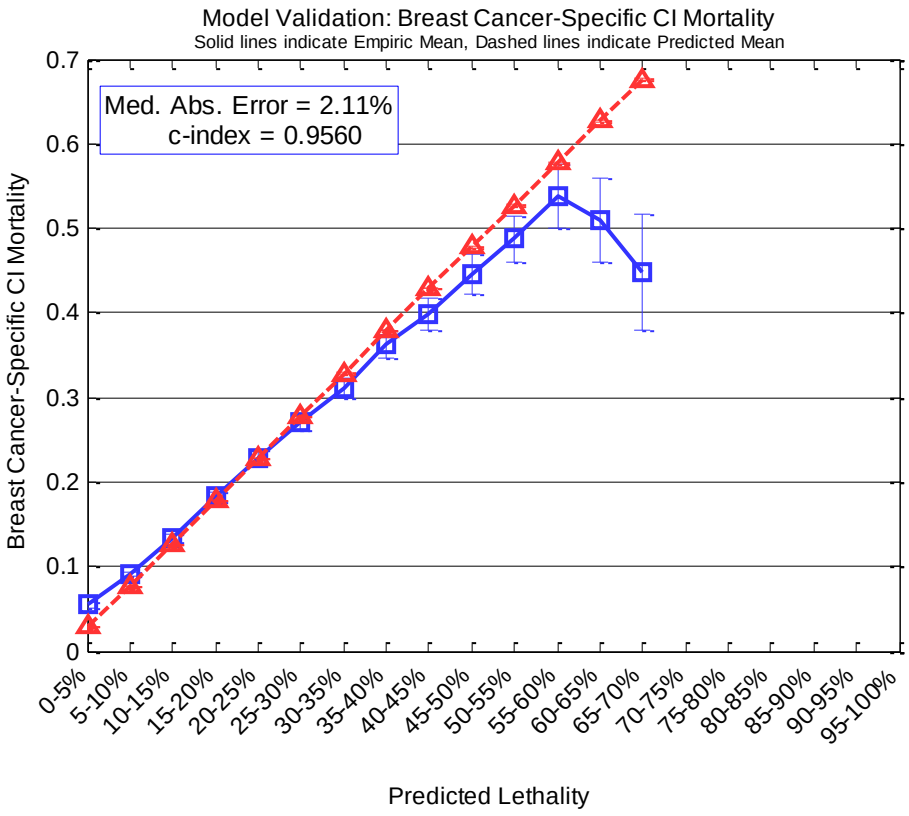


SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {'Predicted Lethality', [0:.1:1], '>'}});

Table and Figure 2b: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 5% predicted lethality bins using the Size+Nodes+PrognosticFactors equation

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0-5%'	97549	'5.47% (0.3%)'	'2.98% (0%)'	'-2.49%'
'5-10%'	93329	'9.11% (0.3%)'	'7.61% (0%)'	'-1.5%'
'10-15%'	66132	'13.36% (0.4%)'	'12.69% (0%)'	'-0.67%'
'15-20%'	43051	'18.22% (0.6%)'	'17.78% (0%)'	'-0.43%'
'20-25%'	30651	'22.88% (0.8%)'	'22.85% (0%)'	'-0.03%'
'25-30%'	20413	'27.05% (1%)'	'27.84% (0%)'	'0.79%'
'30-35%'	14833	'31.14% (1.2%)'	'32.86% (0%)'	'1.72%'
'35-40%'	10293	'36.32% (1.6%)'	'37.87% (0%)'	'1.55%'
'40-45%'	6980	'39.87% (1.8%)'	'42.87% (0%)'	'2.99%'
'45-50%'	4421	'44.51% (2.4%)'	'47.79% (0.1%)'	'3.28%'
'50-55%'	2973	'48.74% (2.8%)'	'52.69% (0.1%)'	'3.95%'
'55-60%'	1712	'53.83% (3.8%)'	'57.75% (0.1%)'	'3.92%'
'60-65%'	902	'50.93% (5%)'	'62.76% (0.1%)'	'11.82%'
'65-70%'	336	'44.82% (6.8%)'	'67.55% (0.1%)'	'22.73%'
'Weighted Mean Error'		'-0.8%'		
'Median Absolute Error'		'2.11%'		
'Weighted Mean Absolute Error'		'1.46%'		
'Maximum Error'		'22.73% (65-70% group)'		
'Concordance Index'		'0.9560'		

'Groups 70-75%, 75-80%, 80-85%, 85-90%, 90-95%, 95-100% excluded due to insufficient follow-up or observed confidence intervals > 20%'



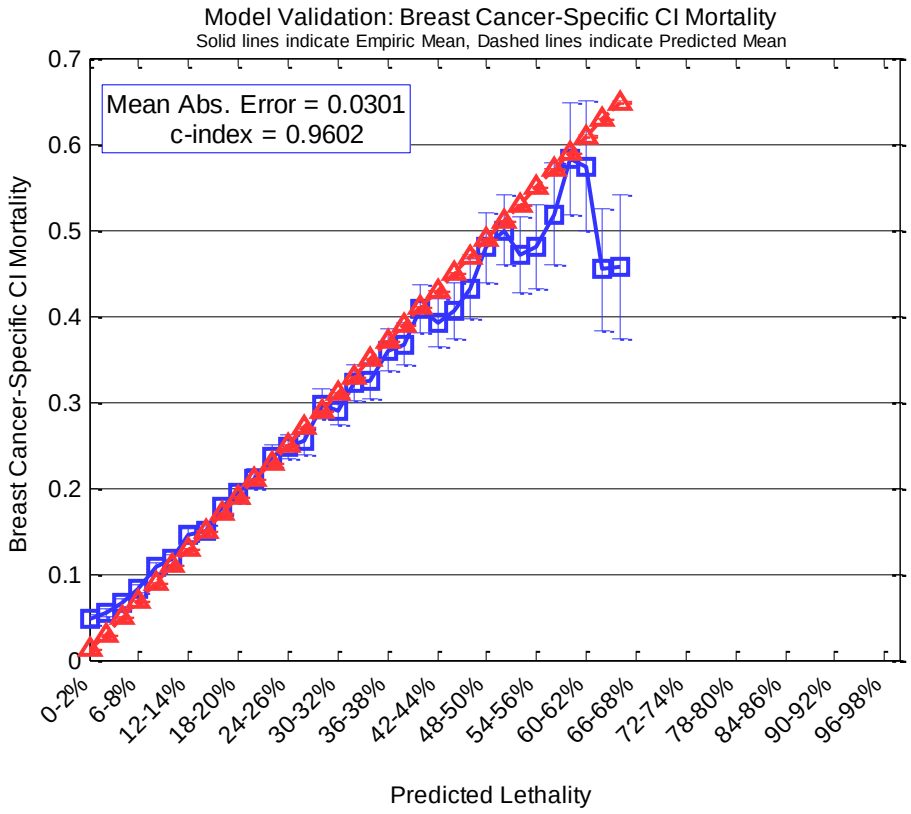
SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {'Predicted Lethality', [0:.05:1], '>'}});

Table and Figure 2c: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 2% predicted lethality bins using the Size+Nodes+PrognosticFactors equation

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0-2%'	27741	'4.64% (0.6%)'	'1.31% (0%)'	'-3.34%'
'2-4%'	47188	'5.4% (0.4%)'	'3.14% (0%)'	'-2.26%'
'4-6%'	44332	'6.73% (0.4%)'	'5.21% (0%)'	'-1.52%'
'6-8%'	39381	'8.64% (0.5%)'	'7.26% (0%)'	'-1.38%'
'8-10%'	32236	'10.9% (0.6%)'	'9.3% (0%)'	'-1.6%'
'10-12%'	30558	'11.69% (0.6%)'	'11.32% (0%)'	'-0.37%'
'12-14%'	24561	'14.54% (0.7%)'	'13.38% (0%)'	'-1.16%'
'14-16%'	20951	'15.55% (0.8%)'	'15.39% (0%)'	'-0.16%'
'16-18%'	17789	'18.21% (0.9%)'	'17.4% (0%)'	'-0.81%'
'18-20%'	15324	'19.82% (1%)'	'19.44% (0%)'	'-0.38%'
'20-22%'	13866	'21.51% (1.1%)'	'21.47% (0%)'	'-0.04%'
'22-24%'	11076	'23.38% (1.3%)'	'23.47% (0%)'	'0.08%'
'24-26%'	10274	'25.69% (1.4%)'	'25.42% (0%)'	'-0.28%'
'26-28%'	8858	'25.2% (1.4%)'	'27.52% (0%)'	'2.32%'
'28-30%'	6990	'30% (1.8%)'	'29.48% (0%)'	'-0.51%'
'30-32%'	6804	'29.16% (1.7%)'	'31.52% (0%)'	'2.36%'
'32-34%'	5520	'33.27% (2.1%)'	'33.53% (0%)'	'0.27%'
'34-36%'	4994	'32.51% (2%)'	'35.5% (0%)'	'2.99%'
'36-38%'	4111	'34.51% (2.5%)'	'37.56% (0%)'	'3.04%'
'38-40%'	3697	'40.02% (2.6%)'	'39.48% (0%)'	'-0.54%'
'40-42%'	3064	'40.22% (2.8%)'	'41.52% (0%)'	'1.3%'
'42-44%'	2803	'40.08% (2.9%)'	'43.47% (0%)'	'3.39%'
'44-46%'	2132	'40.71% (3.2%)'	'45.52% (0.1%)'	'4.81%'
'46-48%'	1913	'41.97% (3.5%)'	'47.45% (0.1%)'	'5.48%'
'48-50%'	1489	'48.61% (4.3%)'	'49.45% (0.1%)'	'0.84%'
'50-52%'	1341	'50.42% (4.2%)'	'51.37% (0.1%)'	'0.95%'
'52-54%'	1152	'47.58% (4.5%)'	'53.32% (0.1%)'	'5.74%'
'54-56%'	934	'50.26% (5.2%)'	'55.42% (0.1%)'	'5.16%'
'56-58%'	712	'51.78% (5.8%)'	'57.42% (0.1%)'	'5.64%'
'58-60%'	546	'56.06% (6.1%)'	'59.64% (0.1%)'	'3.58%'
'60-62%'	424	'57.45% (8.2%)'	'61.47% (0.1%)'	'4.01%'
'62-64%'	340	'44.15% (7%)'	'63.47% (0.1%)'	'19.32%'
'64-66%'	220	'45.69% (8.5%)'	'65.35% (0.1%)'	'19.66%'

'Weighted Mean Error'	'-0.79%'
'Median Absolute Error'	'1.6%'
'Weighted Mean Absolute Error'	'1.47%'
'Maximum Error'	'19.66% (64-66% group)'
'Concordance Index'	'0.9602'

"'Groups 66-100% excluded due to insufficient follow-up or observed confidence intervals > 20%'



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {'Predicted Lethality', [0:.02:1], '>'}});

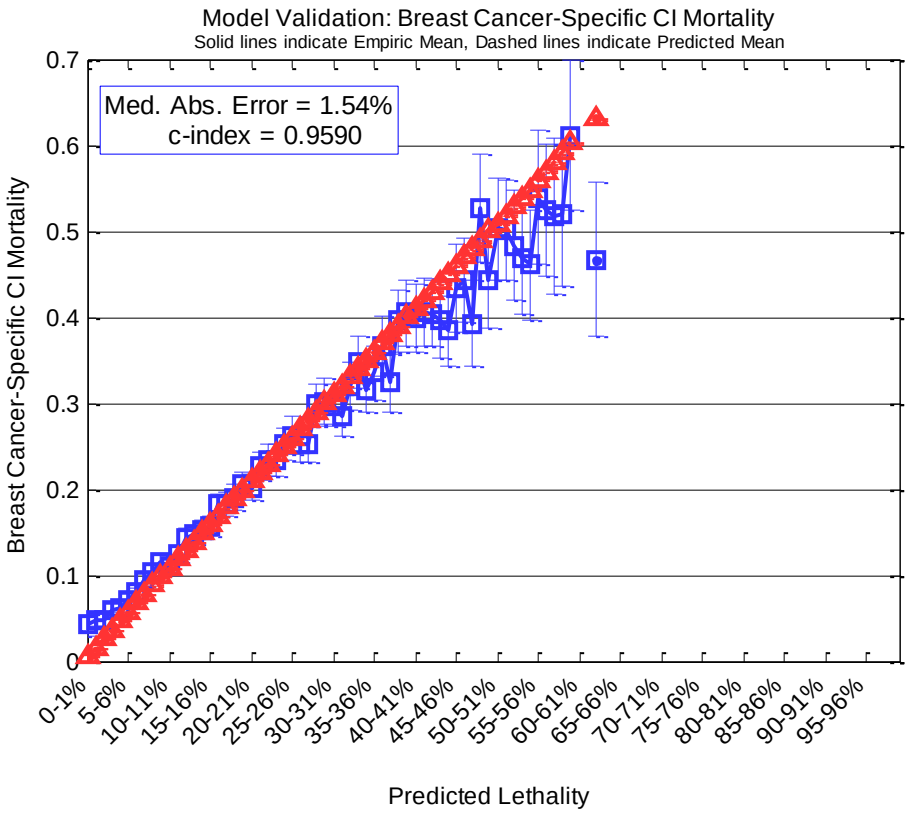
Table and Figure 2d: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 1% predicted lethality bins using the Size+Nodes+PrognosticFactors equation

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0-1%'	8761	'4.26% (1.3%)'	'0.68% (0%)'	'-3.58%'
'1-2%'	18980	'4.82% (0.7%)'	'1.6% (0%)'	'-3.22%'
'2-3%'	23649	'4.73% (0.6%)'	'2.63% (0%)'	'-2.1%'
'3-4%'	23539	'6.01% (0.6%)'	'3.66% (0%)'	'-2.35%'
'4-5%'	22620	'6.26% (0.6%)'	'4.7% (0%)'	'-1.56%'
'5-6%'	21712	'7.21% (0.6%)'	'5.74% (0%)'	'-1.46%'
'6-7%'	20299	'7.92% (0.7%)'	'6.76% (0%)'	'-1.16%'
'7-8%'	19082	'9.42% (0.7%)'	'7.8% (0%)'	'-1.62%'
'8-9%'	17482	'10.39% (0.8%)'	'8.84% (0%)'	'-1.54%'
'9-10%'	14754	'11.5% (0.9%)'	'9.84% (0%)'	'-1.66%'
'10-11%'	16148	'11.01% (0.8%)'	'10.82% (0%)'	'-0.19%'
'11-12%'	14410	'12.43% (0.9%)'	'11.88% (0%)'	'-0.56%'
'12-13%'	12308	'14.41% (1%)'	'12.89% (0%)'	'-1.51%'
'13-14%'	12253	'14.68% (1%)'	'13.88% (0%)'	'-0.8%'
'14-15%'	11013	'15.35% (1.1%)'	'14.92% (0%)'	'-0.43%'
'15-16%'	9938	'15.75% (1.2%)'	'15.9% (0%)'	'0.15%'
'16-17%'	9428	'18.22% (1.3%)'	'16.94% (0%)'	'-1.27%'
'17-18%'	8361	'18.19% (1.4%)'	'17.91% (0%)'	'-0.27%'
'18-19%'	7589	'19.07% (1.5%)'	'18.97% (0%)'	'-0.1%'
'19-20%'	7735	'20.55% (1.5%)'	'19.91% (0%)'	'-0.64%'
'20-21%'	6690	'20.23% (1.6%)'	'20.95% (0%)'	'0.72%'
'21-22%'	7176	'22.66% (1.6%)'	'21.95% (0%)'	'-0.71%'
'22-23%'	5635	'23.32% (1.9%)'	'22.96% (0%)'	'-0.36%'
'23-24%'	5441	'23.41% (1.8%)'	'23.99% (0%)'	'0.58%'
'24-25%'	5709	'25.26% (1.9%)'	'24.99% (0%)'	'-0.26%'
'25-26%'	4565	'26.24% (2.2%)'	'25.94% (0%)'	'-0.3%'
'26-27%'	4417	'25.21% (2%)'	'27.04% (0%)'	'1.82%'
'27-28%'	4441	'25.17% (2.1%)'	'28.01% (0%)'	'2.84%'
'28-29%'	3754	'29.8% (2.5%)'	'28.96% (0%)'	'-0.85%'
'29-30%'	3236	'30.16% (2.7%)'	'30.09% (0%)'	'-0.07%'
'30-31%'	3434	'29.67% (2.4%)'	'31.06% (0%)'	'1.39%'
'31-32%'	3370	'28.58% (2.4%)'	'31.99% (0%)'	'3.41%'
'32-33%'	2892	'31.89% (2.8%)'	'33.03% (0%)'	'1.14%'

'33-34%'	2628	'34.79% (3%)'	'34.09% (0%)'	'-0.7%'
'34-35%'	2509	'31.62% (2.7%)'	'35.01% (0%)'	'3.39%'
'35-36%'	2485	'33.54% (3.1%)'	'36% (0%)'	'2.46%'
'36-37%'	2125	'36.59% (3.6%)'	'37.07% (0%)'	'0.48%'
'37-38%'	1986	'32.36% (3.4%)'	'38.07% (0%)'	'5.71%'
'38-39%'	1946	'39.59% (3.7%)'	'38.98% (0%)'	'-0.61%'
'39-40%'	1751	'40.49% (3.8%)'	'40.05% (0%)'	'-0.44%'
'40-41%'	1600	'39.81% (4%)'	'41.04% (0%)'	'1.23%'
'41-42%'	1464	'40.66% (3.9%)'	'42.04% (0.1%)'	'1.38%'
'42-43%'	1496	'40.44% (3.9%)'	'43.02% (0.1%)'	'2.58%'
'43-44%'	1307	'39.69% (4.4%)'	'43.98% (0.1%)'	'4.29%'
'44-45%'	1113	'38.42% (4.1%)'	'45.06% (0.1%)'	'6.65%'
'45-46%'	1019	'43.44% (5.1%)'	'46.02% (0.1%)'	'2.58%'
'46-47%'	1021	'44.29% (4.9%)'	'47% (0.1%)'	'2.7%'
'47-48%'	892	'39.29% (5%)'	'47.97% (0.1%)'	'8.68%'
'48-49%'	764	'52.62% (6.3%)'	'48.9% (0.1%)'	'-3.72%'
'49-50%'	725	'44.31% (5.7%)'	'50.02% (0.1%)'	'5.72%'
'50-51%'	684	'50.28% (5.9%)'	'50.9% (0.1%)'	'0.62%'
'51-52%'	657	'50.18% (5.8%)'	'51.86% (0.1%)'	'1.67%'
'52-53%'	628	'48.36% (6.4%)'	'52.85% (0.1%)'	'4.49%'
'53-54%'	524	'46.77% (6.3%)'	'53.89% (0.1%)'	'7.12%'
'54-55%'	480	'46.09% (6.4%)'	'54.88% (0.1%)'	'8.79%'
'55-56%'	454	'53.92% (7.8%)'	'55.99% (0.1%)'	'2.06%'
'56-57%'	356	'52.46% (7.7%)'	'56.93% (0.1%)'	'4.47%'
'57-58%'	356	'51.67% (9%)'	'57.92% (0.1%)'	'6.25%'
'58-59%'	301	'51.94% (8.2%)'	'59.09% (0.1%)'	'7.15%'
'59-60%'	245	'61.14% (8.7%)'	'60.31% (0.1%)'	'-0.82%'
'62-63%'	207	'46.74% (8.9%)'	'63.07% (0.1%)'	'16.34%'
'0-1%'	8761	'4.26% (1.3%)'	'0.68% (0%)'	'-3.58%'

'Weighted Mean Error'	'-0.81%'
'Median Absolute Error'	'1.54%'
'Weighted Mean Absolute Error'	'1.51%'
'Maximum Error'	'16.34% (62-63% group)'
'Concordance Index'	'0.9590'

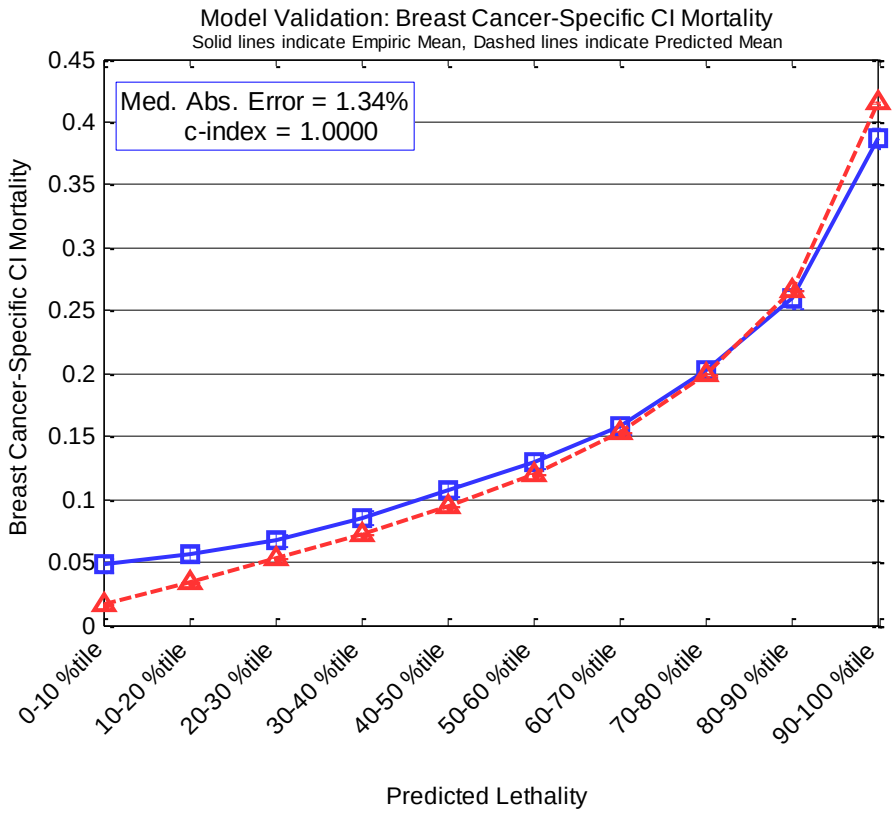
'"Groups 63-100% excluded due to insufficient follow-up or observed confidence intervals > 20%'



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {'Predicted Lethality', [0:.01:1], '>'}});

Table and Figure 2e: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 10% predicted lethality percentiles using the Size+Nodes+PrognosticFactors equation

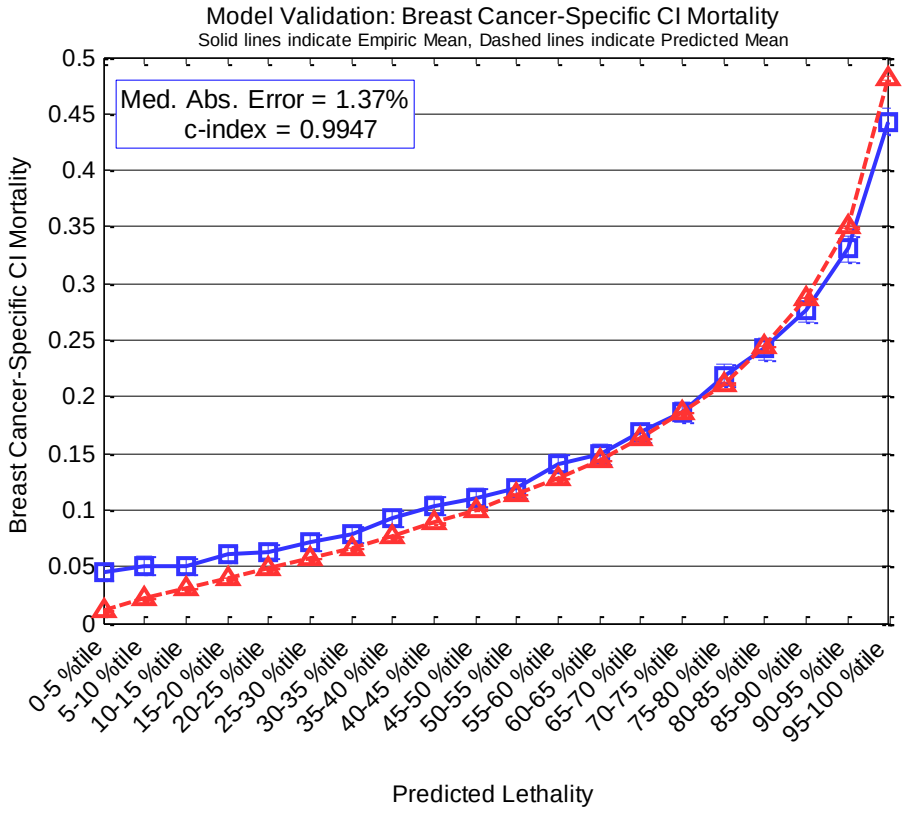
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0-10 %tile'	39399	'4.79% (0.5%)'	'1.62% (0%)'	'-3.17%'
'10-20 %tile'	39360	'5.58% (0.5%)'	'3.48% (0%)'	'-2.1%'
'20-30 %tile'	39381	'6.75% (0.5%)'	'5.27% (0%)'	'-1.47%'
'30-40 %tile'	39377	'8.59% (0.5%)'	'7.21% (0%)'	'-1.38%'
'40-50 %tile'	39378	'10.75% (0.5%)'	'9.45% (0%)'	'-1.29%'
'50-60 %tile'	39381	'12.99% (0.6%)'	'12.08% (0%)'	'-0.92%'
'60-70 %tile'	39376	'15.85% (0.6%)'	'15.37% (0%)'	'-0.48%'
'70-80 %tile'	39379	'20.28% (0.7%)'	'19.88% (0%)'	'-0.4%'
'80-90 %tile'	39379	'25.96% (0.7%)'	'26.61% (0%)'	'0.65%'
'90-100 %tile'	39379	'38.7% (0.8%)'	'41.57% (0.1%)'	'2.87%'
'Weighted Mean Error'		'-0.77%'		
'Median Absolute Error'		'1.34%'		
'Weighted Mean Absolute Error'		'1.47%'		
'Maximum Error'		'-3.17% (0-10 %tile group)'		
'Concordance Index'		'1.0000'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {'Predicted Lethality', [0:10:100], '%'}});

Table and Figure 2f: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 5% predicted lethality percentiles using the Size+Nodes+PrognosticFactors equation

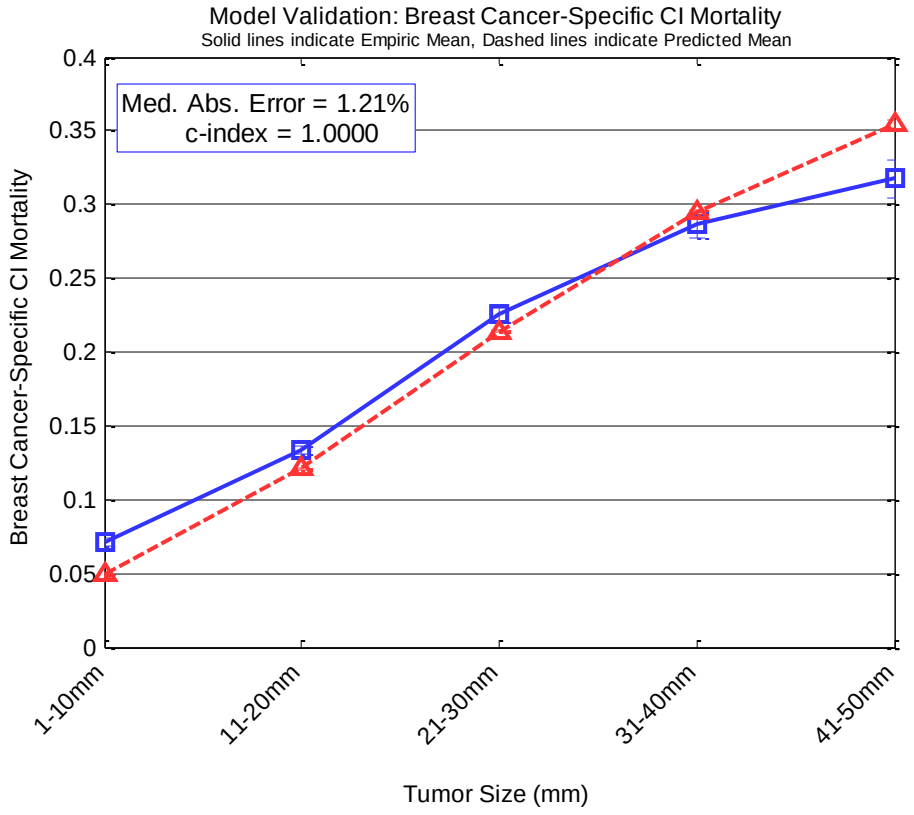
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0-5 %tile'	19689	'4.46% (0.7%)'	'1.07% (0%)'	'-3.39%'
'5-10 %tile'	19710	'5.08% (0.8%)'	'2.17% (0%)'	'-2.91%'
'10-15 %tile'	19669	'5.06% (0.6%)'	'3.05% (0%)'	'-2.01%'
'15-20 %tile'	19691	'6.05% (0.7%)'	'3.91% (0%)'	'-2.14%'
'20-25 %tile'	19763	'6.33% (0.6%)'	'4.81% (0%)'	'-1.52%'
'25-30 %tile'	19618	'7.16% (0.7%)'	'5.74% (0%)'	'-1.42%'
'30-35 %tile'	19731	'7.9% (0.7%)'	'6.69% (0%)'	'-1.21%'
'35-40 %tile'	19646	'9.28% (0.7%)'	'7.72% (0%)'	'-1.56%'
'40-45 %tile'	19689	'10.38% (0.8%)'	'8.84% (0%)'	'-1.54%'
'45-50 %tile'	19689	'11.11% (0.7%)'	'10.07% (0%)'	'-1.04%'
'50-55 %tile'	19727	'11.87% (0.8%)'	'11.35% (0%)'	'-0.51%'
'55-60 %tile'	19654	'14.12% (0.8%)'	'12.8% (0%)'	'-1.32%'
'60-65 %tile'	19697	'14.92% (0.8%)'	'14.43% (0%)'	'-0.49%'
'65-70 %tile'	19679	'16.79% (0.9%)'	'16.31% (0%)'	'-0.48%'
'70-75 %tile'	19690	'18.7% (0.9%)'	'18.57% (0%)'	'-0.13%'
'75-80 %tile'	19689	'21.87% (1%)'	'21.2% (0%)'	'-0.67%'
'80-85 %tile'	19692	'24.27% (1%)'	'24.45% (0%)'	'0.18%'
'85-90 %tile'	19687	'27.64% (1%)'	'28.77% (0%)'	'1.14%'
'90-95 %tile'	19691	'33.04% (1.1%)'	'35.01% (0%)'	'1.97%'
'95-100 %tile'	19688	'44.34% (1.1%)'	'48.13% (0.1%)'	'3.79%'
'Weighted Mean Error'		'-0.76%'		
'Median Absolute Error'		'1.37%'		
'Weighted Mean Absolute Error'		'1.47%'		
'Maximum Error'		'3.79% (95-100 %tile group)'		
'Concordance Index'		'0.9947'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {'Predicted Lethality', [0:5:100], '%'}});

Table and Figure 2g: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 10 mm tumor size bins

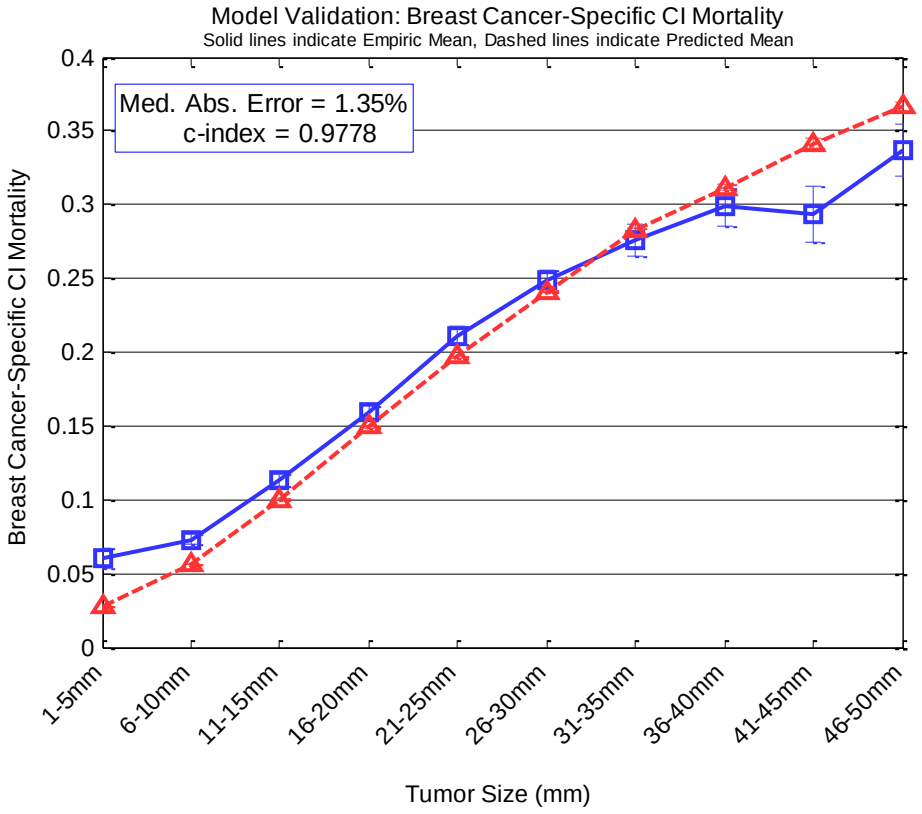
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'1-10mm'	102348	'7.09% (0.3%)'	'4.97% (0%)'	'-2.12%'
'11-20mm'	167513	'13.31% (0.3%)'	'12.11% (0%)'	'-1.21%'
'21-30mm'	81251	'22.54% (0.5%)'	'21.38% (0.1%)'	'-1.16%'
'31-40mm'	29270	'28.63% (0.8%)'	'29.52% (0.1%)'	'0.89%'
'41-50mm'	13407	'31.74% (1.3%)'	'35.47% (0.2%)'	'3.73%'
'Weighted Mean Error'		'-1.11%'		
'Median Absolute Error'		'1.21%'		
'Weighted Mean Absolute Error'		'1.5%'		
'Maximum Error'		'3.73% (41-50mm group)'		
'Concordance Index'		'1.0000'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {DBInfo.TUMOR_SIZE, [0:10:50], '>'}});

Table and Figure 2i: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 5 mm tumor size bins

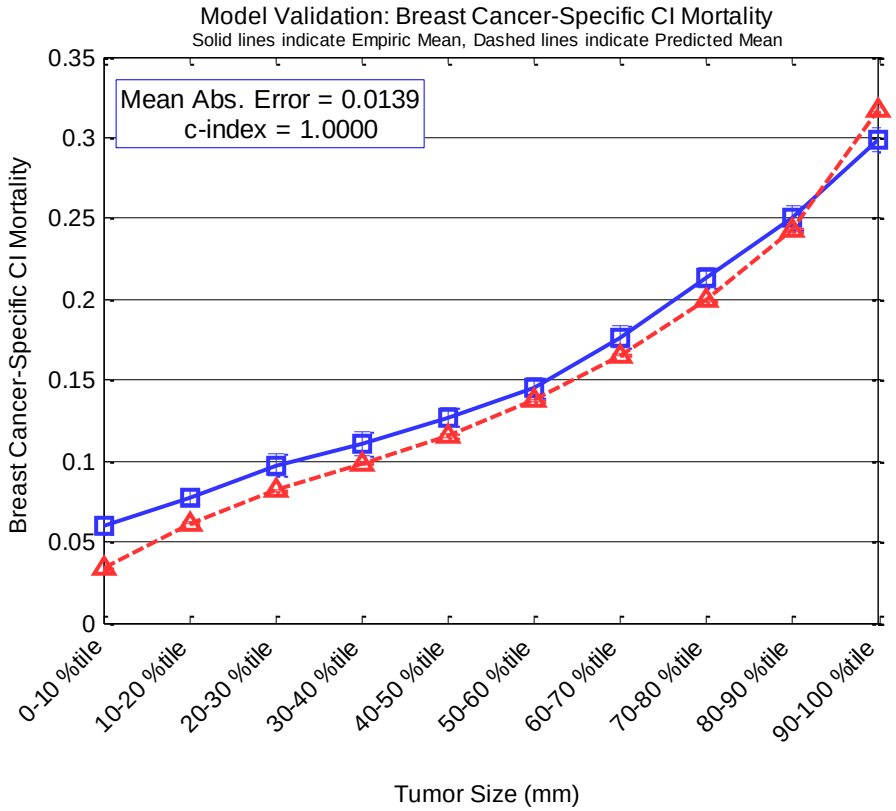
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'1-5mm'	23658	'6.02% (0.7%)'	'2.79% (0.1%)'	'-3.22%'
'6-10mm'	78690	'7.32% (0.3%)'	'5.62% (0%)'	'-1.7%'
'11-15mm'	95984	'11.31% (0.4%)'	'10.01% (0%)'	'-1.3%'
'16-20mm'	71529	'15.92% (0.5%)'	'14.92% (0.1%)'	'-1%'
'21-25mm'	50444	'21.1% (0.6%)'	'19.7% (0.1%)'	'-1.4%'
'26-30mm'	30807	'24.84% (0.8%)'	'24.13% (0.1%)'	'-0.71%'
'31-35mm'	16191	'27.58% (1.1%)'	'28.2% (0.2%)'	'0.62%'
'36-40mm'	13079	'29.86% (1.3%)'	'31.15% (0.2%)'	'1.3%'
'41-45mm'	6356	'29.35% (1.8%)'	'34.16% (0.3%)'	'4.8%'
'46-50mm'	7051	'33.68% (1.8%)'	'36.65% (0.3%)'	'2.96%'
'Weighted Mean Error'		'-1.07%'		
'Median Absolute Error'		'1.35%'		
'Weighted Mean Absolute Error'		'1.47%'		
'Maximum Error'		'4.8% (41-45mm group)'		
'Concordance Index'		'0.9778'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {DBInfo.TUMOR_SIZE, [0:5:50], '>'}});

Table and Figure 2i: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 10% tumor size percentiles

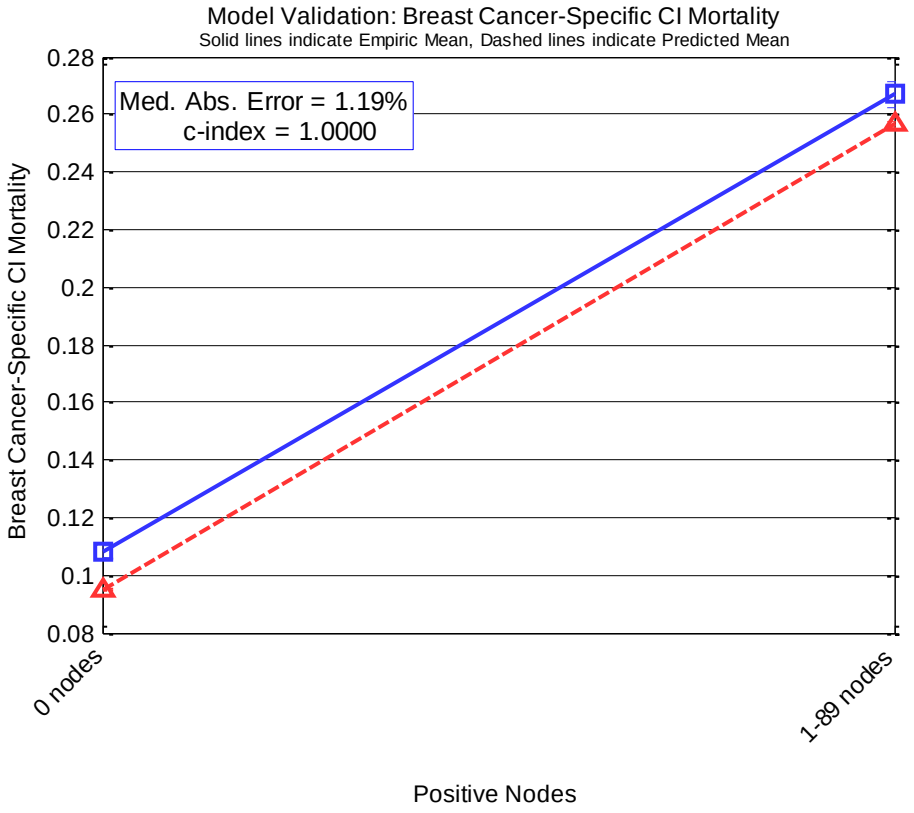
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0-10 %tile'	45520	'5.98% (0.5%)'	'3.44% (0%)'	'-2.54%'
'10-20 %tile'	56828	'7.78% (0.4%)'	'6.19% (0%)'	'-1.59%'
'20-30 %tile'	33292	'9.75% (0.6%)'	'8.22% (0.1%)'	'-1.53%'
'30-40 %tile'	25136	'11.03% (0.7%)'	'9.96% (0.1%)'	'-1.08%'
'40-50 %tile'	37556	'12.73% (0.6%)'	'11.63% (0.1%)'	'-1.1%'
'50-60 %tile'	41558	'14.53% (0.6%)'	'13.81% (0.1%)'	'-0.72%'
'60-70 %tile'	36284	'17.68% (0.6%)'	'16.66% (0.1%)'	'-1.03%'
'70-80 %tile'	44131	'21.35% (0.6%)'	'20.01% (0.1%)'	'-1.34%'
'80-90 %tile'	34872	'25.01% (0.7%)'	'24.45% (0.1%)'	'-0.56%'
'90-100 %tile'	38612	'29.91% (0.7%)'	'31.87% (0.1%)'	'1.96%'
'Weighted Mean Error'		'-1%'		
'Median Absolute Error'		'1.22%'		
'Weighted Mean Absolute Error'		'1.39%'		
'Maximum Error'		'-2.54% (0-10 %tile group)'		
'Concordance Index'		'1.0000'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {DBInfo.TUMOR_SIZE, [0:10:100], '%'}});

Table and Figure 2j: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by lymph nodes positivity status

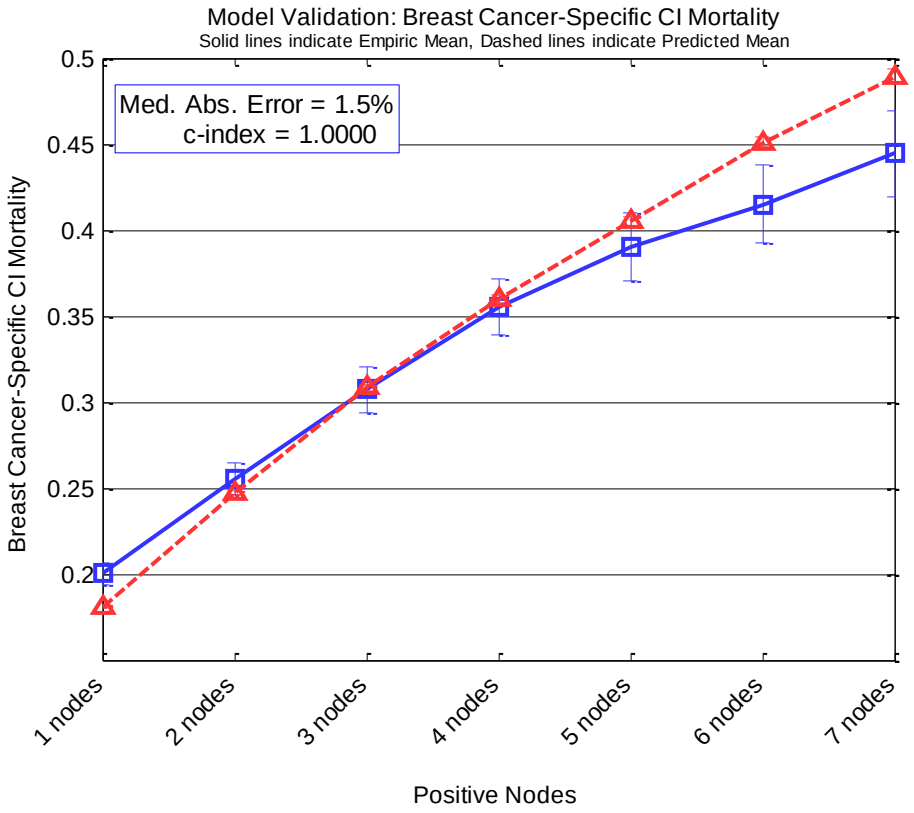
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0 nodes'	277866	'10.81% (0.2%)'	'9.5% (0%)'	'-1.31%'
'1-89 nodes'	115923	'26.7% (0.4%)'	'25.64% (0.1%)'	'-1.07%'
'Weighted Mean Error'		'-1.24%'		
'Median Absolute Error'		'1.19%'		
'Weighted Mean Absolute Error'		'1.24%'		
'Maximum Error'		'-1.31% (0-0 nodes group)'		
'Concordance Index'		'1.0000'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {DBInfo.POSITIVE_NODES, [-1,0,89], '>'}});

Table and Figure 2k: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by number of positive lymph nodes

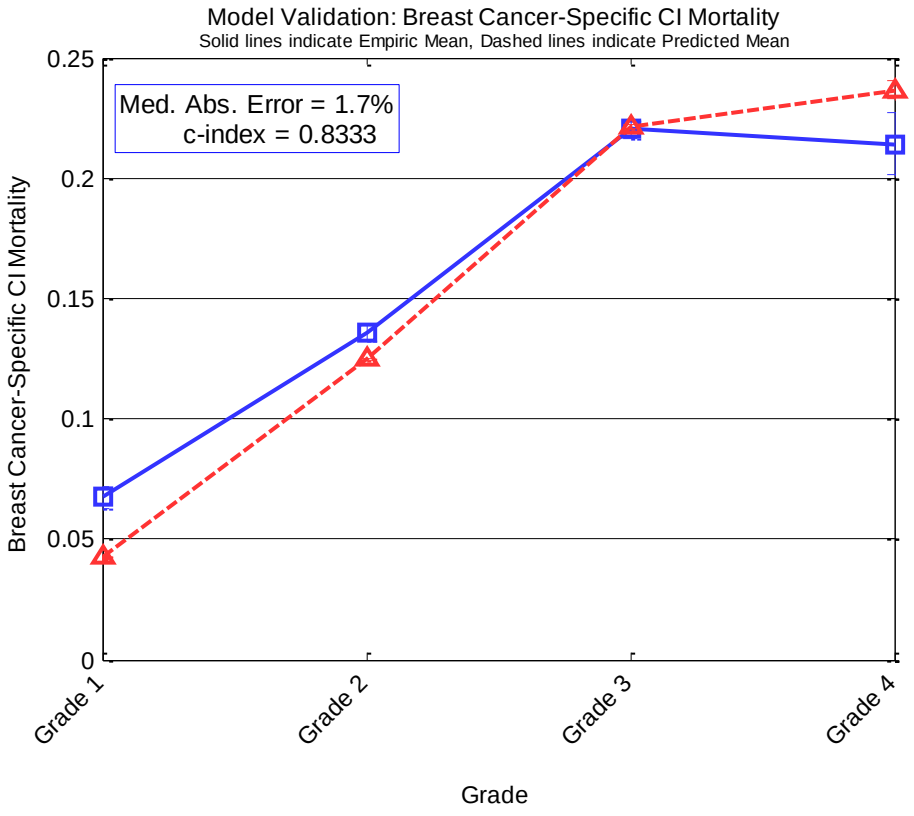
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'1 nodes'	53960	'20.04% (0.6%)'	'18.12% (0.1%)'	'-1.92%'
'2 nodes'	24757	'25.49% (0.9%)'	'24.66% (0.1%)'	'-0.83%'
'3 nodes'	13836	'30.7% (1.3%)'	'30.82% (0.2%)'	'0.12%'
'4 nodes'	8900	'35.54% (1.6%)'	'35.97% (0.2%)'	'0.43%'
'5 nodes'	6250	'38.97% (2%)'	'40.48% (0.3%)'	'1.5%'
'6 nodes'	4655	'41.49% (2.2%)'	'45.11% (0.3%)'	'3.62%'
'7 nodes'	3565	'44.45% (2.5%)'	'48.93% (0.4%)'	'4.49%'
'1 nodes'	53960	'20.04% (0.6%)'	'18.12% (0.1%)'	'-1.92%'
'Weighted Mean Error'		'-0.66%'		
'Median Absolute Error'		'1.5%'		
'Weighted Mean Absolute Error'		'1.48%'		
'Maximum Error'		'4.49% (7 nodes group)'		
'Concordance Index'		'1.0000'		



```
SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base',
Breast.snapFilter, { {DBInfo.POSITIVE_NODES, [1:7], '='}});
```

Table and Figure 2l: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by tumor grade

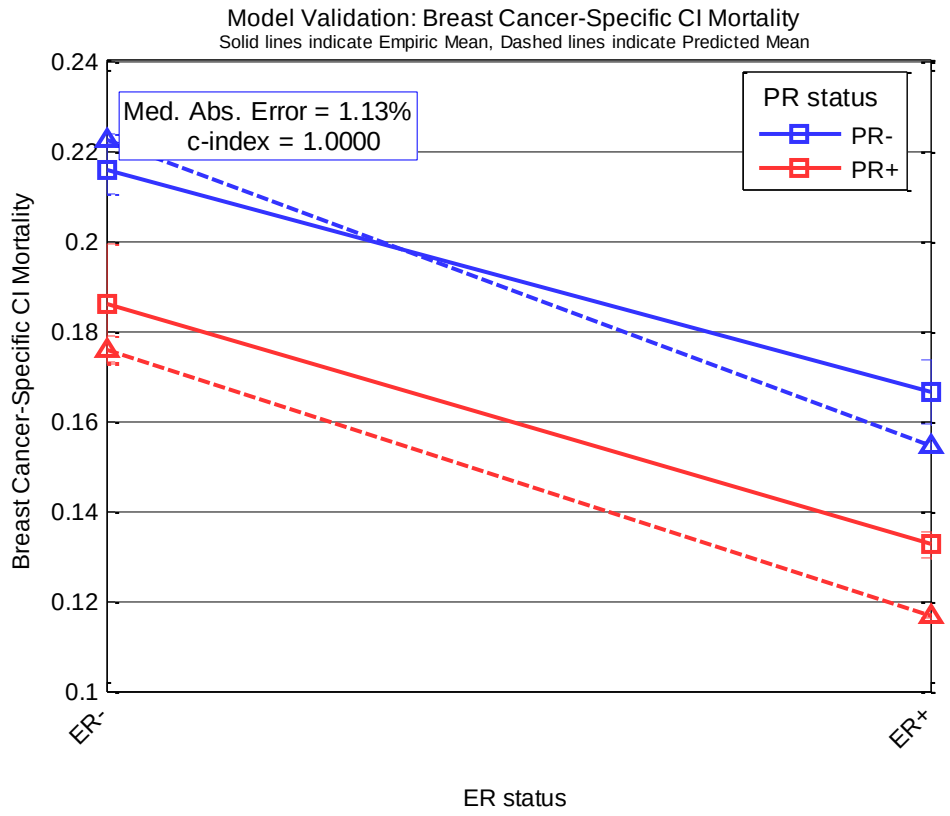
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'Grade 1'	71343	'6.75% (0.5%)'	'4.29% (0%)'	'-2.46%'
'Grade 2'	149898	'13.6% (0.3%)'	'12.47% (0%)'	'-1.13%'
'Grade 3'	119305	'22.01% (0.4%)'	'22.12% (0.1%)'	'0.11%'
'Grade 4'	7021	'21.41% (1.3%)'	'23.67% (0.3%)'	'2.26%'
'Weighted Mean Error'		'-0.91%'		
'Median Absolute Error'		'1.7%'		
'Weighted Mean Absolute Error'		'1.08%'		
'Maximum Error'		'-2.46% (Grade 1 group)'		
'Concordance Index'		'0.8333'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {DBInfo.GRADE, [1:4], '='}});

Table and Figure 2m: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by estrogen and progesterone receptor status

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'ER- / PR-'	62315	'21.58% (0.5%)'	'22.26% (0.1%)'	'0.68%'
'ER- / PR+'	6583	'18.62% (1.3%)'	'17.57% (0.3%)'	'-1.04%'
'ER+ / PR-'	39857	'16.64% (0.7%)'	'15.43% (0.1%)'	'-1.21%'
'ER+ / PR+'	215003	'13.25% (0.3%)'	'11.65% (0%)'	'-1.6%'
'Weighted Mean Error'		'-1.1%'		
'Median Absolute Error'		'1.13%'		
'Weighted Mean Absolute Error'		'1.36%'		
'Maximum Error'		'-1.6% (ER+ / PR+ group)'		
'Concordance Index'		'1.0000'		

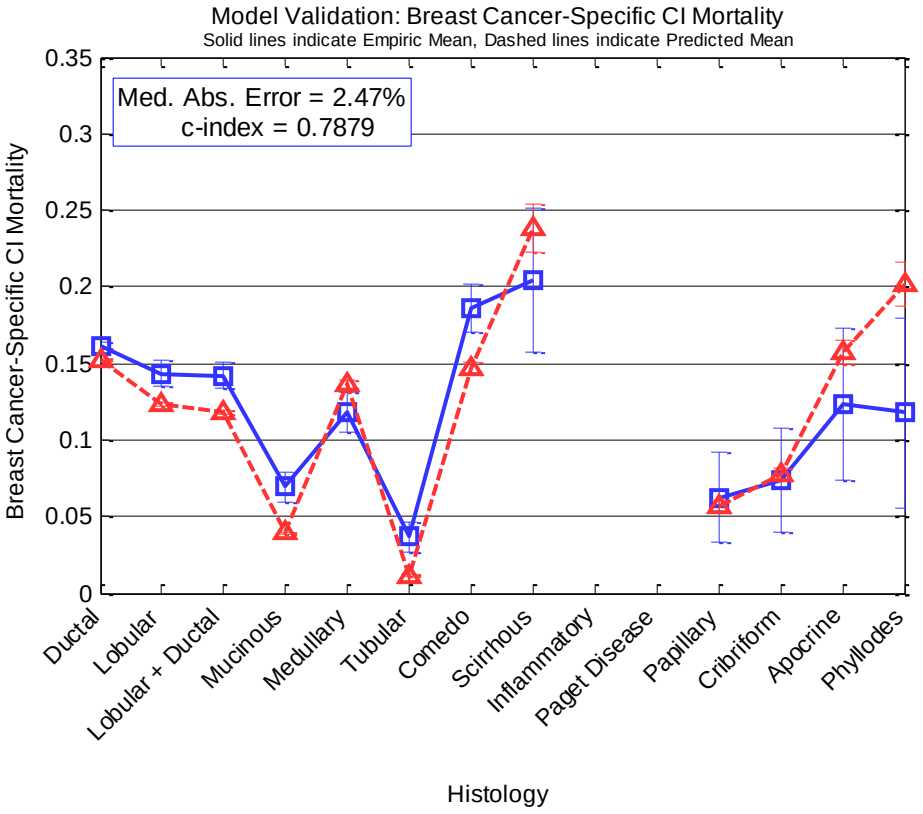


SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {DBInfo.ER_STATUS, [0,1], '='},{DBInfo.PR_STATUS, [0,1], '='}});

Table and Figure 2n: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by histological type

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'Ductal'	289896	'16.16% (0.2%)'	'15.28% (0%)'	'-0.88%'
'Lobular'	28203	'14.36% (0.8%)'	'12.34% (0.1%)'	'-2.02%'
'Lobular + Ductal'	30398	'14.23% (0.9%)'	'11.83% (0.1%)'	'-2.4%'
'Mucinous'	9569	'6.92% (0.9%)'	'3.95% (0.1%)'	'-2.98%'
'Medullary'	3945	'11.82% (1.3%)'	'13.62% (0.2%)'	'1.8%'
'Tubular'	5802	'3.69% (1%)'	'1.16% (0%)'	'-2.53%'
'Comedo'	3330	'18.62% (1.5%)'	'14.64% (0.4%)'	'-3.97%'
'Scirrhous'	389	'20.4% (4.7%)'	'23.86% (1.6%)'	'3.46%'
'Papillary'	717	'6.27% (2.9%)'	'5.73% (0.4%)'	'-0.54%'
'Cribriform'	946	'7.37% (3.5%)'	'7.77% (0.4%)'	'0.4%'
'Apocrine'	929	'12.37% (5%)'	'15.76% (0.8%)'	'3.39%'
'Phyllodes'	134	'11.78% (6.2%)'	'20.14% (1.4%)'	'8.36%'
'Weighted Mean Error'		'-1.15%'		
'Median Absolute Error'		'2.47%'		
'Weighted Mean Absolute Error'		'1.22%'		
'Maximum Error'		'8.36% (Phyllodes group)'		
'Concordance Index'		'0.7879'		

'Inflammatory and Paget Disease excluded due to insufficient follow-up or observed confidence intervals > 20%'



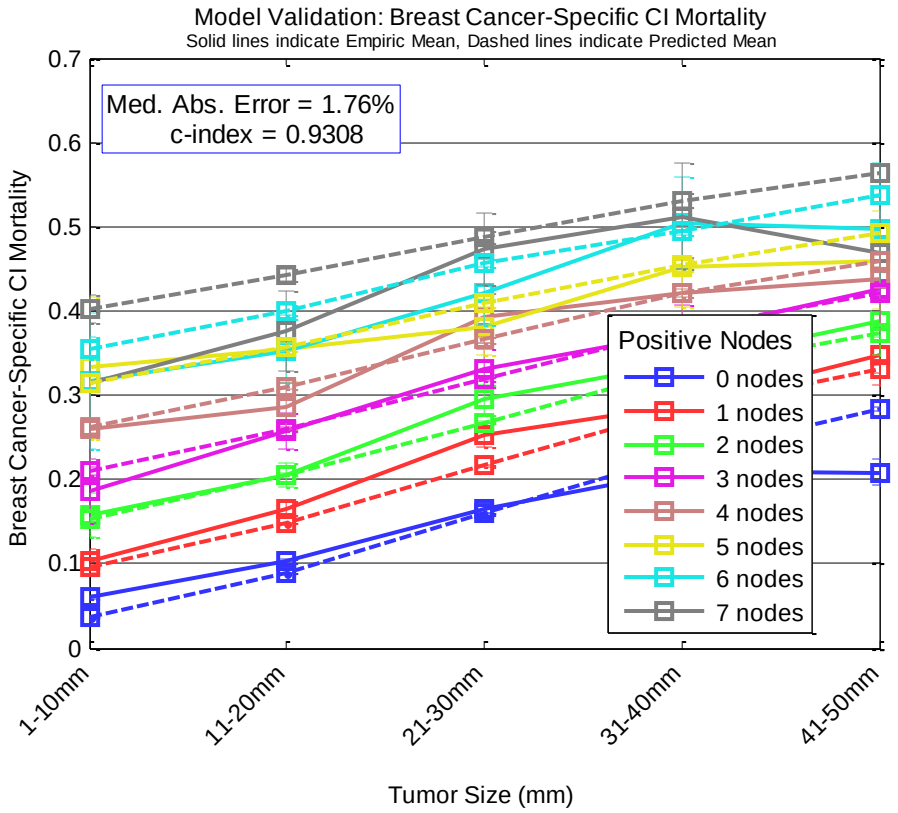
SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {DBInfo.HISTOLOGY, Breast.histologies, '='}});

Table and Figure 2p: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Permutations of 10 mm tumor size bins and number of positive lymph nodes

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'1-10mm / 0 nodes'	90078	'6.03% (0.3%)'	'3.73% (0%)'	'-2.31%'
'1-10mm / 1 nodes'	7519	'10.29% (1.4%)'	'9.68% (0.1%)'	'-0.62%'
'1-10mm / 2 nodes'	2413	'15.73% (2.6%)'	'15.39% (0.2%)'	'-0.34%'
'1-10mm / 3 nodes'	975	'18.6% (3.9%)'	'20.96% (0.4%)'	'2.36%'
'1-10mm / 4 nodes'	555	'26% (5.7%)'	'26.13% (0.7%)'	'0.13%'
'1-10mm / 5 nodes'	376	'33.31% (8.4%)'	'31.48% (1%)'	'-1.82%'
'1-10mm / 6 nodes'	267	'31.71% (8.1%)'	'35.57% (1.2%)'	'3.85%'
'1-10mm / 7 nodes'	165	'31.53% (9.6%)'	'40.24% (1.6%)'	'8.72%'
'11-20mm / 0 nodes'	121378	'10.36% (0.3%)'	'8.89% (0%)'	'-1.47%'
'11-20mm / 1 nodes'	24054	'16.58% (0.9%)'	'14.87% (0.1%)'	'-1.7%'
'11-20mm / 2 nodes'	9945	'20.55% (1.4%)'	'20.6% (0.1%)'	'0.05%'
'11-20mm / 3 nodes'	4934	'25.8% (2.1%)'	'26.06% (0.2%)'	'0.26%'
'11-20mm / 4 nodes'	2939	'28.68% (2.6%)'	'31.01% (0.3%)'	'2.33%'
'11-20mm / 5 nodes'	1884	'35.44% (3.7%)'	'35.75% (0.4%)'	'0.3%'
'11-20mm / 6 nodes'	1369	'35.24% (3.8%)'	'40.08% (0.5%)'	'4.85%'
'11-20mm / 7 nodes'	1010	'37.6% (4.7%)'	'44.2% (0.7%)'	'6.6%'
'21-30mm / 0 nodes'	46451	'16.5% (0.6%)'	'15.92% (0.1%)'	'-0.57%'
'21-30mm / 1 nodes'	14582	'25.27% (1.3%)'	'21.61% (0.1%)'	'-3.66%'
'21-30mm / 2 nodes'	7644	'29.46% (1.8%)'	'26.8% (0.2%)'	'-2.66%'
'21-30mm / 3 nodes'	4562	'33.19% (2.3%)'	'31.87% (0.3%)'	'-1.32%'
'21-30mm / 4 nodes'	2964	'39.23% (3%)'	'36.58% (0.3%)'	'-2.65%'
'21-30mm / 5 nodes'	2223	'37.98% (3.3%)'	'40.92% (0.4%)'	'2.93%'
'21-30mm / 6 nodes'	1610	'42.19% (4%)'	'45.72% (0.5%)'	'3.54%'
'21-30mm / 7 nodes'	1215	'47.39% (4.2%)'	'48.8% (0.6%)'	'1.41%'
'31-40mm / 0 nodes'	14134	'20.97% (1.1%)'	'22.81% (0.1%)'	'1.84%'
'31-40mm / 1 nodes'	5402	'28.86% (2%)'	'28.26% (0.2%)'	'-0.6%'
'31-40mm / 2 nodes'	3220	'33.79% (2.7%)'	'32.99% (0.3%)'	'-0.8%'
'31-40mm / 3 nodes'	2240	'37.32% (3.4%)'	'37.84% (0.4%)'	'0.52%'
'31-40mm / 4 nodes'	1576	'42.07% (4.3%)'	'42.05% (0.5%)'	'-0.02%'
'31-40mm / 5 nodes'	1086	'45.23% (4.8%)'	'45.4% (0.6%)'	'0.17%'
'31-40mm / 6 nodes'	888	'50.34% (5.4%)'	'49.59% (0.7%)'	'-0.76%'
'31-40mm / 7 nodes'	724	'51.24% (6.2%)'	'53.12% (0.8%)'	'1.88%'
'41-50mm / 0 nodes'	5825	'20.87% (1.6%)'	'28.26% (0.2%)'	'7.39%'

'41-50mm / 1 nodes'	2403	'34.73% (3.6%)'	'33.07% (0.4%)'	'-1.65%'
'41-50mm / 2 nodes'	1535	'38.84% (4.1%)'	'37.41% (0.5%)'	'-1.43%'
'41-50mm / 3 nodes'	1125	'42.6% (5.2%)'	'42% (0.7%)'	'-0.59%'
'41-50mm / 4 nodes'	866	'43.75% (5.7%)'	'45.94% (0.7%)'	'2.19%'
'41-50mm / 5 nodes'	681	'46.01% (5.8%)'	'49.25% (0.9%)'	'3.24%'
'41-50mm / 6 nodes'	521	'49.75% (7.8%)'	'53.7% (1%)'	'3.95%'
'41-50mm / 7 nodes'	451	'46.77% (6.8%)'	'56.34% (1%)'	'9.58%'

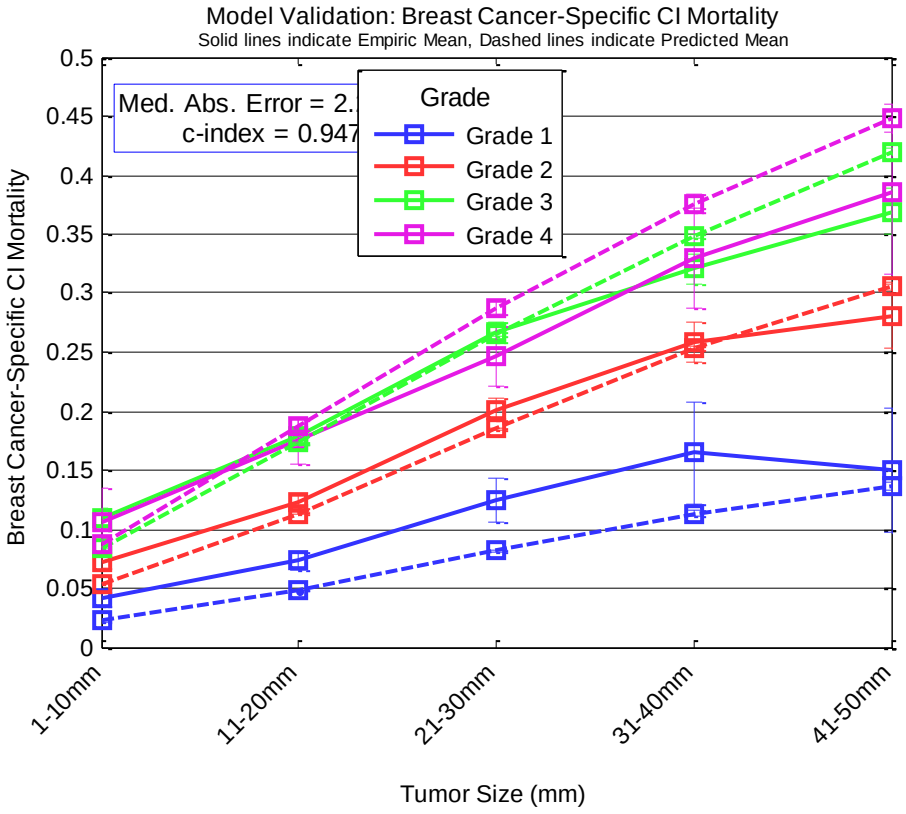
'Weighted Mean Error'	'-1.11%'
'Median Absolute Error'	'1.76%'
'Weighted Mean Absolute Error'	'1.74%'
'Maximum Error'	'9.58% (41-50mm / 7 nodes group)'
'Concordance Index'	'0.9308'



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {DBInfo.TUMOR_SIZE, [0:10:50], '>'},{DBInfo.POSITIVE_NODES, [0:7], '='}});

Table and Figure 2p: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Permutations of 10 mm tumor size bins and tumor grade

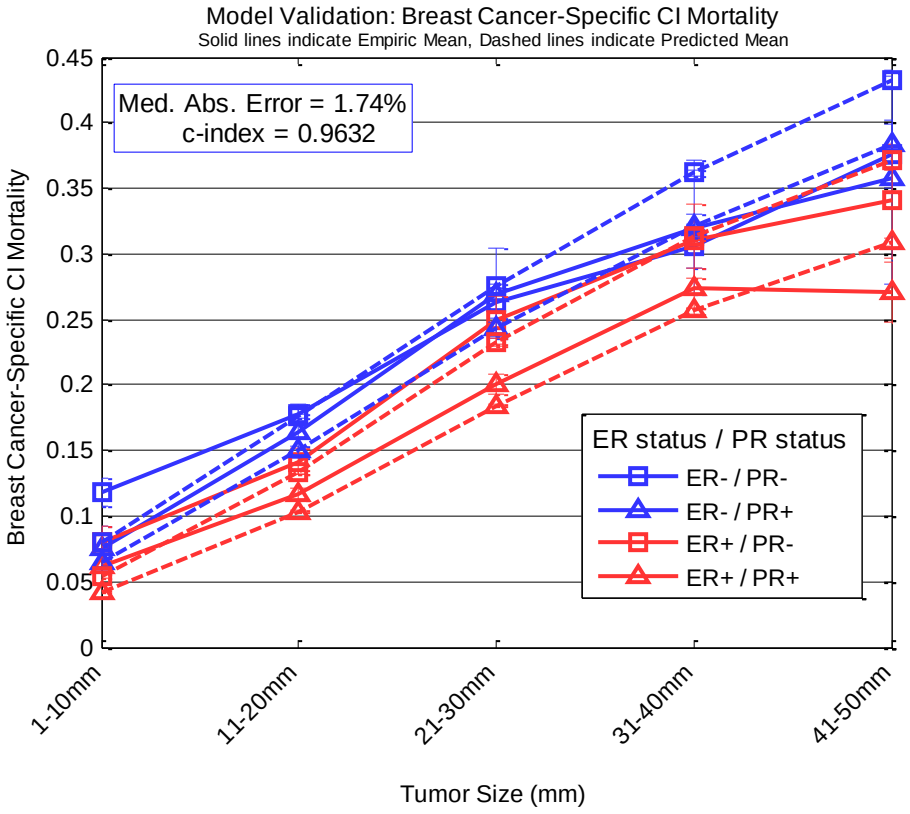
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'1-10mm / Grade 1'	31812	'4.14% (0.6%)'	'2.22% (0%)'	'-1.92%'
'1-10mm / Grade 2'	39531	'7.17% (0.5%)'	'5.39% (0%)'	'-1.78%'
'1-10mm / Grade 3'	16844	'10.95% (0.9%)'	'8.45% (0.1%)'	'-2.5%'
'1-10mm / Grade 4'	1172	'10.59% (2.9%)'	'8.75% (0.5%)'	'-1.84%'
'11-20mm / Grade 1'	29329	'7.31% (0.8%)'	'4.8% (0%)'	'-2.52%'
'11-20mm / Grade 2'	68920	'12.31% (0.5%)'	'11.31% (0%)'	'-1%'
'11-20mm / Grade 3'	47453	'17.85% (0.6%)'	'17.31% (0.1%)'	'-0.54%'
'11-20mm / Grade 4'	2660	'17.47% (1.9%)'	'18.81% (0.4%)'	'1.34%'
'21-30mm / Grade 1'	7311	'12.44% (1.9%)'	'8.18% (0.1%)'	'-4.25%'
'21-30mm / Grade 2'	28569	'20.14% (0.9%)'	'18.52% (0.1%)'	'-1.62%'
'21-30mm / Grade 3'	34447	'26.74% (0.8%)'	'26.52% (0.1%)'	'-0.22%'
'21-30mm / Grade 4'	1917	'24.71% (2.5%)'	'28.76% (0.5%)'	'4.05%'
'31-40mm / Grade 1'	1934	'16.45% (4.3%)'	'11.35% (0.2%)'	'-5.1%'
'31-40mm / Grade 2'	8892	'25.88% (1.7%)'	'25.32% (0.2%)'	'-0.56%'
'31-40mm / Grade 3'	14175	'32.07% (1.3%)'	'34.86% (0.2%)'	'2.79%'
'31-40mm / Grade 4'	866	'32.97% (4.3%)'	'37.62% (0.8%)'	'4.65%'
'41-50mm / Grade 1'	957	'15.05% (5.3%)'	'13.68% (0.4%)'	'-1.37%'
'41-50mm / Grade 2'	3986	'28.03% (2.8%)'	'30.58% (0.3%)'	'2.55%'
'41-50mm / Grade 3'	6386	'36.89% (2%)'	'41.99% (0.3%)'	'5.1%'
'41-50mm / Grade 4'	406	'38.53% (6.9%)'	'44.77% (1.2%)'	'6.24%'
'Weighted Mean Error'		'-0.99%'		
'Median Absolute Error'		'2.21%'		
'Weighted Mean Absolute Error'		'1.57%'		
'Maximum Error'		'6.24% (41-50mm / Grade 4 group)'		
'Concordance Index'		'0.9474'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {DBInfo.TUMOR_SIZE, [0:10:50], '>'},{DBInfo.GRADE, [1:4], '='}});

Table and Figure 2q: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Permutations of 10 mm tumor size bins and estrogen/progesterone receptor status

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'1-10mm / ER- / PR-'	10804	'11.81% (1.1%)'	'7.98% (0.1%)'	'-3.83%'
'1-10mm / ER- / PR+'	1490	'7.48% (1.8%)'	'6.44% (0.3%)'	'-1.04%'
'1-10mm / ER+ / PR-'	10917	'7.98% (1.2%)'	'5.41% (0.1%)'	'-2.57%'
'1-10mm / ER+ / PR+'	59828	'6.23% (0.5%)'	'4.26% (0%)'	'-1.97%'
'11-20mm / ER- / PR-'	23658	'17.76% (0.8%)'	'17.61% (0.1%)'	'-0.15%'
'11-20mm / ER- / PR+'	2757	'16.34% (1.9%)'	'14.98% (0.3%)'	'-1.37%'
'11-20mm / ER+ / PR-'	16386	'14.17% (1%)'	'13.41% (0.1%)'	'-0.76%'
'11-20mm / ER+ / PR+'	96180	'11.69% (0.4%)'	'10.36% (0%)'	'-1.33%'
'21-30mm / ER- / PR-'	17041	'26.26% (1.1%)'	'27.53% (0.2%)'	'1.27%'
'21-30mm / ER- / PR+'	1502	'26.99% (3.5%)'	'24.28% (0.5%)'	'-2.71%'
'21-30mm / ER+ / PR-'	8114	'24.96% (1.8%)'	'23.26% (0.2%)'	'-1.7%'
'21-30mm / ER+ / PR+'	40345	'20.06% (0.8%)'	'18.44% (0.1%)'	'-1.62%'
'31-40mm / ER- / PR-'	7408	'30.62% (1.7%)'	'36.18% (0.3%)'	'5.56%'
'31-40mm / ER- / PR+'	590	'32% (5.1%)'	'32.17% (0.9%)'	'0.17%'
'31-40mm / ER+ / PR-'	3047	'30.98% (2.9%)'	'31.42% (0.4%)'	'0.44%'
'31-40mm / ER+ / PR+'	12834	'27.41% (1.5%)'	'25.64% (0.2%)'	'-1.77%'
'41-50mm / ER- / PR-'	3404	'37.56% (2.6%)'	'43.18% (0.4%)'	'5.62%'
'41-50mm / ER- / PR+'	244	'35.84% (8.1%)'	'38.32% (1.5%)'	'2.47%'
'41-50mm / ER+ / PR-'	1393	'34.03% (4.3%)'	'37.12% (0.7%)'	'3.1%'
'41-50mm / ER+ / PR+'	5816	'27.09% (2.3%)'	'30.87% (0.3%)'	'3.78%'
'Weighted Mean Error'		'-1.03%'		
'Median Absolute Error'		'1.74%'		
'Weighted Mean Absolute Error'		'1.71%'		
'Maximum Error'		'5.62% (41-50mm / ER- / PR- group)'		
'Concordance Index'		'0.9632'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {DBInfo.TUMOR_SIZE, [0:10:50], '>'},{DBInfo.ER_STATUS, [0,1], '='},{DBInfo.PR_STATUS, [0,1], '='}});

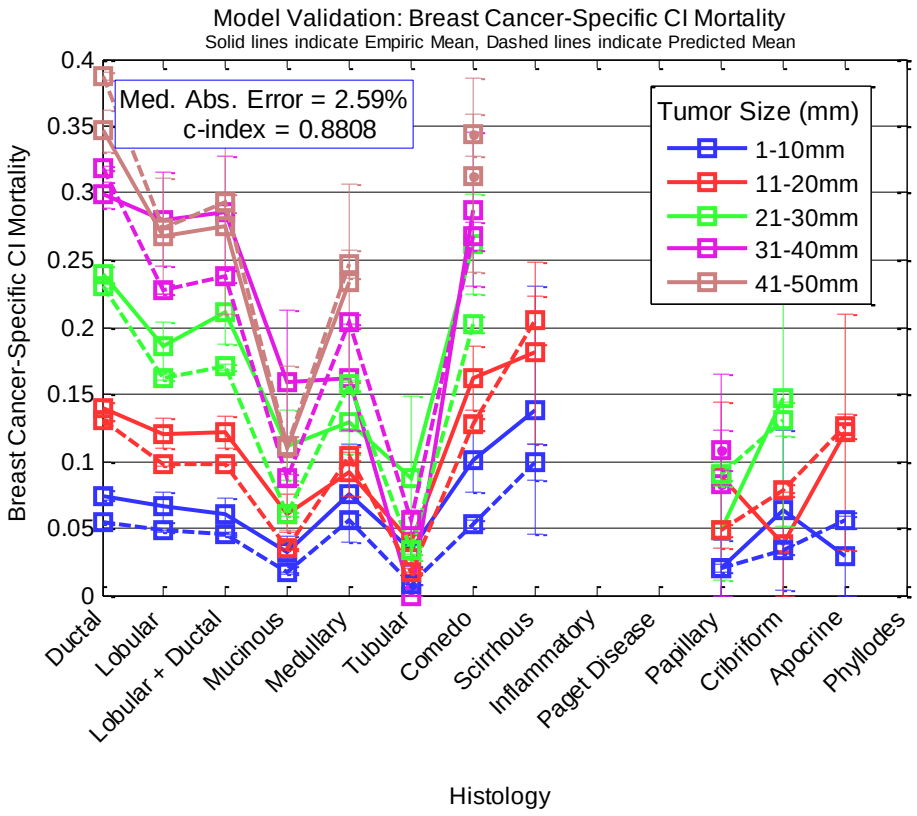
Table and Figure 2r: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Permutations of 10 mm tumor size bins and histological type

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'Ductal / 1-10mm'	75544	'7.46% (0.4%)'	'5.38% (0%)'	'-2.08%'
'Ductal / 11-20mm'	124551	'14.01% (0.3%)'	'13.05% (0%)'	'-0.96%'
'Ductal / 21-30mm'	59713	'23.95% (0.6%)'	'23.06% (0.1%)'	'-0.89%'
'Ductal / 31-40mm'	21084	'29.88% (1%)'	'31.82% (0.2%)'	'1.94%'
'Ductal / 41-50mm'	9004	'34.67% (1.5%)'	'38.73% (0.3%)'	'4.06%'
'Lobular / 1-10mm'	5879	'6.57% (1.2%)'	'4.78% (0.1%)'	'-1.79%'
'Lobular / 11-20mm'	11874	'12.08% (1.2%)'	'9.75% (0.1%)'	'-2.33%'
'Lobular / 21-30mm'	6312	'18.55% (1.9%)'	'16.25% (0.2%)'	'-2.3%'
'Lobular / 31-40mm'	2544	'28.01% (3.5%)'	'22.82% (0.4%)'	'-5.19%'
'Lobular / 41-50mm'	1594	'26.8% (4.4%)'	'27.34% (0.5%)'	'0.54%'
'Lobular + Ductal / 1-10mm'	6995	'6.03% (1.3%)'	'4.48% (0.1%)'	'-1.54%'
'Lobular + Ductal / 11-20mm'	13686	'12.18% (1.2%)'	'9.84% (0.1%)'	'-2.33%'
'Lobular + Ductal / 21-30mm'	6519	'21.09% (2.3%)'	'17.06% (0.2%)'	'-4.04%'
'Lobular + Ductal / 31-40mm'	2082	'28.55% (4.2%)'	'23.8% (0.4%)'	'-4.75%'
'Lobular + Ductal / 41-50mm'	1116	'27.48% (6.5%)'	'29.3% (0.6%)'	'1.82%'
'Mucinous / 1-10mm'	2837	'3.28% (1.1%)'	'1.68% (0%)'	'-1.61%'
'Mucinous / 11-20mm'	4157	'6.09% (1.4%)'	'3.48% (0.1%)'	'-2.61%'
'Mucinous / 21-30mm'	1710	'11.19% (2.5%)'	'6.08% (0.2%)'	'-5.11%'
'Mucinous / 31-40mm'	604	'15.92% (5.4%)'	'8.66% (0.4%)'	'-7.25%'
'Mucinous / 41-50mm'	261	'10.94% (6.2%)'	'11.18% (0.7%)'	'0.25%'
'Medullary / 1-10mm'	351	'7.6% (3.7%)'	'5.56% (0.5%)'	'-2.04%'
'Medullary / 11-20mm'	1609	'9.25% (1.8%)'	'10.37% (0.3%)'	'1.12%'
'Medullary / 21-30mm'	1308	'12.87% (2.3%)'	'15.69% (0.3%)'	'2.82%'
'Medullary / 31-40mm'	502	'16.25% (4%)'	'20.43% (0.5%)'	'4.18%'
'Medullary / 41-50mm'	175	'23.3% (7.4%)'	'24.69% (1%)'	'1.39%'
'Tubular / 1-10mm'	3938	'3.39% (1.2%)'	'0.77% (0%)'	'-2.62%'
'Tubular / 11-20mm'	1617	'4.02% (2.1%)'	'1.67% (0.1%)'	'-2.35%'
'Tubular / 21-30mm'	185	'8.78% (6.1%)'	'3.3% (0.3%)'	'-5.48%'
'Tubular / 31-40mm'	43	'0% (0%)'	'5.56% (0.9%)'	'5.56%'

'Comedo / 1-10mm'	946	'10.02% (2.3%)'	'5.32% (0.3%)'	'-4.69%'
'Comedo / 11-20mm'	1213	'16.22% (2.3%)'	'12.78% (0.4%)'	'-3.43%'
'Comedo / 21-30mm'	682	'26.17% (3.7%)'	'20.24% (0.7%)'	'-5.93%'
'Comedo / 31-40mm'	313	'28.79% (5.7%)'	'26.77% (1%)'	'-2.03%'
'Comedo / 41-50mm'	176	'31.3% (7.2%)'	'34.33% (1.5%)'	'3.04%'
'Scirrhous / 1-10mm'	78	'13.82% (9.2%)'	'9.87% (1.3%)'	'-3.95%'
'Scirrhous / 11-20mm'	179	'18.09% (6.8%)'	'20.49% (1.8%)'	'2.4%'
'Papillary / 1-10mm'	213	'2.06% (2.1%)'	'2.02% (0.3%)'	'-0.04%'
'Papillary / 11-20mm'	266	'8.94% (5.5%)'	'4.84% (0.4%)'	'-4.1%'
'Papillary / 21-30mm'	156	'4.82% (3.8%)'	'9.03% (0.9%)'	'4.2%'
'Papillary / 31-40mm'	50	'8.25% (8.3%)'	'10.84% (1.5%)'	'2.59%'
'Cribriform / 1-10mm'	325	'6.38% (6%)'	'3.43% (0.3%)'	'-2.95%'
'Cribriform / 11-20mm'	439	'3.82% (3.8%)'	'7.82% (0.5%)'	'4%'
'Cribriform / 21-30mm'	130	'14.74% (9.6%)'	'13.1% (1.3%)'	'-1.64%'
'Apocrine / 1-10mm'	234	'2.95% (2.9%)'	'5.61% (0.6%)'	'2.66%'
'Apocrine / 11-20mm'	368	'12.12% (8.8%)'	'12.63% (0.8%)'	'0.5%'

'Weighted Mean Error'	'-1.19%'
'Median Absolute Error'	'2.59%'
'Weighted Mean Absolute Error'	'1.68%'
'Maximum Error'	'-7.25% (Mucinous / 31-40mm group)'
'Concordance Index'	'0.8808'

'Many groups excluded due to insufficient follow-up or observed confidence intervals > 20%'

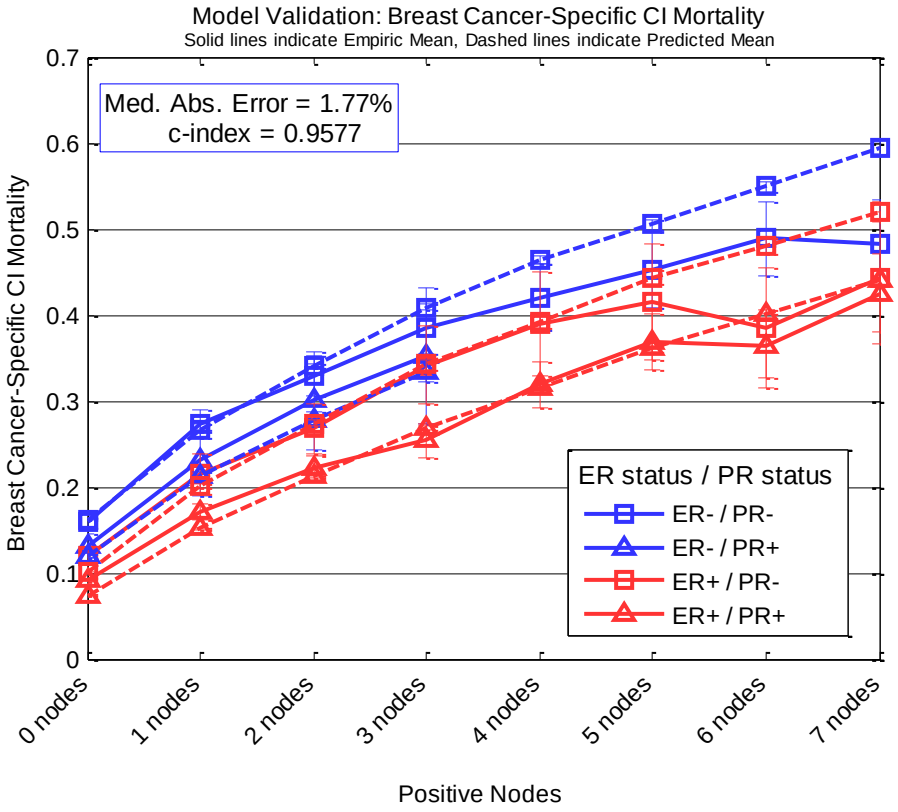


SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, {{DBInfo.HISTOLOGY, Breast.histologies, '='},{DBInfo.TUMOR_SIZE, [0:10:50], '>'}});

Table and Figure 2s: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Permutations of number of positive lymph nodes and estrogen/progesterone receptor status

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0 nodes / ER- / PR-'	42735	'15.89% (0.6%)'	'16.19% (0.1%)'	'0.31%'
'0 nodes / ER- / PR+'	4504	'13.05% (1.4%)'	'12.09% (0.2%)'	'-0.97%'
'0 nodes / ER+ / PR-'	28058	'11.92% (0.7%)'	'10.03% (0.1%)'	'-1.89%'
'0 nodes / ER+ / PR+'	152052	'9.18% (0.3%)'	'7.43% (0%)'	'-1.75%'
'1 nodes / ER- / PR-'	8671	'27.38% (1.6%)'	'26.53% (0.2%)'	'-0.84%'
'1 nodes / ER- / PR+'	901	'23.06% (4.2%)'	'21.26% (0.6%)'	'-1.8%'
'1 nodes / ER+ / PR-'	5517	'21.46% (2.4%)'	'20.11% (0.2%)'	'-1.35%'
'1 nodes / ER+ / PR+'	30135	'17.11% (1%)'	'15.19% (0.1%)'	'-1.92%'
'2 nodes / ER- / PR-'	4046	'32.99% (2.3%)'	'34.07% (0.3%)'	'1.07%'
'2 nodes / ER- / PR+'	477	'30% (5.7%)'	'27.9% (0.8%)'	'-2.1%'
'2 nodes / ER+ / PR-'	2485	'26.76% (2.9%)'	'27.43% (0.4%)'	'0.67%'
'2 nodes / ER+ / PR+'	13459	'22.21% (1.4%)'	'21.19% (0.1%)'	'-1.02%'
'3 nodes / ER- / PR-'	2416	'38.43% (3%)'	'40.87% (0.4%)'	'2.43%'
'3 nodes / ER- / PR+'	239	'35.18% (7.9%)'	'33.39% (1.3%)'	'-1.79%'
'3 nodes / ER+ / PR-'	1398	'34.11% (4.5%)'	'34.24% (0.6%)'	'0.13%'
'3 nodes / ER+ / PR+'	7457	'25.44% (2%)'	'26.79% (0.2%)'	'1.35%'
'4 nodes / ER- / PR-'	1654	'42.02% (3.8%)'	'46.32% (0.5%)'	'4.3%'
'4 nodes / ER+ / PR-'	900	'38.86% (6.1%)'	'39.14% (0.7%)'	'0.28%'
'4 nodes / ER+ / PR+'	4631	'31.92% (2.7%)'	'31.59% (0.3%)'	'-0.33%'
'5 nodes / ER- / PR-'	1146	'45.25% (4.5%)'	'50.5% (0.6%)'	'5.25%'
'5 nodes / ER+ / PR-'	623	'41.52% (6.9%)'	'44.33% (0.8%)'	'2.81%'
'5 nodes / ER+ / PR+'	3249	'36.79% (3.3%)'	'36.12% (0.3%)'	'-0.67%'
'6 nodes / ER- / PR-'	941	'48.88% (4.4%)'	'54.9% (0.6%)'	'6.02%'
'6 nodes / ER+ / PR-'	492	'38.51% (6.9%)'	'47.93% (0.9%)'	'9.43%'
'6 nodes / ER+ / PR+'	2282	'36.39% (3.7%)'	'40.17% (0.4%)'	'3.78%'
'7 nodes / ER- / PR-'	706	'48.36% (5.1%)'	'59.46% (0.7%)'	'11.1%'
'7 nodes / ER+ / PR-'	384	'44.32% (7.6%)'	'51.95% (1.2%)'	'7.63%'
'7 nodes / ER+ / PR+'	1738	'42.52% (4.5%)'	'44.01% (0.5%)'	'1.49%'
'Weighted Mean Error'		'-1.03%'		
'Median Absolute Error'		'1.77%'		
'Weighted Mean Absolute Error'		'1.54%'		
'Maximum Error'		'11.1% (7 nodes / ER- / PR- group)'		
'Concordance Index'		'0.9577'		

'Groups 4 nodes / ER- / PR+, 5 nodes / ER- / PR+, 6 nodes / ER- / PR+, 7 nodes / ER- / PR+ excluded due to insufficient follow-up or observed confidence intervals > 20%'

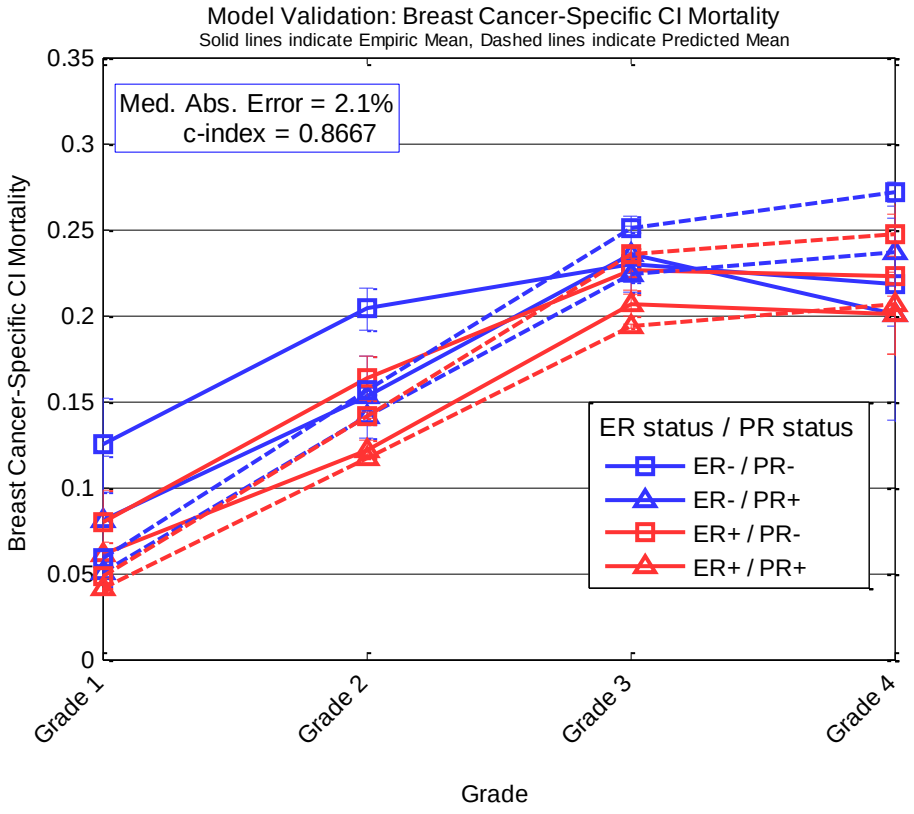


SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {DBInfo.POSITIVE_NODES, [0:7], '='},{DBInfo.ER_STATUS, [0,1], '='},{DBInfo.PR_STATUS, [0,1], '='}});

Table and Figure 2t: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Permutations of tumor grade and estrogen/progesterone receptor status

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'Grade 1 / ER- / PR-'	1833	'12.46% (2.7%)'	'5.92% (0.2%)'	'-6.54%'
'Grade 1 / ER- / PR+'	624	'8.04% (3.8%)'	'5.03% (0.3%)'	'-3.01%'
'Grade 1 / ER+ / PR-'	7540	'7.92% (1.9%)'	'4.81% (0.1%)'	'-3.11%'
'Grade 1 / ER+ / PR+'	50825	'6.16% (0.6%)'	'4.14% (0%)'	'-2.02%'
'Grade 2 / ER- / PR-'	11565	'20.36% (1.2%)'	'15.61% (0.2%)'	'-4.76%'
'Grade 2 / ER- / PR+'	1917	'15.24% (2.4%)'	'14.09% (0.4%)'	'-1.15%'
'Grade 2 / ER+ / PR-'	16128	'16.32% (1.3%)'	'14.18% (0.2%)'	'-2.14%'
'Grade 2 / ER+ / PR+'	98142	'12.2% (0.5%)'	'11.71% (0.1%)'	'-0.48%'
'Grade 3 / ER- / PR-'	42201	'22.95% (0.7%)'	'25.01% (0.1%)'	'2.06%'
'Grade 3 / ER- / PR+'	3086	'23.57% (2.2%)'	'22.38% (0.5%)'	'-1.19%'
'Grade 3 / ER+ / PR-'	11797	'22.57% (1.4%)'	'23.59% (0.3%)'	'1.03%'
'Grade 3 / ER+ / PR+'	44434	'20.66% (0.8%)'	'19.36% (0.1%)'	'-1.3%'
'Grade 4 / ER- / PR-'	2299	'21.8% (2.5%)'	'27.14% (0.6%)'	'5.35%'
'Grade 4 / ER- / PR+'	204	'20.1% (6.2%)'	'23.68% (2%)'	'3.59%'
'Grade 4 / ER+ / PR-'	584	'22.24% (4.5%)'	'24.66% (1.3%)'	'2.42%'
'Grade 4 / ER+ / PR+'	2462	'20.1% (2.4%)'	'20.62% (0.5%)'	'0.52%'
'Weighted Mean Error'		'-0.76%'		
'Median Absolute Error'		'2.1%'		
'Weighted Mean Absolute Error'		'1.54%'		
'Maximum Error'		'-6.54% (Grade 1 / ER- / PR- group)'		
'Concordance Index'		'0.8667'		

'Groups 75-80%, 80-85%, 85-90%, 90-95%, 95-100% excluded due to insufficient follow-up or observed confidence intervals > 20%'



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, { {DBInfo.GRADE, [1:4], '='},{DBInfo.ER_STATUS, [0,1], '='},{DBInfo.PR_STATUS, [0,1], '='}});

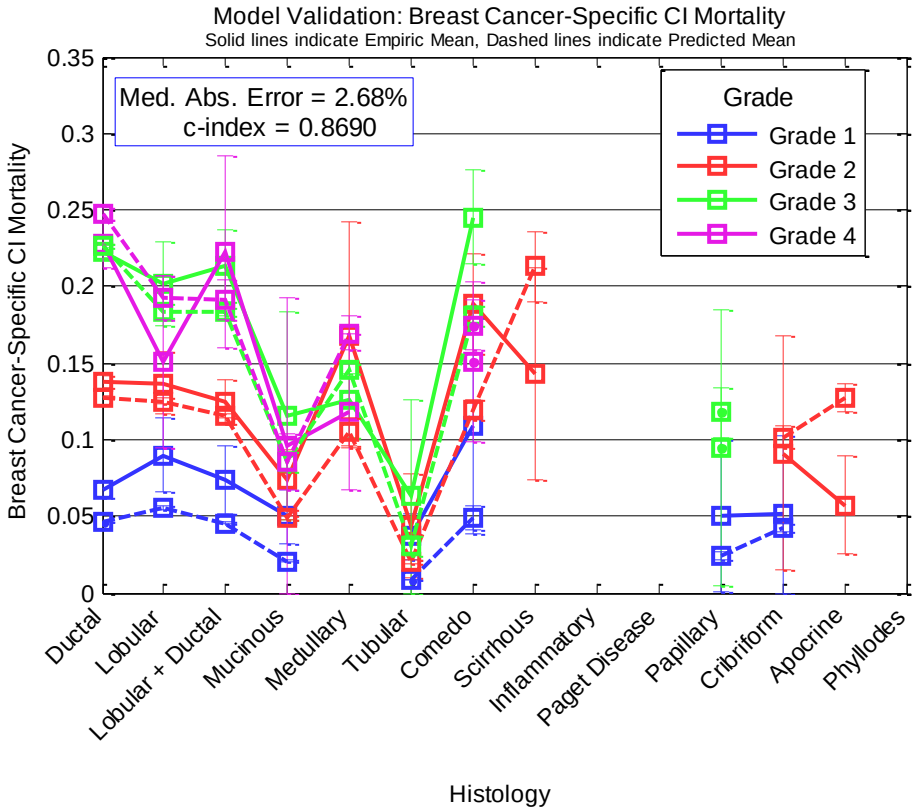
Table and Figure 2u: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Permutations of tumor grade and histological type

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'Ductal / Grade 1'	47528	'6.76% (0.5%)'	'4.61% (0%)'	'-2.15%'
'Ductal / Grade 2'	114160	'13.82% (0.4%)'	'12.77% (0.1%)'	'-1.05%'
'Ductal / Grade 3'	100368	'22.3% (0.4%)'	'22.67% (0.1%)'	'0.38%'
'Ductal / Grade 4'	5091	'22.79% (1.6%)'	'24.78% (0.4%)'	'1.99%'
'Lobular / Grade 1'	4885	'8.95% (2.4%)'	'5.52% (0.1%)'	'-3.43%'
'Lobular / Grade 2'	9911	'13.69% (2%)'	'12.51% (0.2%)'	'-1.18%'
'Lobular / Grade 3'	2735	'20.2% (2.8%)'	'18.38% (0.4%)'	'-1.81%'
'Lobular / Grade 4'	291	'15.08% (5.6%)'	'19.25% (1.4%)'	'4.17%'
'Lobular + Ductal / Grade 1'	5728	'7.34% (2.2%)'	'4.55% (0.1%)'	'-2.78%'
'Lobular + Ductal / Grade 2'	14914	'12.46% (1.5%)'	'11.5% (0.1%)'	'-0.96%'
'Lobular + Ductal / Grade 3'	6133	'21.31% (2.3%)'	'18.35% (0.3%)'	'-2.96%'
'Lobular + Ductal / Grade 4'	380	'22.28% (6.3%)'	'19.15% (1.3%)'	'-3.13%'
'Mucinous / Grade 1'	3891	'4.96% (1.7%)'	'2.06% (0%)'	'-2.91%'
'Mucinous / Grade 2'	2370	'7.36% (1.9%)'	'4.86% (0.1%)'	'-2.5%'
'Mucinous / Grade 3'	369	'11.55% (6.8%)'	'8.53% (0.6%)'	'-3.03%'
'Mucinous / Grade 4'	42	'9.61% (9.6%)'	'8.55% (1.8%)'	'-1.05%'
'Medullary / Grade 2'	199	'16.84% (7.4%)'	'10.53% (0.9%)'	'-6.31%'
'Medullary / Grade 3'	2029	'12.55% (2.4%)'	'14.6% (0.3%)'	'2.05%'
'Medullary / Grade 4'	239	'11.78% (5.1%)'	'16.95% (1.1%)'	'5.17%'
'Tubular / Grade 1'	4303	'3.66% (1.4%)'	'0.85% (0%)'	'-2.82%'
'Tubular / Grade 2'	521	'4.35% (3.4%)'	'2.06% (0.1%)'	'-2.29%'
'Tubular / Grade 3'	60	'6.29% (6.3%)'	'3.06% (0.6%)'	'-3.23%'
'Comedo / Grade 1'	111	'10.91% (7.1%)'	'4.89% (0.7%)'	'-6.02%'
'Comedo / Grade 2'	755	'18.93% (3.3%)'	'11.96% (0.7%)'	'-6.96%'
'Comedo / Grade 3'	1227	'24.54% (3%)'	'18.08% (0.7%)'	'-6.46%'
'Comedo / Grade 4'	215	'15.08% (5.2%)'	'17.5% (1.7%)'	'2.42%'
'Scirrhous / Grade 2'	132	'14.32% (6.9%)'	'21.3% (2.3%)'	'6.99%'
'Papillary / Grade 1'	208	'5.02% (5%)'	'2.44% (0.2%)'	'-2.58%'
'Papillary / Grade 3'	76	'9.44% (9%)'	'11.77% (1.6%)'	'2.34%'
'Cribriform / Grade 1'	449	'5.15% (5.1%)'	'4.26% (0.3%)'	'-0.89%'
'Cribriform / Grade 2'	303	'9.12% (7.7%)'	'10.18% (0.8%)'	'1.06%'

'Apocrine / Grade 2'	416	'5.72% (3.2%)'	'12.77% (0.9%)'	'7.05%'

'Weighted Mean Error'	'-0.89%'
'Median Absolute Error'	'2.68%'
'Weighted Mean Absolute Error'	'1.25%'
'Maximum Error'	'7.05% (Apocrine / Grade 2 group)'
'Concordance Index'	'0.8690'

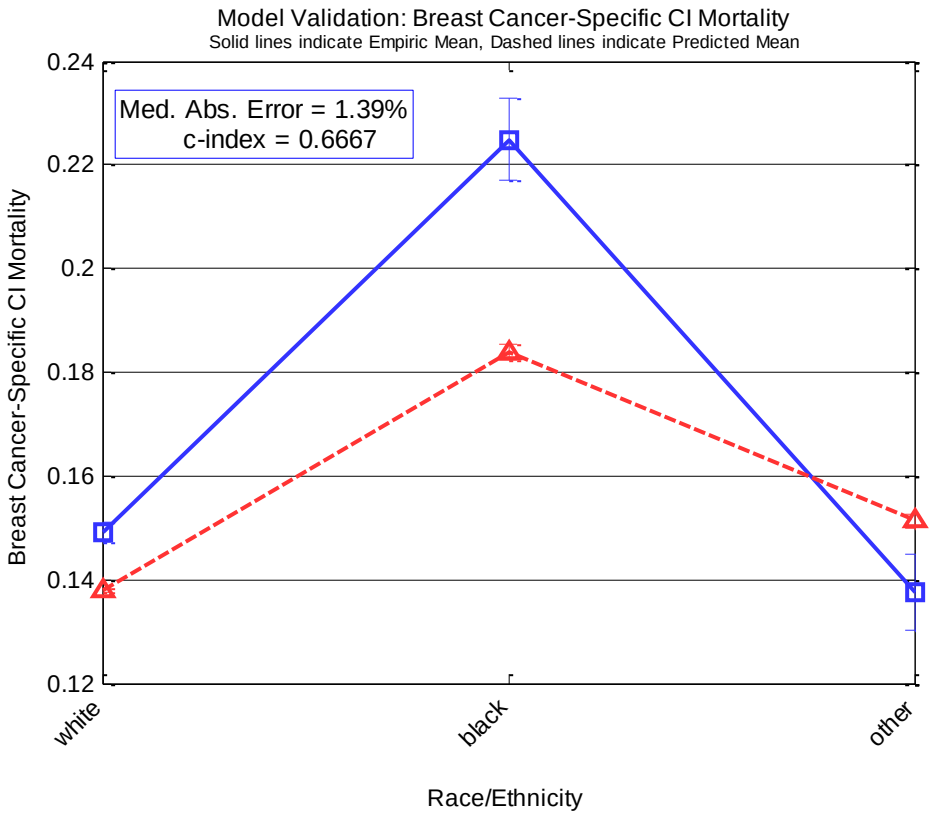
Many groups excluded due to insufficient follow-up or observed confidence intervals > 20%'



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, {{DBInfo.HISTOLOGY, Breast.histologies, '='}, {DBInfo.GRADE, [1:4], '='}});

Table and Figure 2v: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Grouped by race

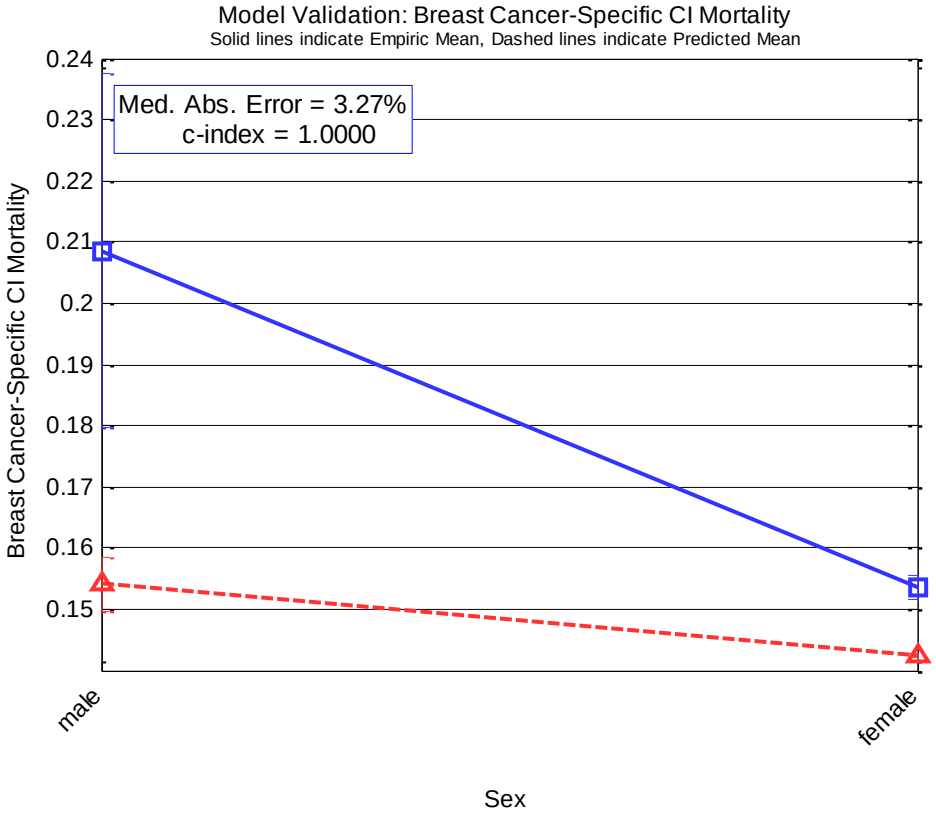
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'white'	331854	'14.91% (0.2%)'	'13.8% (0%)'	'-1.11%'
'black'	30763	'22.49% (0.8%)'	'18.37% (0.2%)'	'-4.12%'
'other'	29826	'13.75% (0.7%)'	'15.14% (0.1%)'	'1.39%'
'Weighted Mean Error'		'-1.16%'		
'Median Absolute Error'		'1.39%'		
'Weighted Mean Absolute Error'		'1.37%'		
'Maximum Error'		'-4.12% (black group)'		
'Concordance Index'		'0.6667'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, {{DBInfo.RACE_ETHNICITY, [0,1,2,98], '>'}});

Table and Figure 2w: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Grouped by sex

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'male'	2530	'20.86% (2.9%)'	'15.42% (0.4%)'	'-5.45%'
'female'	391259	'15.35% (0.2%)'	'14.25% (0%)'	'-1.1%'
'Weighted Mean Error'		'-1.13%'		
'Median Absolute Error'		'3.27%'		
'Weighted Mean Absolute Error'		'1.13%'		
'Maximum Error'		'-5.45% (male group)'		
'Concordance Index'		'1.0000'		

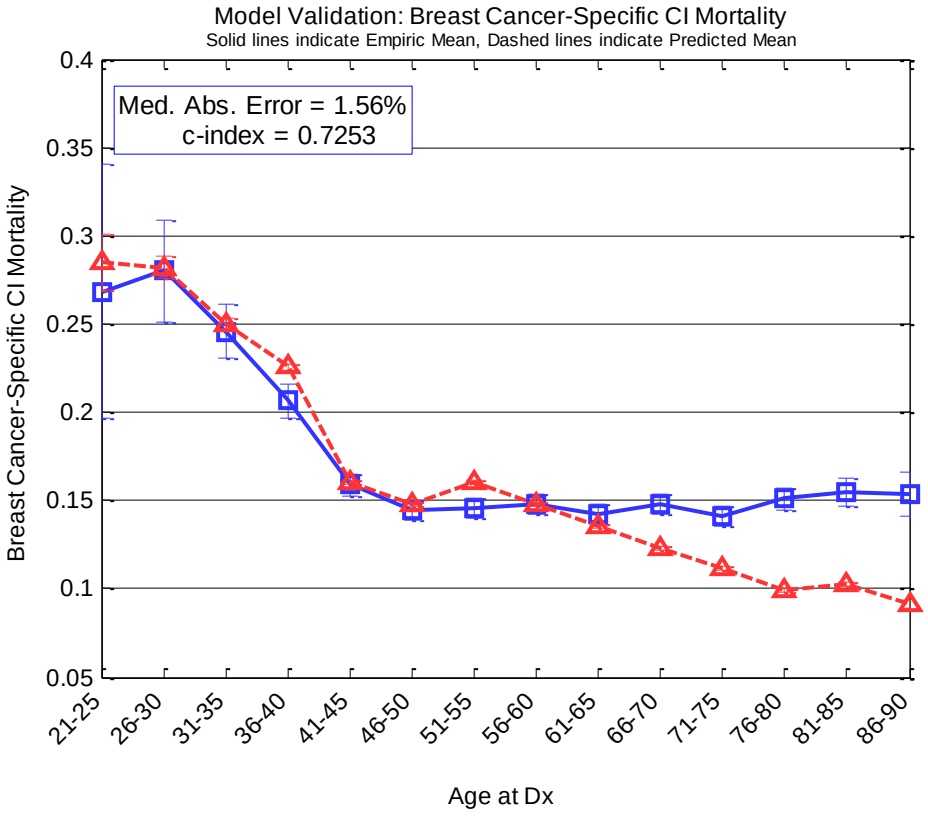


SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, {{DBInfo.SEX, [1,2], '='}});

Table and Figure 2x: **Verification of the SNAP method on the SEER dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Grouped by age

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'21-25'	425	'26.83% (7.2%)'	'28.5% (1.5%)'	'1.67%'
'26-30'	2305	'28.01% (2.9%)'	'28.19% (0.6%)'	'0.18%'
'31-35'	7741	'24.57% (1.5%)'	'24.94% (0.3%)'	'0.37%'
'36-40'	18411	'20.68% (1%)'	'22.57% (0.2%)'	'1.89%'
'41-45'	34962	'15.88% (0.7%)'	'16% (0.1%)'	'0.12%'
'46-50'	47709	'14.43% (0.6%)'	'14.77% (0.1%)'	'0.34%'
'51-55'	48852	'14.55% (0.6%)'	'15.99% (0.1%)'	'1.44%'
'56-60'	49057	'14.8% (0.6%)'	'14.82% (0.1%)'	'0.02%'
'61-65'	46459	'14.27% (0.6%)'	'13.55% (0.1%)'	'-0.72%'
'66-70'	43787	'14.83% (0.5%)'	'12.33% (0.1%)'	'-2.5%'
'71-75'	39299	'14.09% (0.6%)'	'11.21% (0.1%)'	'-2.88%'
'76-80'	30750	'15.1% (0.6%)'	'9.95% (0.1%)'	'-5.15%'
'81-85'	17141	'15.48% (0.8%)'	'10.27% (0.1%)'	'-5.21%'
'86-90'	5635	'15.34% (1.3%)'	'9.12% (0.2%)'	'-6.22%'
'Weighted Mean Error'		'-1.04%'		
'Median Absolute Error'		'1.56%'		
'Weighted Mean Absolute Error'		'1.71%'		
'Maximum Error'		'-6.22% (86-90 group)'		
'Concordance Index'		'0.7253'		

'Groups 21-25, 26-30, 86-90, 91-95, 96-100 excluded due to insufficient follow-up or observed confidence intervals > 20%'



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'SEER_10_Breast_Base', Breast.snapFilter, {{DBInfo.AGE_AT_DX, [20:5:90], '>'}});

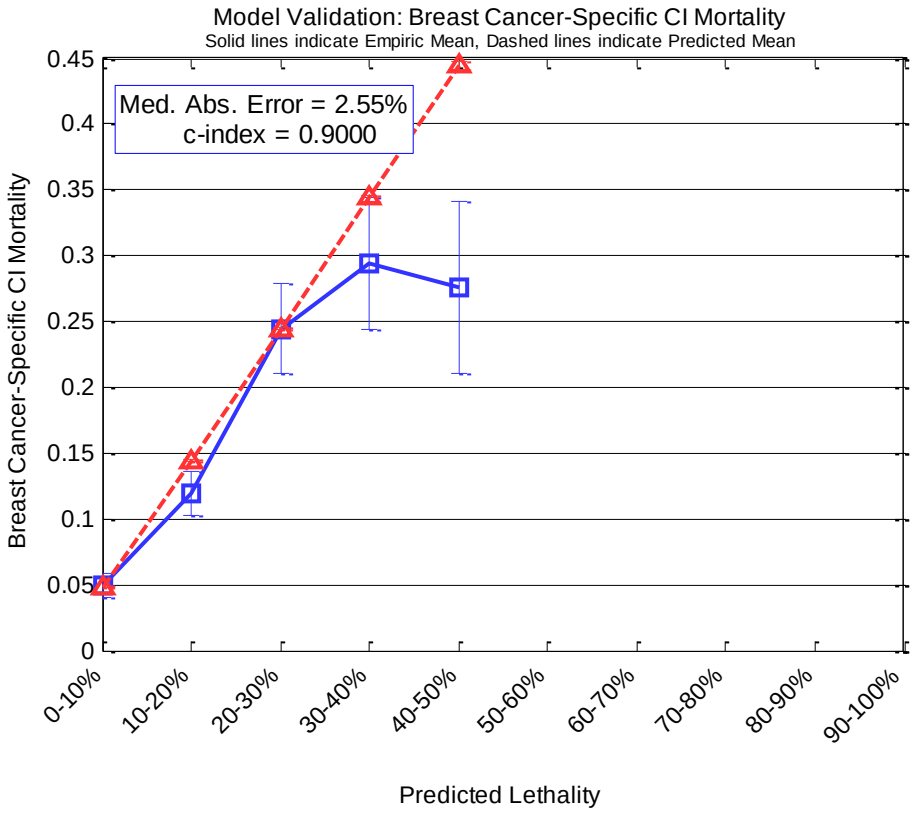
II Validation on the Partners dataset

Table and Figure 2aa: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 10% predicted lethality bins using the Size+Nodes+PrognosticFactors equation

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0-10%'	6015	'4.94% (0.9%)'	'4.84% (0.1%)'	'-0.1%'
'10-20%'	3099	'11.89% (1.7%)'	'14.44% (0.1%)'	'2.55%'
'20-30%'	1499	'24.43% (3.4%)'	'24.47% (0.1%)'	'0.04%'
'30-40%'	730	'29.41% (5%)'	'34.39% (0.2%)'	'4.98%'
'40-50%'	327	'27.57% (6.6%)'	'44.41% (0.3%)'	'16.84%'

'Weighted Mean Error'	'1.41%'
'Median Absolute Error'	'2.55%'
'Weighted Mean Absolute Error'	'1.52%'
'Maximum Error'	'16.84% (40-50% group)'
'Concordance Index'	'0.9000'

'Groups 50-60%, 60-70%, 70-80%, 80-90%, 90-100% excluded due to insufficient follow-up or observed confidence intervals > 20%'

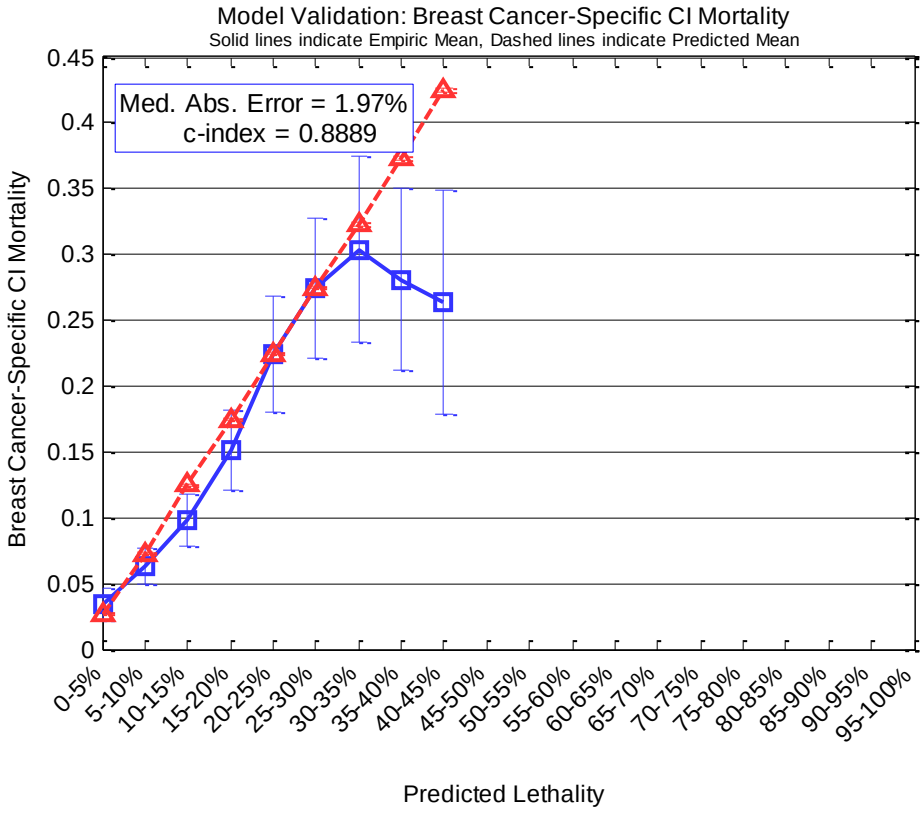


```
SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'Partners_09_Breast',
Breast.snapFilter, { {'Predicted Lethality', [0:.1:1], '>'}});
```

Table and Figure 2bb: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 5% predicted lethality bins using the Size+Nodes+PrognosticFactors equation

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0-5%'	3225	'3.48% (1.2%)'	'2.72% (0%)'	'-0.76%'
'5-10%'	2790	'6.32% (1.4%)'	'7.29% (0.1%)'	'0.96%'
'10-15%'	1866	'9.83% (2%)'	'12.47% (0.1%)'	'2.64%'
'15-20%'	1233	'15.14% (3%)'	'17.42% (0.1%)'	'2.28%'
'20-25%'	902	'22.43% (4.4%)'	'22.46% (0.1%)'	'0.03%'
'25-30%'	597	'27.41% (5.3%)'	'27.51% (0.1%)'	'0.1%'
'30-35%'	432	'30.38% (7%)'	'32.35% (0.1%)'	'1.97%'
'35-40%'	298	'28.12% (6.9%)'	'37.35% (0.2%)'	'9.23%'
'40-45%'	197	'26.36% (8.5%)'	'42.48% (0.2%)'	'16.12%'
'Weighted Mean Error'		'1.29%'		
'Median Absolute Error'		'1.97%'		
'Weighted Mean Absolute Error'		'1.71%'		
'Maximum Error'		'16.12% (40-45% group)'		
'Concordance Index'		'0.8889'		

'Groups 45-100% excluded due to insufficient follow-up or observed confidence intervals > 20%'



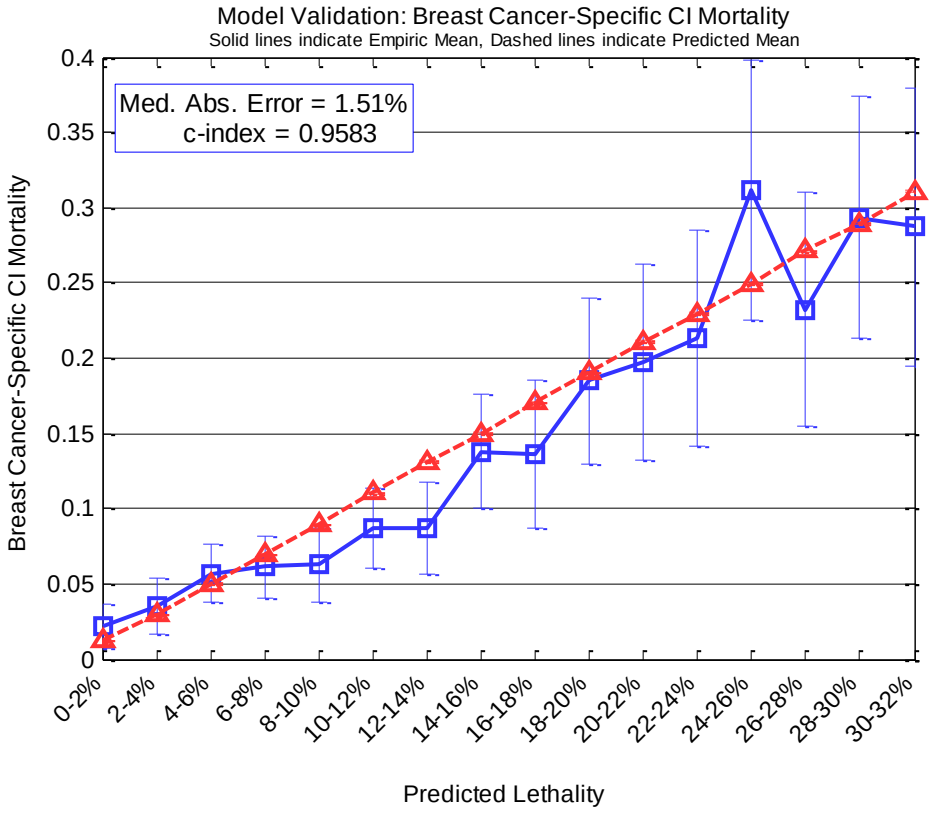
SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'Partners_09_Breast', Breast.snapFilter, { {'Predicted Lethality', [0:.05:1], '>'}});

Table and Figure 2cc: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 2% predicted lethality bins using the Size+Nodes+PrognosticFactors equation

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0-2%'	1124	'2.18% (1.5%)'	'1.24% (0%)'	'-0.94%'
'2-4%'	1428	'3.5% (1.8%)'	'3.02% (0%)'	'-0.48%'
'4-6%'	1311	'5.71% (1.9%)'	'5.04% (0%)'	'-0.68%'
'6-8%'	1276	'6.14% (2%)'	'7.01% (0%)'	'0.87%'
'8-10%'	876	'6.27% (2.5%)'	'8.95% (0%)'	'2.68%'
'10-12%'	826	'8.67% (2.7%)'	'11.06% (0%)'	'2.39%'
'12-14%'	713	'8.75% (3%)'	'13.14% (0%)'	'4.39%'
'14-16%'	617	'13.8% (3.8%)'	'15% (0%)'	'1.2%'
'16-18%'	497	'13.66% (4.9%)'	'17.06% (0.1%)'	'3.41%'
'18-20%'	446	'18.49% (5.5%)'	'19.07% (0.1%)'	'0.58%'
'20-22%'	387	'19.7% (6.5%)'	'21.08% (0.1%)'	'1.39%'
'22-24%'	337	'21.31% (7.1%)'	'22.95% (0.1%)'	'1.64%'
'24-26%'	302	'31.13% (8.6%)'	'24.94% (0.1%)'	'-6.19%'
'26-28%'	246	'23.24% (7.7%)'	'27.16% (0.1%)'	'3.91%'
'28-30%'	227	'29.35% (8%)'	'28.97% (0.1%)'	'-0.38%'
'30-32%'	207	'28.72% (9.2%)'	'31.06% (0.1%)'	'2.35%'

'Weighted Mean Error'	'0.85%'
'Median Absolute Error'	'1.51%'
'Weighted Mean Absolute Error'	'1.7%'
'Maximum Error'	'-6.19% (24-26% group)'
'Concordance Index'	'0.9583'

'Groups 32-100% excluded due to insufficient follow-up or observed confidence intervals > 20%'

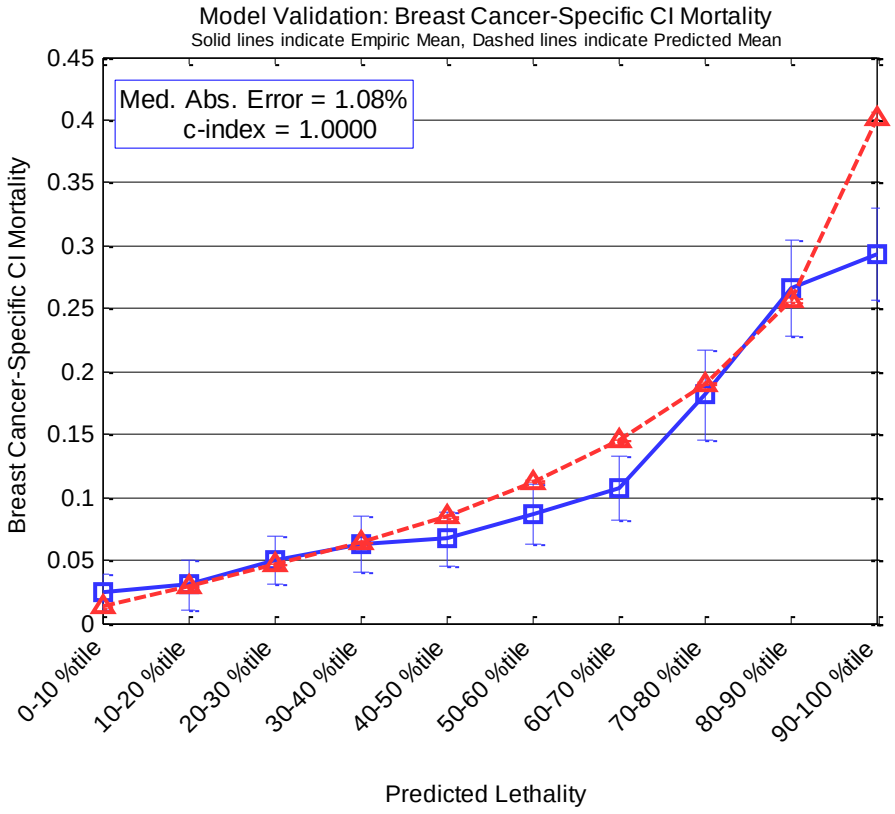


SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'Partners_09_Breast', Breast.snapFilter, { {'Predicted Lethality', [0:.02:.32], '>'}});

Table and Figure 2dd: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 10% predicted lethality percentiles using the Size+Nodes+PrognosticFactors equation

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0-10 %tile'	1182	'2.47% (1.5%)'	'1.29% (0%)'	'-1.19%'
'10-20 %tile'	1183	'3.09% (2%)'	'2.93% (0%)'	'-0.16%'
'20-30 %tile'	1182	'4.97% (1.9%)'	'4.65% (0%)'	'-0.32%'
'30-40 %tile'	1185	'6.29% (2.2%)'	'6.45% (0%)'	'0.16%'
'40-50 %tile'	1180	'6.7% (2.1%)'	'8.43% (0%)'	'1.73%'
'50-60 %tile'	1183	'8.66% (2.4%)'	'11.27% (0.1%)'	'2.61%'
'60-70 %tile'	1182	'10.77% (2.5%)'	'14.53% (0.1%)'	'3.77%'
'70-80 %tile'	1182	'18.17% (3.6%)'	'19.03% (0.1%)'	'0.86%'
'80-90 %tile'	1183	'26.61% (3.9%)'	'25.63% (0.1%)'	'-0.98%'
'90-100 %tile'	1181	'29.33% (3.7%)'	'40.18% (0.5%)'	'10.85%'
'Weighted Mean Error'		'1.73%'		
'Median Absolute Error'		'1.08%'		
'Weighted Mean Absolute Error'		'2.26%'		
'Maximum Error'		'10.85% (90-100 %tile group)'		
'Concordance Index'		'1.0000'		

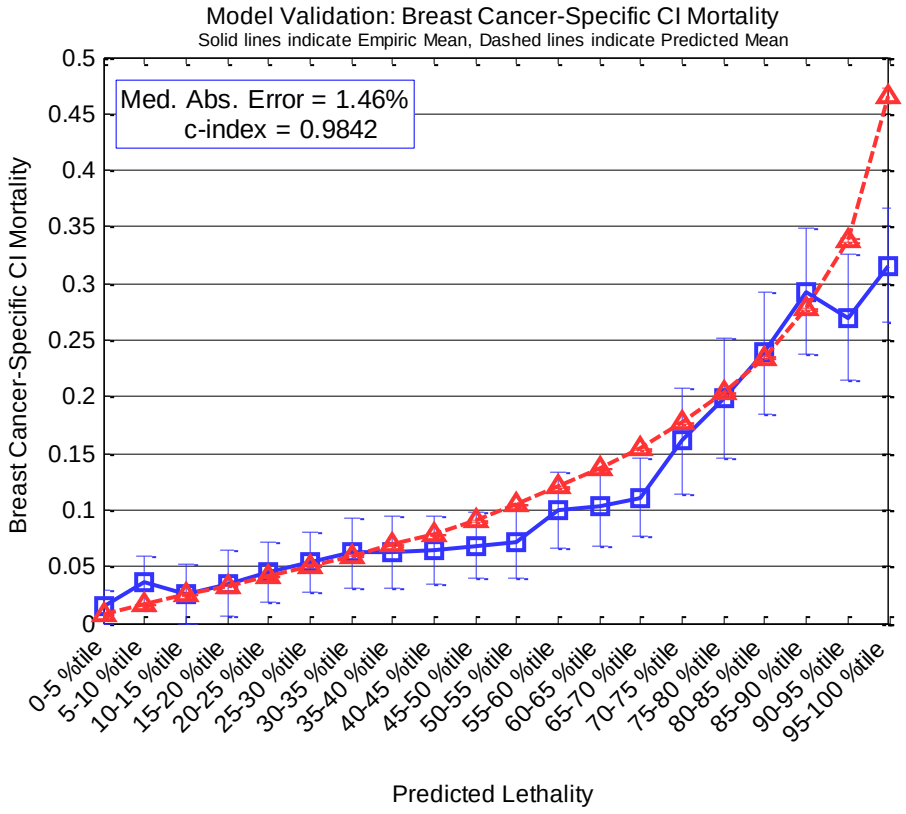
'Groups 32-100% excluded due to insufficient follow-up or observed confidence intervals > 20%'



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'Partners_09_Breast', Breast.snapFilter, { {'Predicted Lethality', [0:10:100], '%'}});

Table and Figure 2ee: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 5% predicted lethality percentiles using the Size+Nodes+PrognosticFactors equation

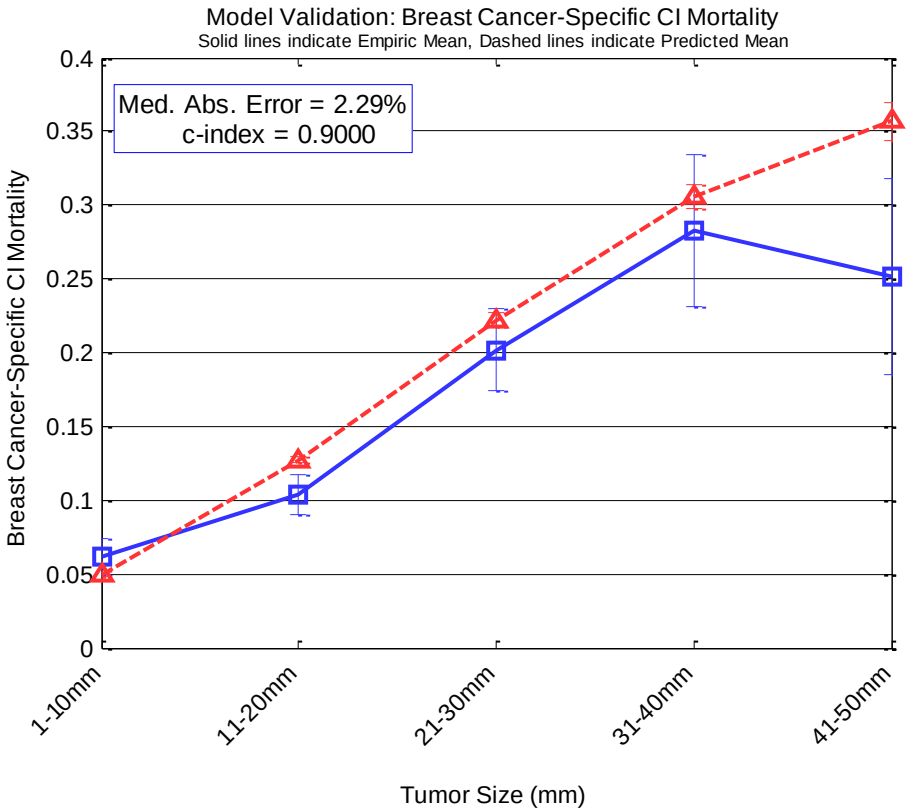
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0-5 %tile'	591	'1.45% (1.4%)'	'0.83% (0%)'	'-0.62%'
'5-10 %tile'	591	'3.54% (2.4%)'	'1.74% (0%)'	'-1.79%'
'10-15 %tile'	592	'2.59% (2.6%)'	'2.52% (0%)'	'-0.07%'
'15-20 %tile'	591	'3.53% (3%)'	'3.34% (0%)'	'-0.18%'
'20-25 %tile'	591	'4.54% (2.7%)'	'4.19% (0%)'	'-0.35%'
'25-30 %tile'	591	'5.35% (2.7%)'	'5.12% (0%)'	'-0.24%'
'30-35 %tile'	592	'6.2% (3.1%)'	'5.99% (0%)'	'-0.21%'
'35-40 %tile'	593	'6.28% (3.2%)'	'6.9% (0%)'	'0.62%'
'40-45 %tile'	589	'6.47% (2.9%)'	'7.85% (0%)'	'1.38%'
'45-50 %tile'	591	'6.88% (3%)'	'9.02% (0%)'	'2.14%'
'50-55 %tile'	591	'7.24% (3.3%)'	'10.51% (0%)'	'3.27%'
'55-60 %tile'	592	'9.99% (3.4%)'	'12.03% (0%)'	'2.03%'
'60-65 %tile'	591	'10.3% (3.5%)'	'13.67% (0%)'	'3.37%'
'65-70 %tile'	591	'11.1% (3.5%)'	'15.4% (0%)'	'4.29%'
'70-75 %tile'	591	'16.09% (4.7%)'	'17.7% (0.1%)'	'1.61%'
'75-80 %tile'	591	'19.89% (5.2%)'	'20.36% (0.1%)'	'0.47%'
'80-85 %tile'	591	'23.9% (5.4%)'	'23.48% (0.1%)'	'-0.42%'
'85-90 %tile'	592	'29.3% (5.5%)'	'27.77% (0.1%)'	'-1.53%'
'90-95 %tile'	591	'27.02% (5.5%)'	'33.76% (0.2%)'	'6.74%'
'95-100 %tile'	590	'31.56% (5.1%)'	'46.61% (0.6%)'	'15.05%'
'Weighted Mean Error'		'1.78%'		
'Median Absolute Error'		'1.46%'		
'Weighted Mean Absolute Error'		'2.32%'		
'Maximum Error'		'15.05% (95-100 %tile group)'		
'Concordance Index'		'0.9842'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'Partners_09_Breast', Breast.snapFilter, { {'Predicted Lethality', [0:5:100], '%'}});

Table and Figure 2ff: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 10 mm tumor size bins

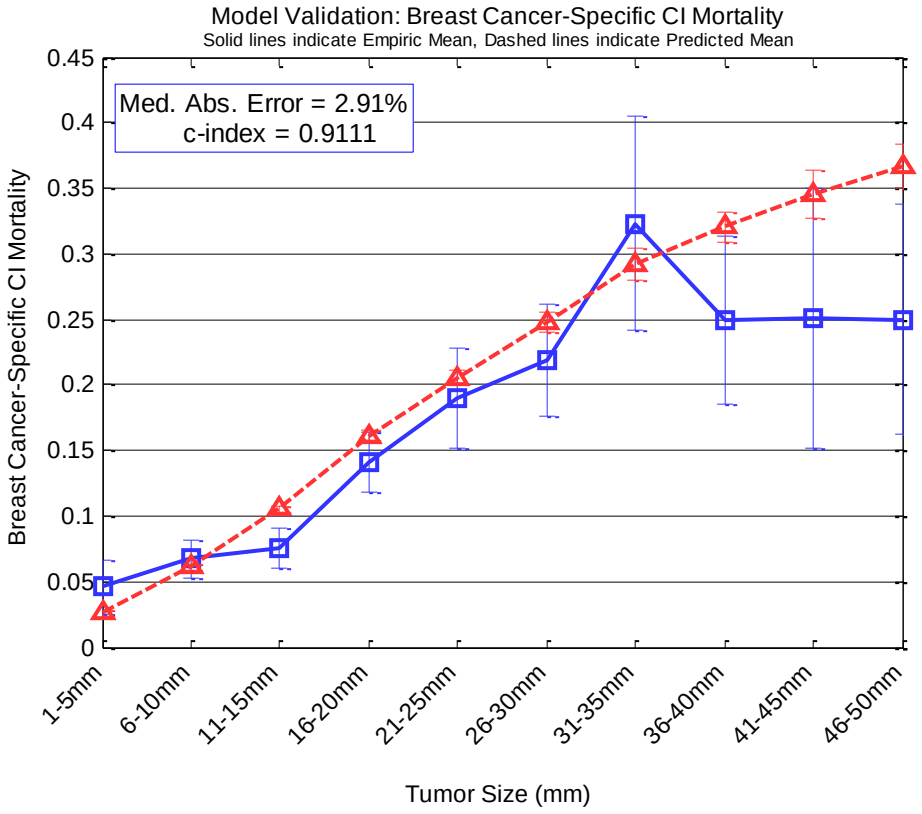
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'1-10mm'	4091	'6.21% (1.2%)'	'5.02% (0.2%)'	'-1.19%'
'11-20mm'	4625	'10.33% (1.3%)'	'12.73% (0.2%)'	'2.4%'
'21-30mm'	2049	'20.16% (2.8%)'	'22.22% (0.5%)'	'2.05%'
'31-40mm'	739	'28.29% (5.1%)'	'30.58% (0.9%)'	'2.29%'
'41-50mm'	320	'25.14% (6.6%)'	'35.69% (1.3%)'	'10.55%'
'Weighted Mean Error'		'1.31%'		
'Median Absolute Error'		'2.29%'		
'Weighted Mean Absolute Error'		'2.13%'		
'Maximum Error'		'10.55% (41-50mm group)'		
'Concordance Index'		'0.9000'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'Partners_09_Breast', Breast.snapFilter, { {DBInfo.TUMOR_SIZE, [0:10:50], '>'}});

Table and Figure 2gg: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 5 mm tumor size bins

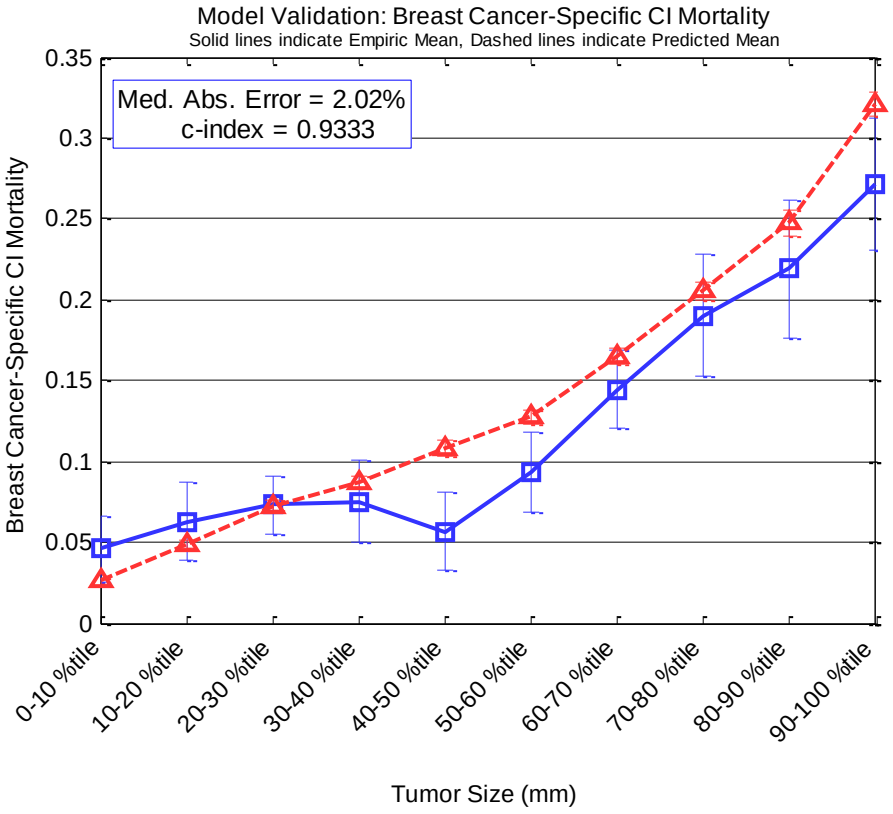
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'1-5mm'	1296	'4.61% (2.1%)'	'2.63% (0.2%)'	'-1.98%'
'6-10mm'	2795	'6.75% (1.4%)'	'6.12% (0.2%)'	'-0.63%'
'11-15mm'	2817	'7.56% (1.5%)'	'10.53% (0.3%)'	'2.97%'
'16-20mm'	1808	'14.09% (2.3%)'	'16.17% (0.4%)'	'2.08%'
'21-25mm'	1248	'19.01% (3.8%)'	'20.58% (0.6%)'	'1.57%'
'26-30mm'	801	'21.92% (4.3%)'	'24.77% (0.8%)'	'2.85%'
'31-35mm'	380	'32.32% (8.1%)'	'29.19% (1.2%)'	'-3.13%'
'36-40mm'	359	'24.88% (6.4%)'	'32.05% (1.2%)'	'7.17%'
'41-45mm'	152	'25.09% (9.9%)'	'34.55% (1.9%)'	'9.46%'
'46-50mm'	168	'25.02% (8.8%)'	'36.71% (1.7%)'	'11.7%'
'Weighted Mean Error'		'1.42%'		
'Median Absolute Error'		'2.91%'		
'Weighted Mean Absolute Error'		'2.35%'		
'Maximum Error'		'11.7% (46-50mm group)'		
'Concordance Index'		'0.9111'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'Partners_09_Breast', Breast.snapFilter, { {DBInfo.TUMOR_SIZE, [0:5:50], '>'}});

Table and Figure 2hh: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by 10% tumor size percentiles

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0-10 %tile'	1296	'4.61% (2.1%)'	'2.63% (0.2%)'	'-1.98%'
'10-20 %tile'	1371	'6.27% (2.4%)'	'4.91% (0.3%)'	'-1.35%'
'20-30 %tile'	1424	'7.3% (1.8%)'	'7.29% (0.3%)'	'-0.01%'
'30-40 %tile'	1121	'7.51% (2.6%)'	'8.77% (0.4%)'	'1.26%'
'40-50 %tile'	784	'5.65% (2.4%)'	'10.83% (0.5%)'	'5.18%'
'50-60 %tile'	1159	'9.35% (2.5%)'	'12.76% (0.4%)'	'3.41%'
'60-70 %tile'	1561	'14.46% (2.4%)'	'16.51% (0.5%)'	'2.06%'
'70-80 %tile'	1248	'19.01% (3.8%)'	'20.58% (0.6%)'	'1.57%'
'80-90 %tile'	801	'21.92% (4.3%)'	'24.77% (0.8%)'	'2.85%'
'90-100 %tile'	1059	'27.16% (4.1%)'	'32.12% (0.7%)'	'4.96%'
'Weighted Mean Error'		'1.5%'		
'Median Absolute Error'		'2.02%'		
'Weighted Mean Absolute Error'		'2.25%'		
'Maximum Error'		'5.18% (40-50 %tile group)'		
'Concordance Index'		'0.9333'		

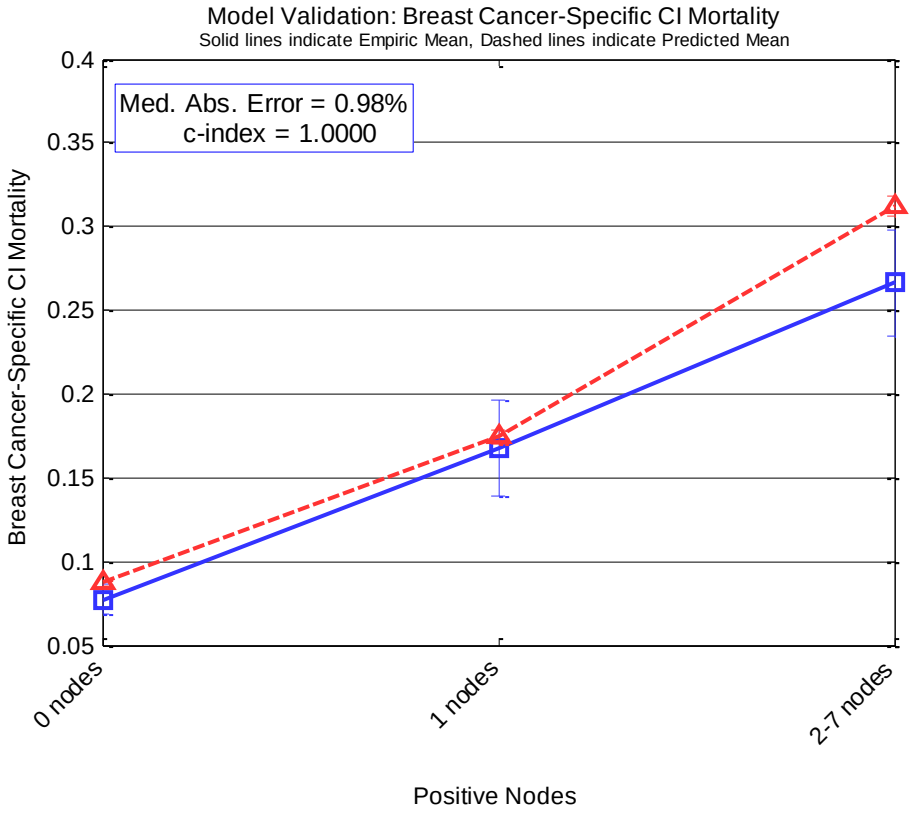


SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'Partners_09_Breast', Breast.snapFilter, { {DBInfo.TUMOR_SIZE, [0:10:100], '%'}});

Table and Figure 2ii: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by number of positive lymph nodes

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'0 nodes'	8287	'7.72% (0.9%)'	'8.7% (0.2%)'	'0.98%'
'1 nodes'	1719	'16.75% (2.9%)'	'17.46% (0.4%)'	'0.71%'
'2-7 nodes'	1818	'26.65% (3.2%)'	'31.24% (0.6%)'	'4.59%'
'Weighted Mean Error'	'1.5%'			
'Median Absolute Error'	'0.98%'			
'Weighted Mean Absolute Error'	'1.5%'			
'Maximum Error'	'4.59% (2-7 nodes group)'			
'Concordance Index'	'1.0000'			

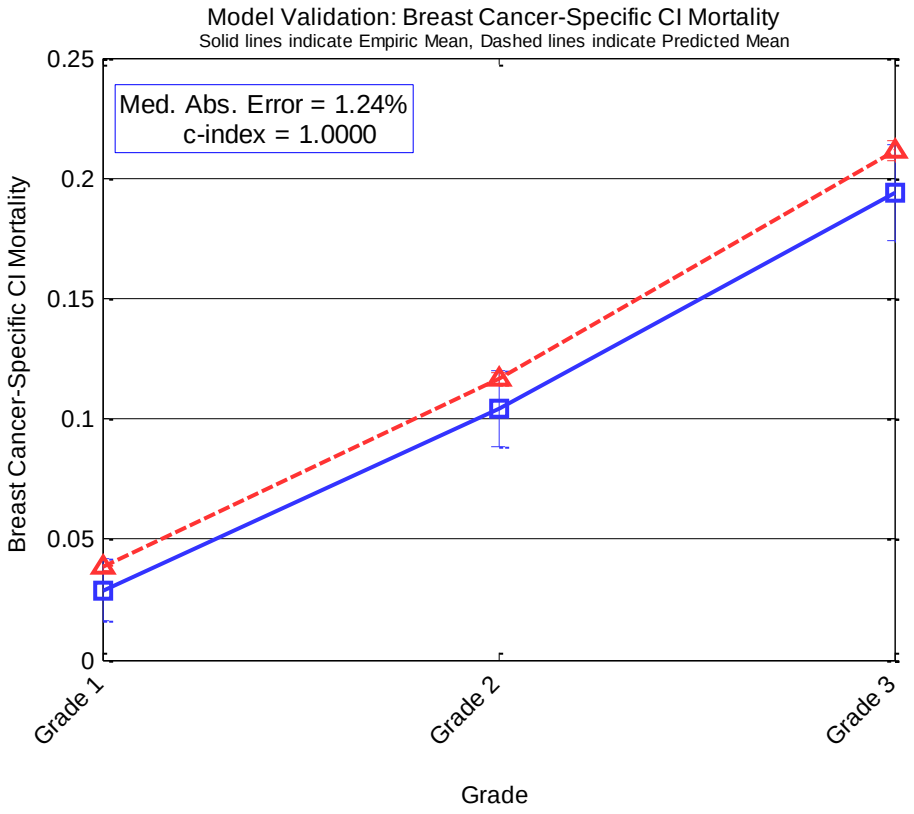
'Groups 2-7 nodes combined due to insufficient follow-up



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'Partners_09_Breast', Breast.snapFilter, { {DBInfo.POSITIVE_NODES, [-1:1,7], '>'}});

Table and Figure 2ijj: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by tumor grade

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'Grade 1'	2078	'2.87% (1.3%)'	'3.84% (0.1%)'	'0.97%'
'Grade 2'	4941	'10.43% (1.6%)'	'11.67% (0.3%)'	'1.24%'
'Grade 3'	3542	'19.4% (2%)'	'21.12% (0.4%)'	'1.72%'
'Weighted Mean Error'		'1.35%'		
'Median Absolute Error'		'1.24%'		
'Weighted Mean Absolute Error'		'1.35%'		
'Maximum Error'		'1.72% (Grade 3 group)'		
'Concordance Index'		'1.0000'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'Partners_09_Breast', Breast.snapFilter, { {DBInfo.GRADE, [1:3], '='}});

Table and Figure 2ikk: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by estrogen receptor status

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'ER- / PR-'	1547	'16.33% (2.8%)'	'21.8% (0.7%)'	'5.47%'
'ER- / PR+'	187	'21.09% (8.8%)'	'18.05% (1.8%)'	'-3.04%'
'ER+ / PR-'	667	'13.05% (4.1%)'	'15.35% (1%)'	'2.3%'
'ER+ / PR+'	6960	'9.81% (1.6%)'	'11.28% (0.2%)'	'1.47%'
'Weighted Mean Error'		'2.1%'		
'Median Absolute Error'		'2.67%'		
'Weighted Mean Absolute Error'		'2.22%'		
'Maximum Error'		'5.47% (ER- / PR- group)'		
'Concordance Index'		'0.8333'		

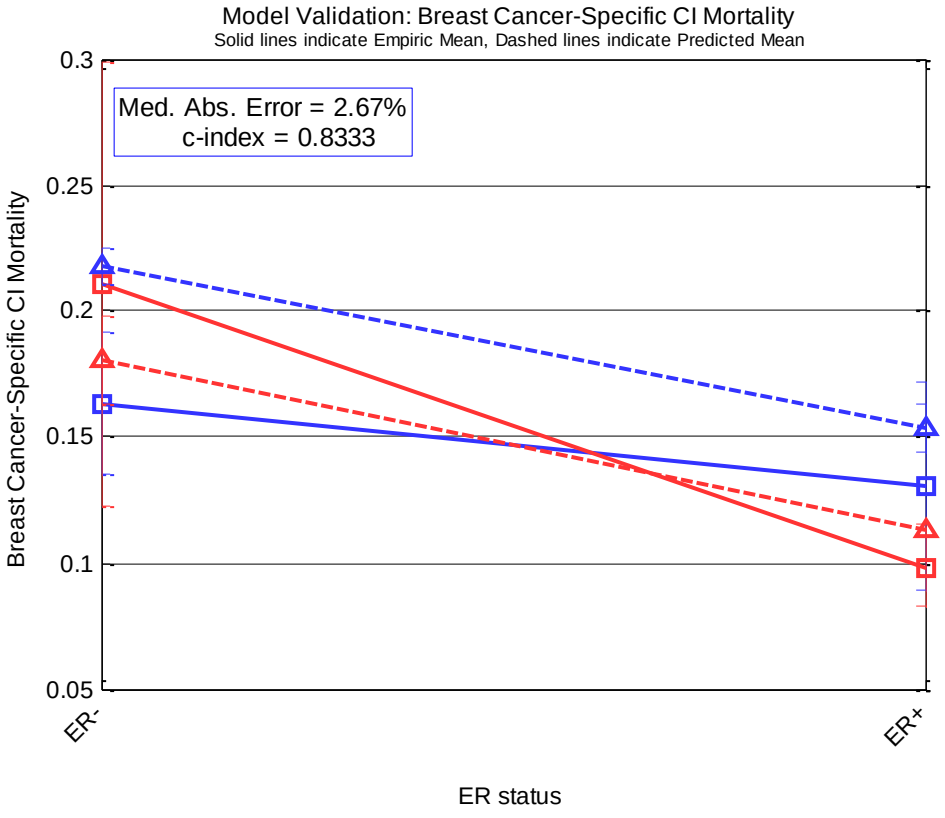
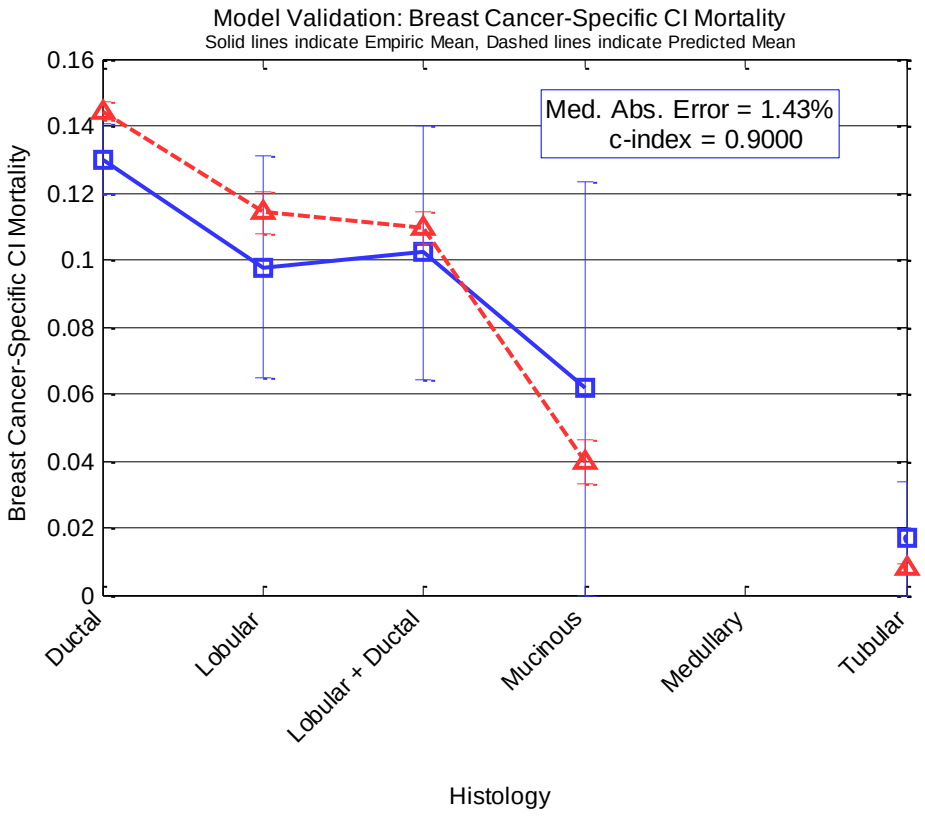


Table and Figure 2ill: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Patients grouped by histological type

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'Ductal'	8714	'13.01% (1%)'	'14.44% (0.3%)'	'1.43%'
'Lobular'	791	'9.79% (3.3%)'	'11.41% (0.6%)'	'1.63%'
'Lobular + Ductal'	1495	'10.22% (3.8%)'	'10.94% (0.5%)'	'0.72%'
'Mucinous'	145	'6.16% (6.2%)'	'3.98% (0.7%)'	'-2.17%'
'Tubular'	136	'1.7% (1.7%)'	'0.81% (0.1%)'	'-0.89%'
'Weighted Mean Error'		'1.28%'		
'Median Absolute Error'		'1.43%'		
'Weighted Mean Absolute Error'		'1.35%'		
'Maximum Error'		'-2.17% (Mucinous group)'		
'Concordance Index'		'0.9000'		

'Medullary group excluded due to insufficient follow-up or observed confidence intervals > 20%'

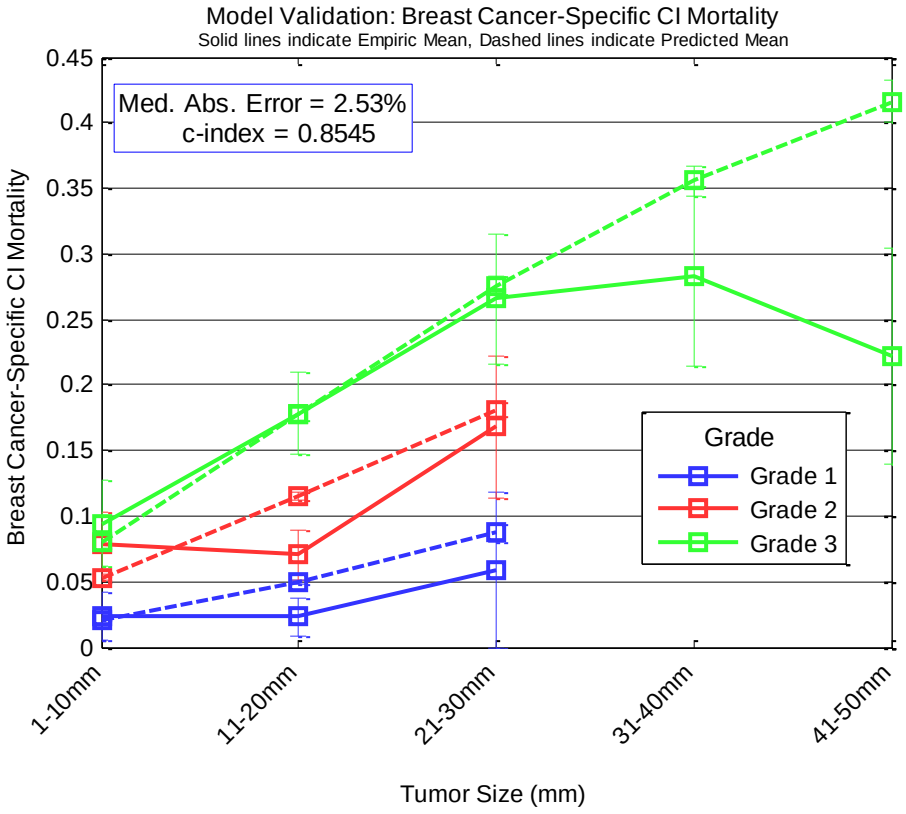


SNAP.validate({'c', 'ci'}, 180, @Breast.getCummDeathRisks, 'Partners_09_Breast', Breast.snapFilter, { {DBInfo.HISTOLOGY, Breast.histologies(1:6), '='}});

Table and Figure 2mm: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Permutations of 10 mm tumor size bins and tumor grade

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'1-10mm / Grade 1'	1142	'2.34% (1.8%)'	'2.13% (0.1%)'	'-0.21%'
'1-10mm / Grade 2'	1698	'7.83% (2.5%)'	'5.31% (0.2%)'	'-2.53%'
'1-10mm / Grade 3'	721	'9.41% (3.3%)'	'8.06% (0.5%)'	'-1.35%'
'11-20mm / Grade 1'	742	'2.29% (1.5%)'	'4.96% (0.2%)'	'2.67%'
'11-20mm / Grade 2'	2063	'7.03% (1.8%)'	'11.51% (0.3%)'	'4.48%'
'11-20mm / Grade 3'	1405	'17.82% (3.1%)'	'17.8% (0.5%)'	'-0.02%'
'21-30mm / Grade 1'	143	'5.9% (5.9%)'	'8.7% (0.7%)'	'2.8%'
'21-30mm / Grade 2'	796	'16.83% (5.4%)'	'18.09% (0.5%)'	'1.26%'
'21-30mm / Grade 3'	910	'26.55% (4.9%)'	'27.6% (0.7%)'	'1.05%'
'31-40mm / Grade 3'	359	'28.25% (6.9%)'	'35.54% (1.1%)'	'7.29%'
'41-50mm / Grade 3'	147	'22.2% (8.2%)'	'41.63% (1.5%)'	'19.44%'
'Weighted Mean Error'		'1.34%'		
'Median Absolute Error'		'2.53%'		
'Weighted Mean Absolute Error'		'2.43%'		
'Maximum Error'		'19.44% (41-50mm / Grade 3 group)'		
'Concordance Index'		'0.8545'		

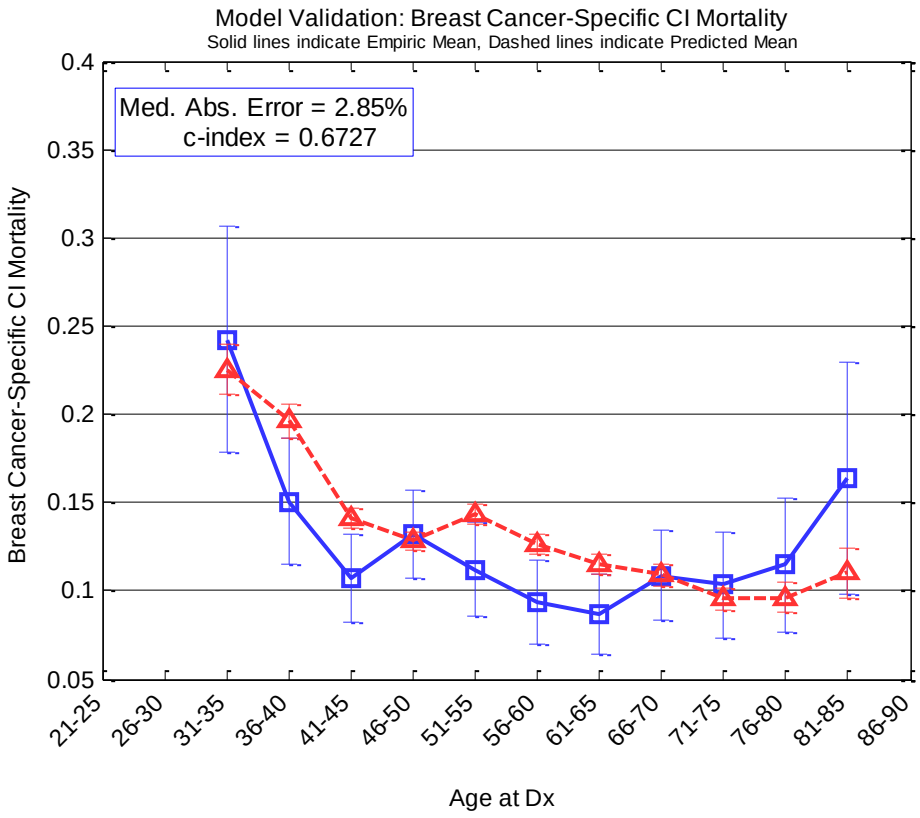
'"Groups excluded due to insufficient follow-up or observed confidence intervals > 20%'



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'Partners_09_Breast', Breast.snapFilter, { {DBInfo.TUMOR_SIZE, [0:10:50], '>'},{DBInfo.GRADE, [1:4], '='}});

Table and Figure 2nn: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Permutations of 5 year age groups

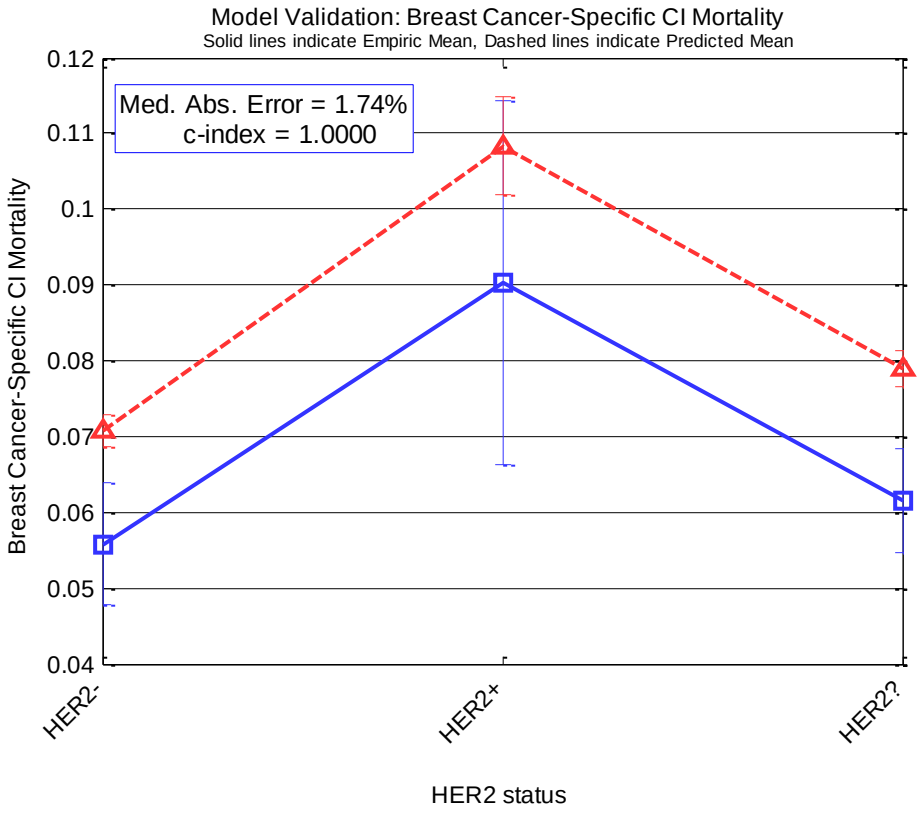
Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'31-35'	384	'24.23% (6.4%)'	'22.54% (1.4%)'	'-1.69%'
'36-40'	901	'15.08% (3.6%)'	'19.62% (0.9%)'	'4.55%'
'41-45'	1422	'10.71% (2.5%)'	'14.11% (0.6%)'	'3.4%'
'46-50'	1893	'13.17% (2.5%)'	'12.84% (0.5%)'	'-0.33%'
'51-55'	1650	'11.18% (2.7%)'	'14.35% (0.6%)'	'3.17%'
'56-60'	1519	'9.33% (2.4%)'	'12.62% (0.5%)'	'3.3%'
'61-65'	1374	'8.69% (2.3%)'	'11.54% (0.5%)'	'2.85%'
'66-70'	1063	'10.89% (2.6%)'	'10.94% (0.6%)'	'0.06%'
'71-75'	802	'10.33% (3%)'	'9.57% (0.6%)'	'-0.76%'
'76-80'	448	'11.46% (3.7%)'	'9.63% (0.8%)'	'-1.83%'
'81-85'	196	'16.37% (6.5%)'	'11.01% (1.4%)'	'-5.36%'
'Weighted Mean Error'		'1.66%'		
'Median Absolute Error'		'2.85%'		
'Weighted Mean Absolute Error'		'2.31%'		
'Maximum Error'		'-5.36% (81-85 group)'		
'Concordance Index'		'0.6727'		



SNAP.validate({'c', 'ci', 'm', 0}, [180], @Breast.getCummDeathRisks, 'Partners_09_Breast', Breast.snapFilter, { {DBInfo.AGE_AT_DX, [20:5:90], '>'}});

Table and Figure 2oo: **Verification of the SNAP method on the Partners dataset** (patients after 1987, parameters for the outcome calculator, see TABLE I). Grouped by HER2 status—values are 7-year survival due to insufficient long-term follow-up

Group†	N	Observed Lethality (SEM)	Predicted Lethality (SEM)	Model Error (pred – obs)
'HER2-'	5729	'5.58% (0.8%)'	'7.08% (0.2%)'	'1.5%'
'HER2+'	976	'9.03% (2.4%)'	'10.83% (0.6%)'	'1.8%'
'HER2 unknown	5119	'6.15% (0.7%)'	'7.89% (0.2%)'	'1.74%'
'Weighted Mean Error'		'1.63%'		
'Median Absolute Error'		'1.74%'		
'Weighted Mean Absolute Error'		'1.63%'		
'Maximum Error'		'1.8% (HER2+ group)'		
'Concordance Index'		'1.0000'		



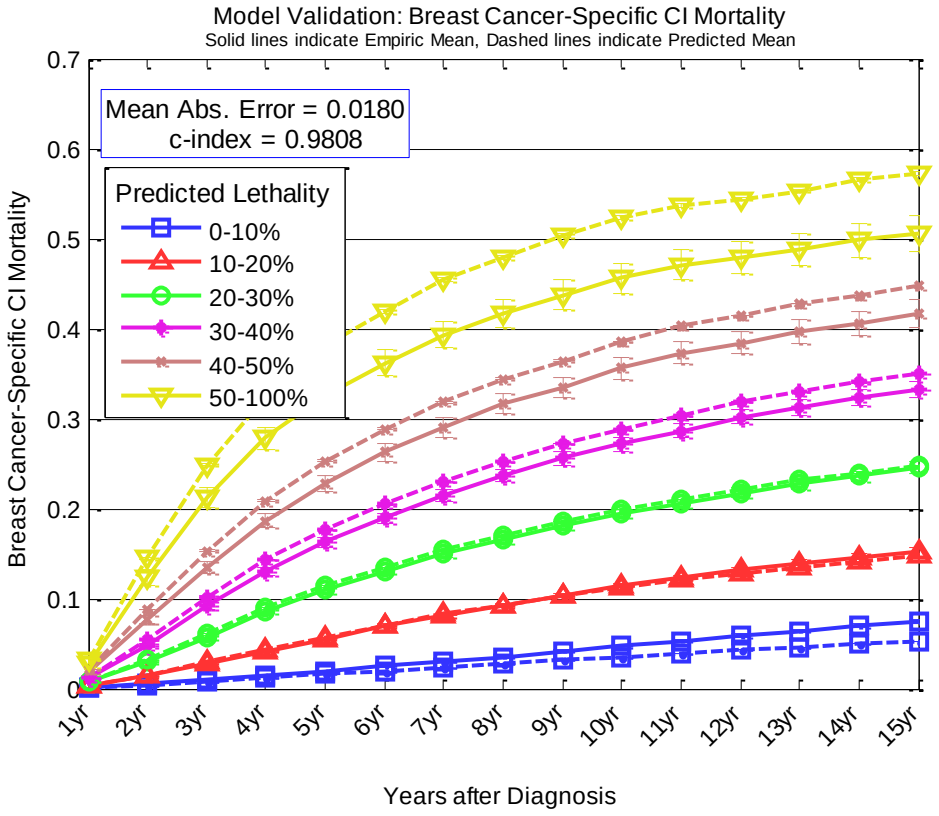
SNAP.validate({'c', 'ci', 'm', 0}, [84], @Breast.getCummDeathRisks, 'Partners_09_Breast', Breast.snapFilter, { {DBInfo.HER2_STATUS, [0,1,9], '='}});

Figure 3. Validation of the time course of lethality. Validation of death distribution and conditional survival calculations. Exact values for figures omitted due to space constraints.

Figure 3a: SEER patients stratified by 10% predicted lethality deciles
Figure 3b: SEER patients stratified by 10mm tumor size bins
Figure 3c: SEER patients stratified by positive nodes
Figure 3d: SEER patients stratified by age

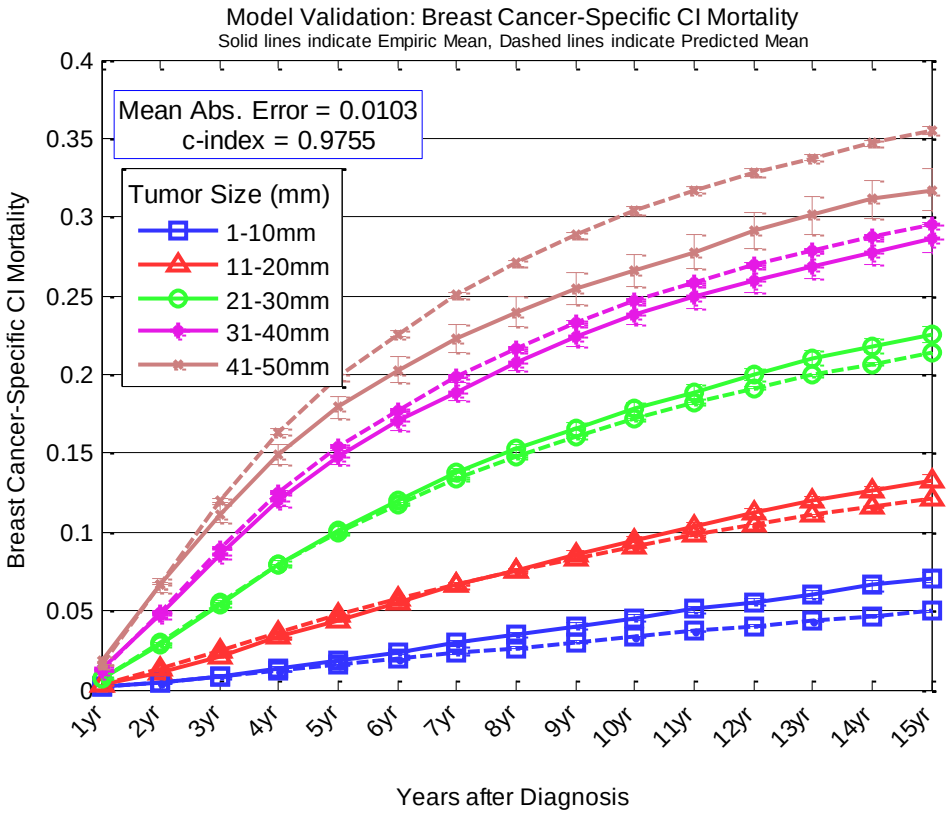
Figure 3aa: Partners patients stratified by 10% predicted lethality deciles
Figure 3bb: Partners patients stratified by 10mm tumor size bins
Figure 3cc: Partners patients stratified by positive nodes
Figure 3dd: Partners patients stratified by age

Figure3a: SEER patients stratified by 10% predicted lethality deciles



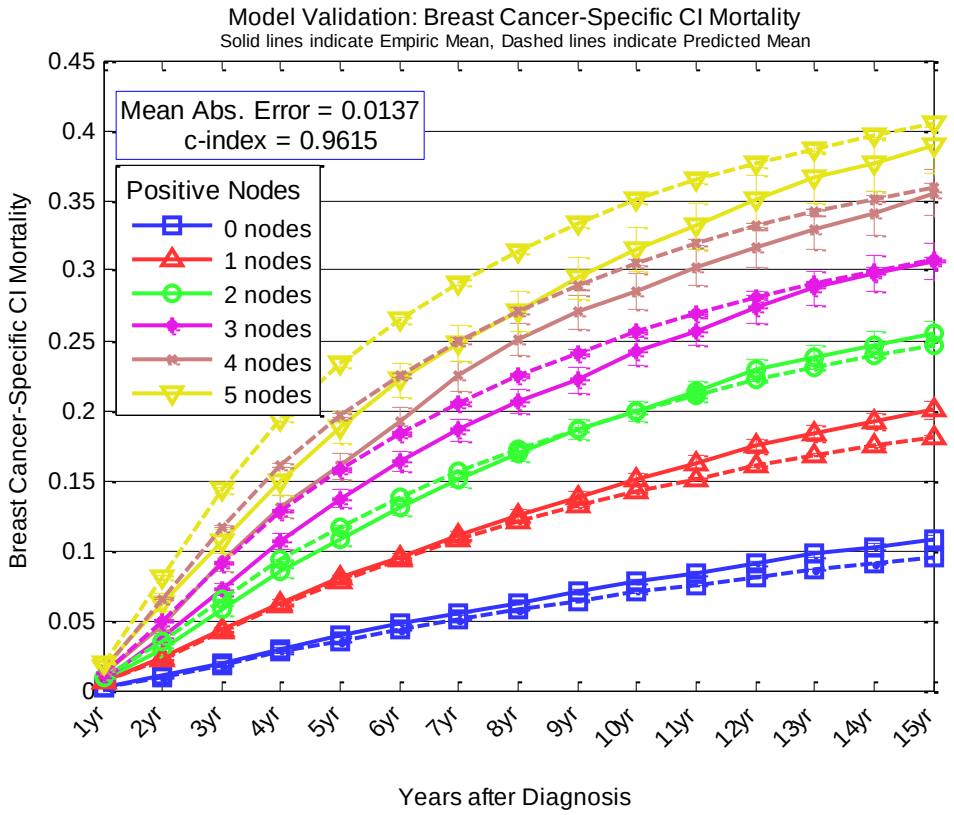
'Weighted Mean Error' '-0.18%'
'Mean Absolute Error' '1.8%'
'Weighted Mean Absolute Error' '0.81%'
'Maximum Error' '6.73% (50-100% / 14yr group)'
'Concordance Index' '0.9808'

Figure 3b: SEER patients stratified by 10mm tumor size bins



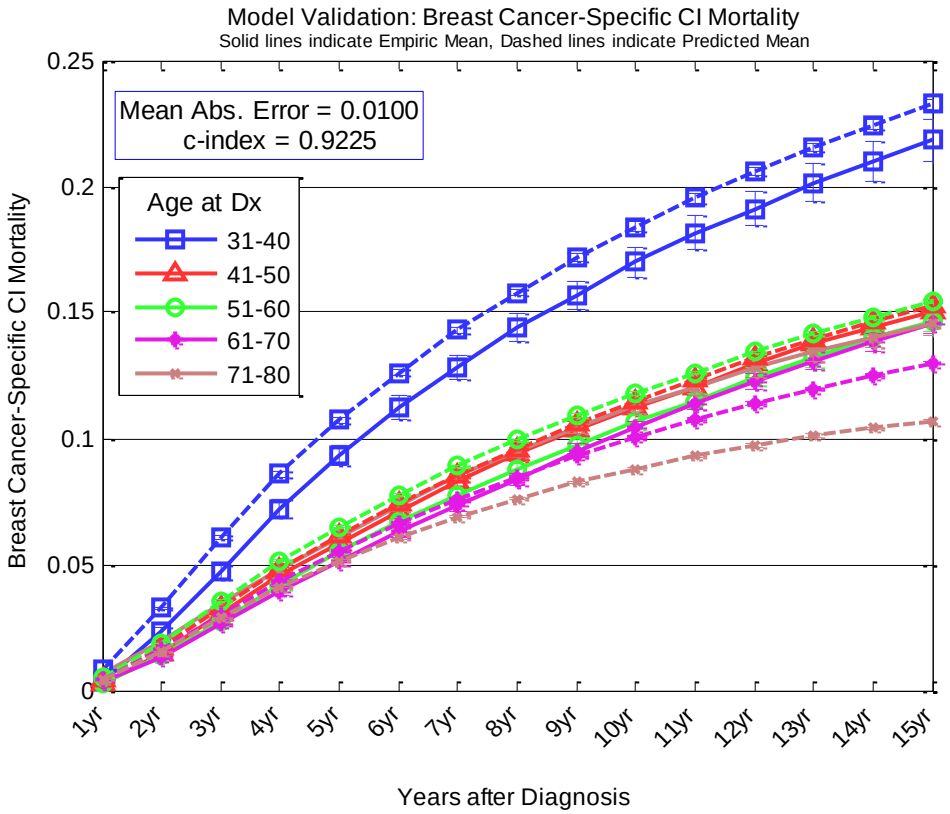
'Weighted Mean Error' '-0.3%'
'Mean Absolute Error' '1.03%'
'Weighted Mean Absolute Error' '0.67%'
'Maximum Error' '3.91% (41-50mm / 11yr group)'
'Concordance Index' '0.9755'

Figure 3c: SEER patients stratified by positive nodes



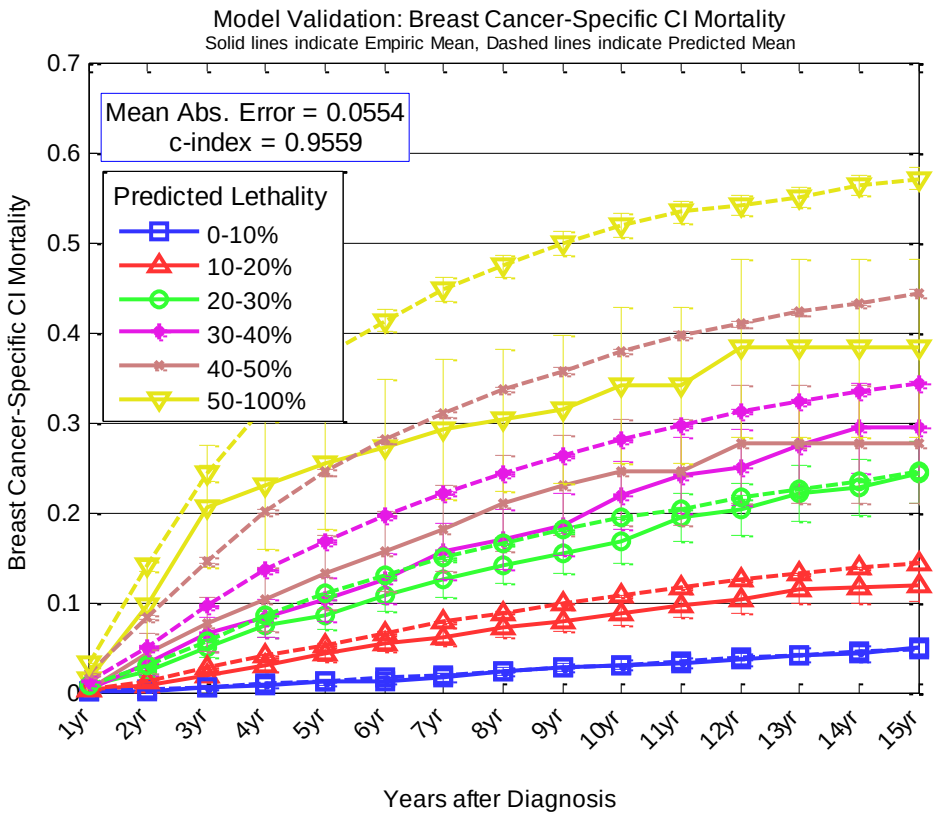
'Weighted Mean Error' '-0.38%'
'Mean Absolute Error' '1.37%'
'Weighted Mean Absolute Error' '0.71%'
'Maximum Error' '4.56% (5 nodes / 5yr group)'
'Concordance Index' '0.9615'

Figure 3d: SEER patients stratified by age



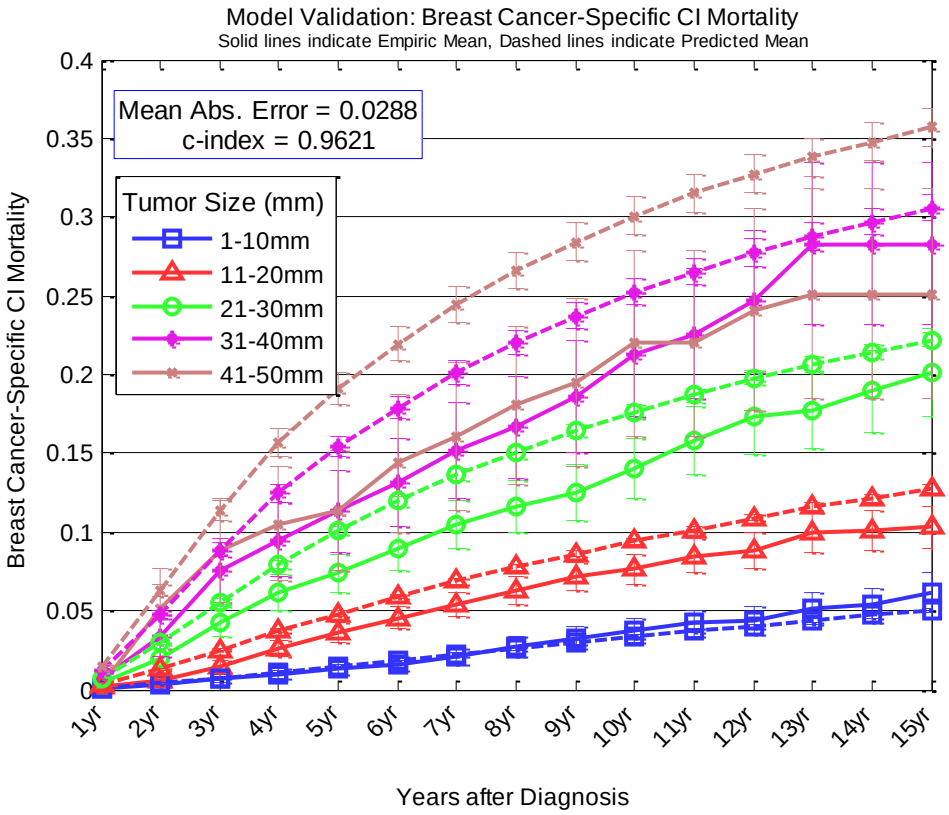
'Weighted Mean Error' '-0.04%'
'Mean Absolute Error' '1%'
'Weighted Mean Absolute Error' '0.9%'
'Maximum Error' '-3.87% (71-80 / 15yr group)'
'Concordance Index' '0.9225'

Figure3aa: Partners patients stratified by 10% predicted lethality deciles



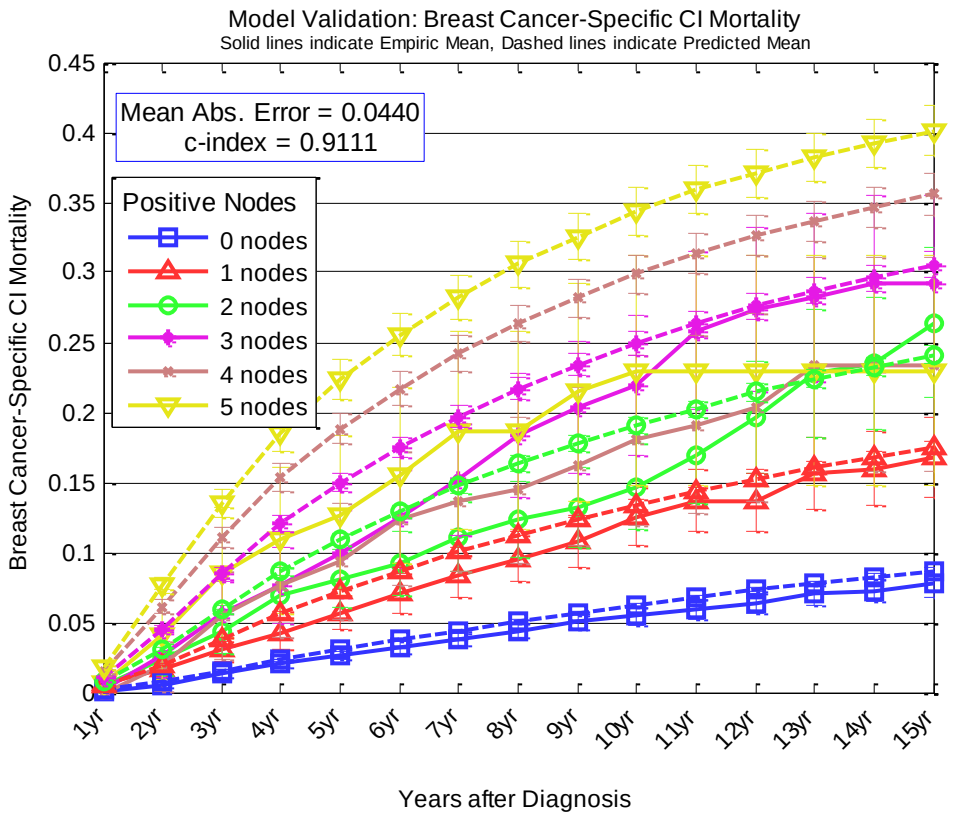
'Weighted Mean Error' '1.43%'
'Mean Absolute Error' '5.54%'
'Weighted Mean Absolute Error' '1.45%'
'Maximum Error' '19.3% (50-100% / 11yr group)'
'Concordance Index' '0.9559'

Figure 3bb: Partners patients stratified by 10mm tumor size bins



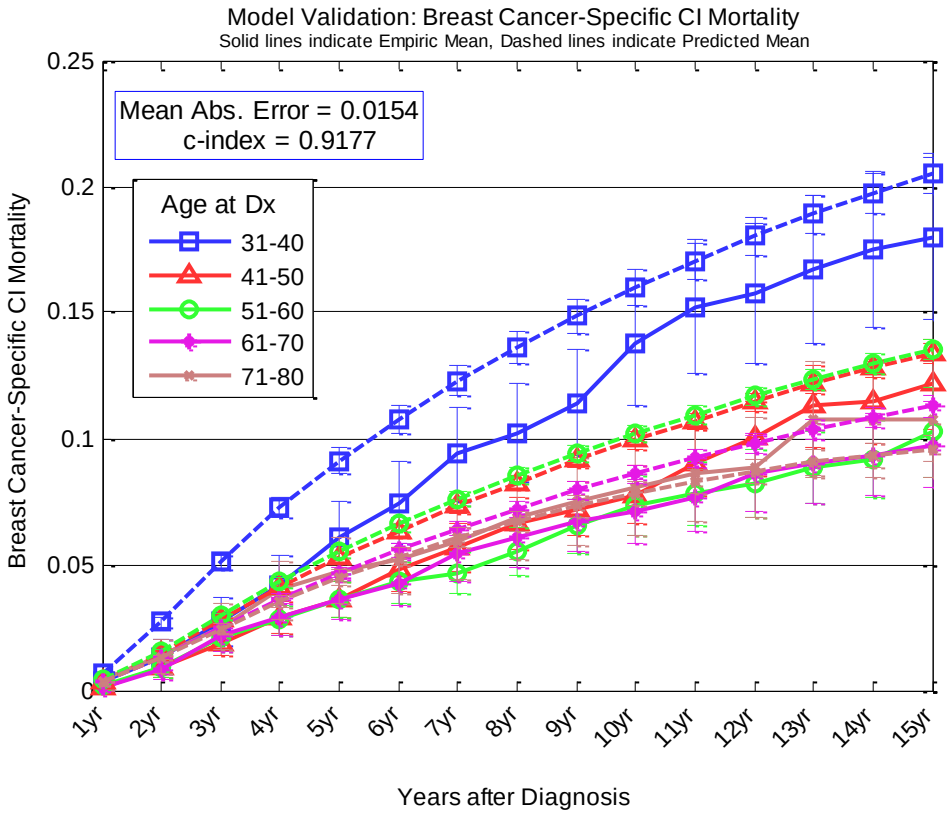
'Weighted Mean Error' '1.29%'
'Mean Absolute Error' '2.88%'
'Weighted Mean Absolute Error' '1.49%'
'Maximum Error' '10.55% (41-50mm / 15yr group)'
'Concordance Index' '0.9621'

Figure 3cc: Partners patients stratified by positive nodes



'Weighted Mean Error' '1.14%'
'Mean Absolute Error' '4.4%'
'Weighted Mean Absolute Error' '1.16%'
'Maximum Error' '17.16% (5 nodes / 15yr group)'
'Concordance Index' '0.9111'

Figure 3dd: Partners patients stratified by age



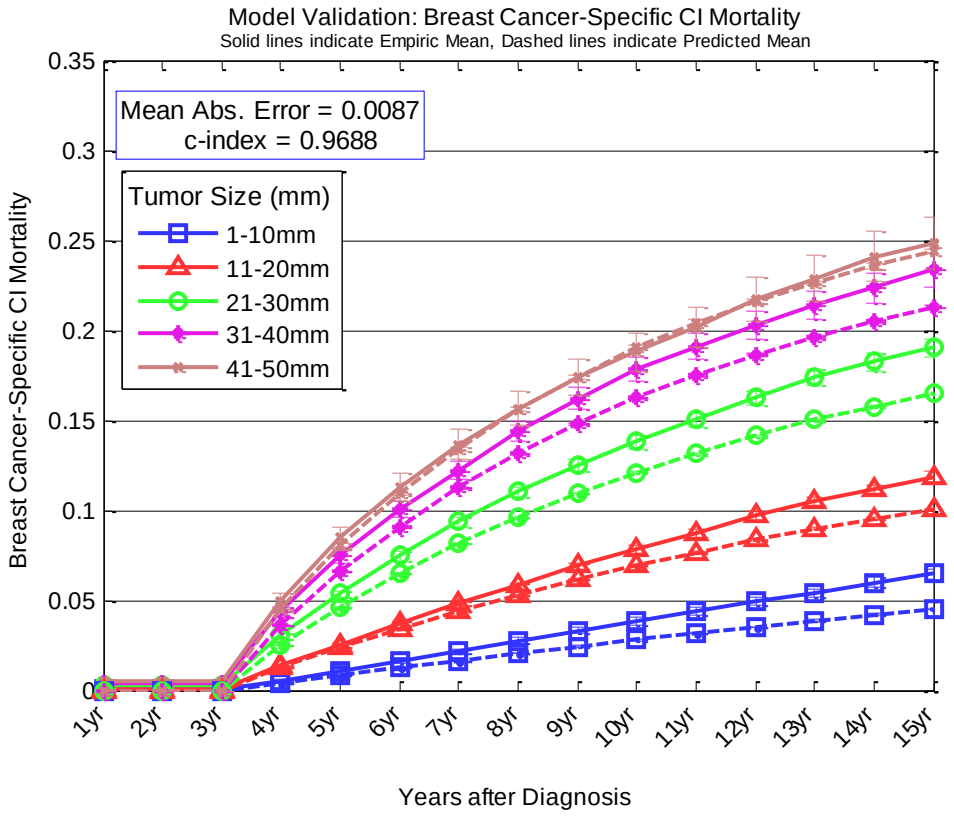
'Weighted Mean Error'	'1.51%'
'Mean Absolute Error'	'1.54%'
'Weighted Mean Absolute Error'	'1.6%'
'Maximum Error'	'3.75% (51-60 / 14yr group)'
'Concordance Index'	'0.9177'

Figure 4. Validation of the conditional survival calculations. Exact values for figures omitted due to space constraints.

Figure 4a: SEER patients stratified by 10mm tumor size bins, 3yr conditional survival
Figure 4b: SEER patients stratified by 10mm tumor size bins, 6yr conditional survival
Figure 4c: SEER patients stratified by 10mm tumor size bins, 9yr conditional survival

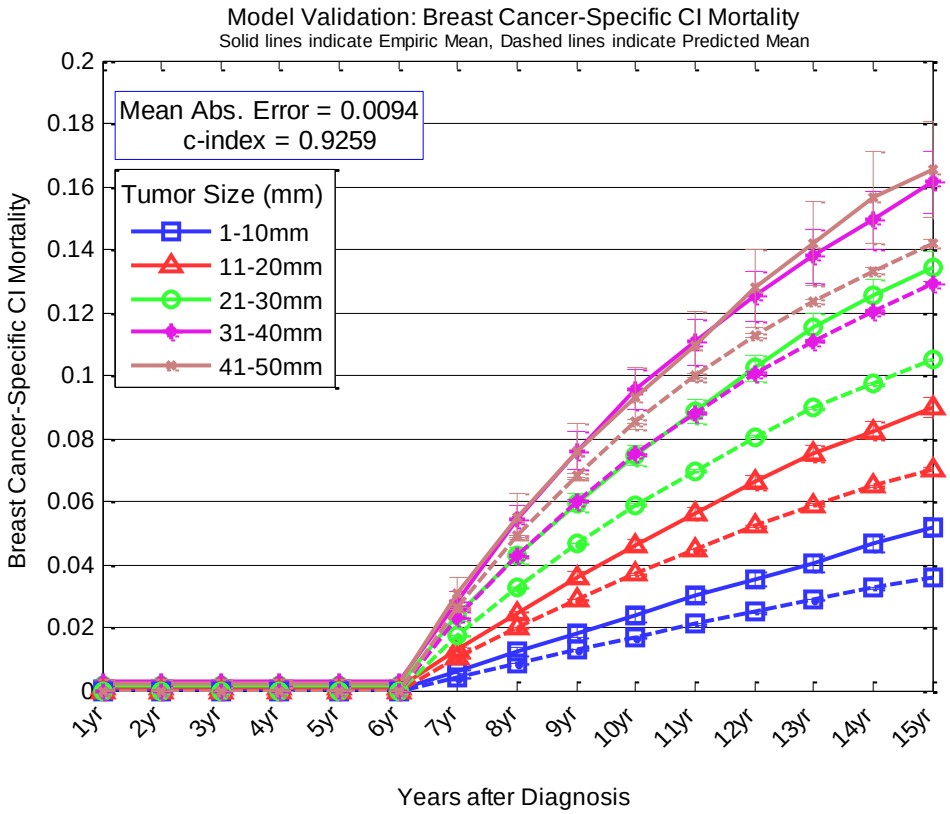
Figure 4aa: Partners patients stratified by 10% predicted lethality deciles
Figure 4bb: Partners patients stratified by 10mm tumor size bins
Figure 4cc: Partners patients stratified by positive nodes
Figure 4dd: Partners patients stratified by age

Figure 4a: SEER patients stratified by 10mm tumor size bins, 3yr conditional survival



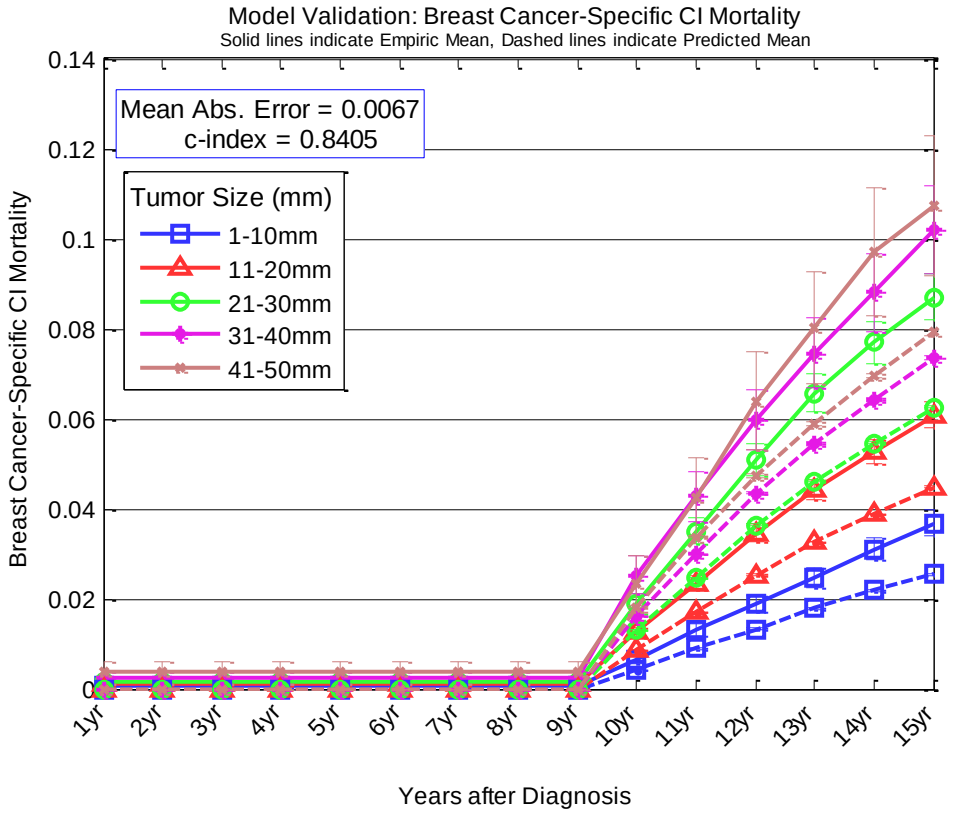
'Weighted Mean Error' '-0.88%'
'Mean Absolute Error' '0.87%'
'Weighted Mean Absolute Error' '0.88%'
'Maximum Error' '-2.52% (21-30mm / 15yr group)'
'Concordance Index' '0.9688'

Figure 4b: SEER patients stratified by 10mm tumor size bins, 6yr conditional survival



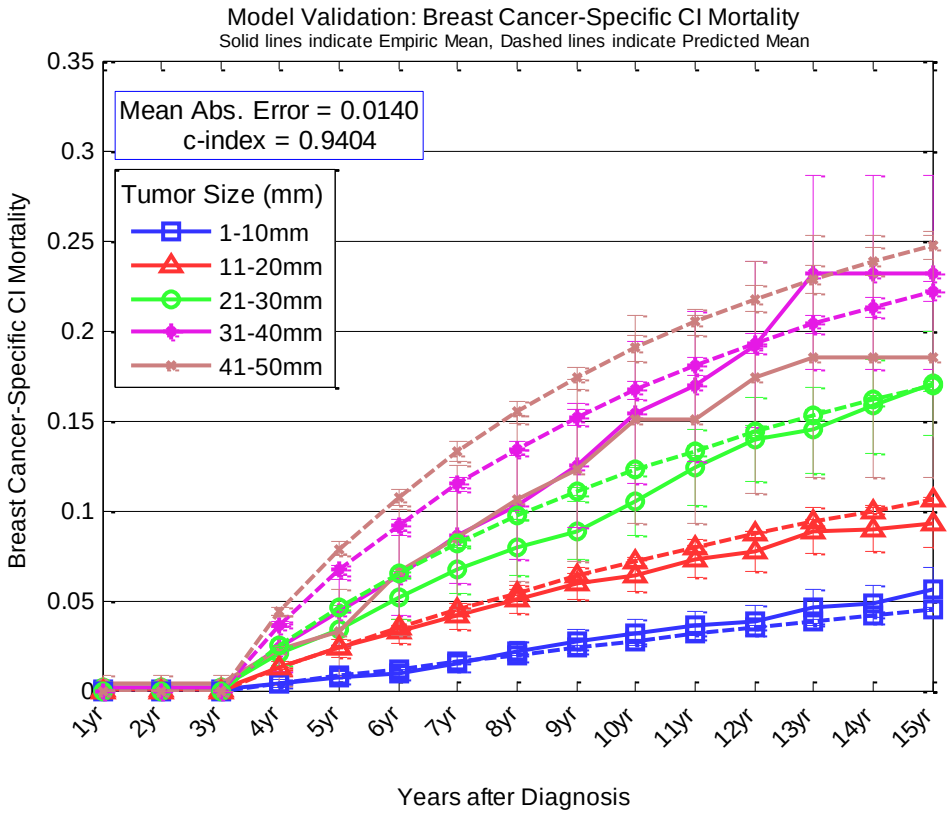
'Weighted Mean Error' '-0.81%'
'Mean Absolute Error' '0.94%'
'Weighted Mean Absolute Error''0.81%'
'Maximum Error' '-3.25% (31-40mm / 15yr group)'
'Concordance Index' '0.9259'

Figure 4c: SEER patients stratified by 10mm tumor size bins, 9yr conditional survival



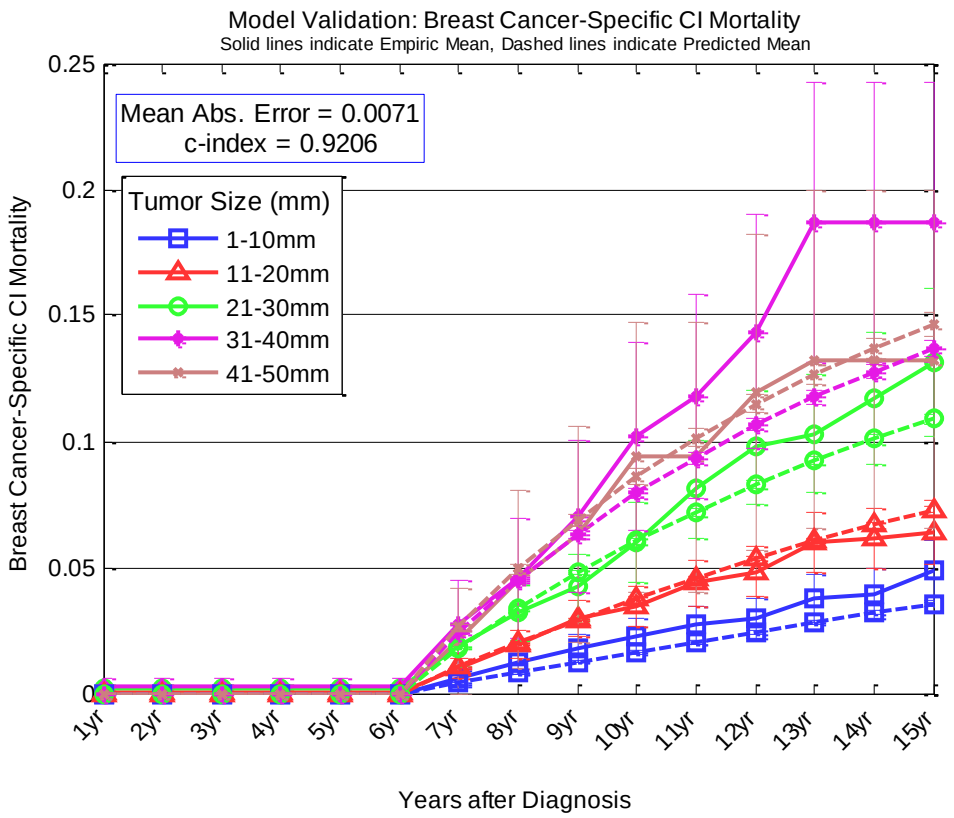
'Weighted Mean Error' '-0.52%'
'Mean Absolute Error' '0.67%'
'Weighted Mean Absolute Error' '0.52%'
'Maximum Error' '-2.85% (31-40mm / 15yr group)'
'Concordance Index' '0.8405'

Figure 4aa: Partners patients stratified by 10mm tumor size bins, 3yr conditional survival



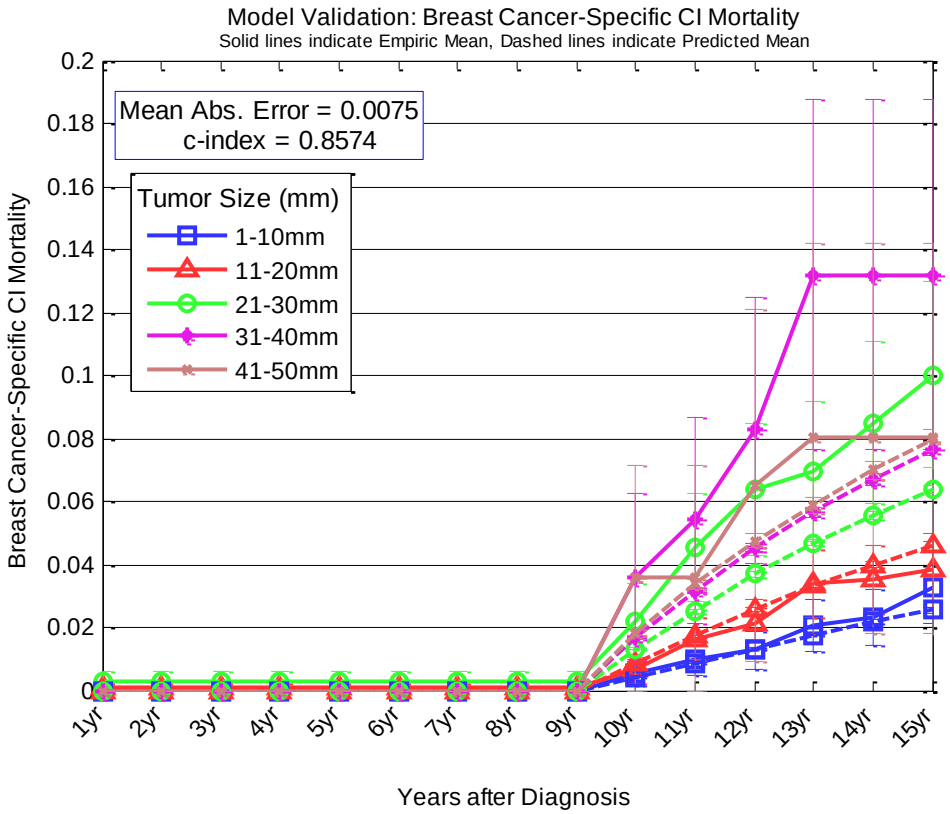
'Weighted Mean Error'	'0.34%'
'Mean Absolute Error'	'1.4%'
'Weighted Mean Absolute Error'	'0.63%'
'Maximum Error'	'6.2% (41-50mm / 15yr group)'
'Concordance Index'	'0.9404'

Figure 4a: SEER patients stratified by 10mm tumor size bins, 6yr conditional survival



'Weighted Mean Error' '-0.27%'
'Mean Absolute Error' '0.71%'
'Weighted Mean Absolute Error' '0.44%'
'Maximum Error' '-6.95% (31-40mm / 13yr group)'
'Concordance Index' '0.9206'

Figure 4b: SEER patients stratified by 10mm tumor size bins, 9yr conditional survival



'Weighted Mean Error' '-0.29%'
'Mean Absolute Error' '0.75%'
'Weighted Mean Absolute Error''0.4%'
'Maximum Error' '-7.53% (31-40mm / 13yr group)'
'Concordance Index' '0.8574"

CODE IN THE TREATMENT CALCULATOR

The javascript code performing the life expectancy and mortality calculations for www.cancermath.net is provided below. The code begins by initializing several lengthy arrays (such as the life expectancy tables)—the code corresponding to Step 1 described above begins at the top of page 20.

```
/*~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
  This web calculator estimates the risk of breast cancer death
  that reflects expectations at the current time.
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~*/

/*~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
   © James Michaelson PhD
   May be freely used for any scientific purpose; For permission to use commercially or in a
website,
   contact Dr. Michaelson at james.michaelson@gmail.com
   For the mathematical essentials used below, see:
     Michaelson JS et al. "The effect of tumor size and lymph node status on breast carcinoma
lethality"
     Cancer. 2003;98:2133-2143.
  ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~*/

  /*********************************************************************
* A set of seven 15-part step functions to represent the fraction
* of deaths that occurs in each of the 15 years after diagnosis.
* This is the probability density function of the SEER cohort from which we derived our
parameters,
* normalized to 1 at 15 years.  Each distribution represents the death distribution for a given
predicted lethality decile of patients (deciles 7-10 are consolidated due to lack of follow-up
for patients with extremely high lethality.
*********************************************************************/
var L_cancer_distribution = [];
L_cancer_distribution[0] =    [0.019616, 0.033607, 0.050191, 0.061750, 0.060530, 0.064742,
0.067020, 0.071466, 0.081533, 0.073175, 0.081652, 0.079388, 0.091390, 0.085183, 0.078758];
L_cancer_distribution[1] =    [0.023136, 0.057584, 0.084479, 0.084391, 0.085485, 0.088679,
0.078667, 0.073739, 0.073411, 0.064442, 0.066278, 0.065975, 0.057491, 0.049183, 0.047060];
L_cancer_distribution[2] =    [0.028354, 0.081731, 0.105380, 0.110125, 0.093966, 0.082921,
0.078921, 0.066581, 0.062425, 0.057623, 0.045785, 0.054887, 0.046125, 0.040354, 0.044822];
L_cancer_distribution[3] =    [0.032086, 0.103774, 0.125460, 0.110931, 0.092170, 0.079606,
0.074475, 0.068409, 0.061230, 0.048345, 0.048421, 0.052404, 0.035408, 0.037259, 0.030023];
L_cancer_distribution[4] =    [0.042404, 0.131218, 0.134476, 0.118682, 0.099011, 0.081084,
0.066663, 0.063178, 0.047991, 0.052718, 0.044478, 0.029628, 0.034241, 0.024338, 0.029889];
L_cancer_distribution[5] =    [0.049900, 0.167947, 0.162144, 0.130179, 0.090684, 0.076706,
0.064070, 0.050783, 0.042789, 0.041432, 0.035461, 0.020914, 0.021077, 0.023692, 0.022222];
L_cancer_distribution[6] =    [0.063152, 0.224963, 0.201910, 0.133052, 0.110058, 0.052619,
0.057881, 0.036207, 0.044003, 0.028356, 0.012792, 0.000000, 0.009988, 0.025019, 0.000000];



/*********************************************************************
* Array of probability of dying between year x and x+1, where x is age, starting at age x=0,
taken from:
*       -National Vital Statistics Reports Vol 58 No 10, March 3, 2010, United States Life Tables
2005,
*       Table 3. Life table for females: United States, 2005.
* adjusted to exclude the probability of dying from breast cancer using data from:
*  -National Vital Statistics Reports Vol 57, No 14, April 17, 2009, Deaths: Final Data for 2006,
*  Table 10. Number of deaths from 113 selected causes by age: United States, 2006
*********************************************************************/

var nvsr_death_prob_yearly_female = new Array(0.006156, 0.000410, 0.000256, 0.000182, 0.000159,
0.000154, 0.000144, 0.000135, 0.000125, 0.000114, 0.000105, 0.000106, 0.000125, 0.000164,
0.000219, 0.000281, 0.000340, 0.000387, 0.000418, 0.000436, 0.000453, 0.000472, 0.000487,
0.000496, 0.000503, 0.000500, 0.000510, 0.000526, 0.000552, 0.000586, 0.000628, 0.000675,
0.000729, 0.000776, 0.000832, 0.000847, 0.000920, 0.001013, 0.001129, 0.001260, 0.001393,
0.001528, 0.001674, 0.001834, 0.002009, 0.002106, 0.002300, 0.002498, 0.002698, 0.002907,
0.003135, 0.003388, 0.003660, 0.003947, 0.004251, 0.004431, 0.004783, 0.005194, 0.005694,
0.006295, 0.007019, 0.007830, 0.008668, 0.009465, 0.010239, 0.010940, 0.011811, 0.012838,
0.014040, 0.015426, 0.016994, 0.018792, 0.020874, 0.023266, 0.025993, 0.028807, 0.032169,
0.035899, 0.040034, 0.044614, 0.049682, 0.055283, 0.061466, 0.068281, 0.075782, 0.083538,
0.092578, 0.102473, 0.113279, 0.125054, 0.137849, 0.151714, 0.166692, 0.182818, 0.200118,
0.218606, 0.238283, 0.259134, 0.281126, 0.304208, 0.328472, 0.353512, 0.379374, 0.405932,
```

```
0.433044, 0.460555, 0.488301, 0.516111, 0.543815, 0.571243, 0.598232, 0.624632, 0.650303,
0.675123, 0.698989, 0.721816, 0.743539, 0.764111, 0.783504, 0.801707, 0.818724, 0.834572,
0.849280, 0.862885);



/*****************************************************************
*  Expectation of life in years at age x, starting at age x=0, taken from:
*       -National Vital Statistics Reports Vol 58 No 10, March 3, 2010, United States Life Tables
2005,
*       Table 3. Life table for females: United States, 2005.
* adjusted to exclude the probability of dying from breast cancer using data from:
*  -National Vital Statistics Reports Vol 57, No 14, April 17, 2009, Deaths: Final Data for 2006,
*  Table 10. Number of deaths from 113 selected causes by age: United States, 2006
*****************************************************************************/

var nvsr_life_expect_female = new Array(80.195482, 79.689126, 78.721607, 77.741637, 76.755697,
75.767824, 74.779417, 73.790115, 72.800010, 71.809049, 70.817179, 69.824563, 68.831912,
67.840455, 66.851500, 65.866034, 64.884407, 63.906306, 62.930853, 61.956960, 60.983767,
60.011179, 59.039281, 58.067804, 57.096372, 56.124854, 55.152654, 54.180514, 53.208739,
52.237825, 51.268137, 50.300015, 49.333629, 48.369231, 47.406383, 46.445419, 45.484350,
44.525756, 43.570382, 42.619046, 41.672166, 40.729583, 39.791132, 38.857000, 37.927461,
37.002789, 36.079831, 35.161857, 34.248664, 33.339968, 32.435716, 31.536154, 30.641666,
29.752393, 28.868313, 27.989425, 27.111765, 26.239653, 25.374035, 24.516471, 23.668605,
22.832368, 22.008603, 21.196664, 20.394423, 19.600223, 18.811494, 18.030360, 17.258344,
16.496985, 15.747623, 15.011224, 14.289144, 13.583117, 12.894762, 12.225539, 11.573332,
10.941386, 10.330175, 9.740125, 9.171611, 8.624953, 8.100407, 7.598166, 7.118352, 6.661027,
6.222625, 5.806468, 5.412324, 5.039878, 4.688755, 4.358496, 4.048582, 3.758430, 3.487400,
3.234803, 2.999905, 2.781936, 2.580095, 2.393547, 2.221429, 2.063450, 1.918373, 1.785391,
1.663708, 1.552553, 1.451177, 1.358858, 1.274907, 1.198669, 1.129520, 1.066876, 1.010187,
0.958937, 0.912649, 0.870878, 0.833213, 0.799274, 0.768703, 0.741143, 0.716094, 0.692070,
0.661053, 0.568558, 0.000000);


//The following function performs all of the the web calculations
function updateGraph(){

     if ( typeof updateGraph.counter == 'undefined' ) { //show the disclaimer the first time
function is called
        tb_show(null,
"/cancer/limitations.html?placeValuesBeforeTB_=savedValues&TB_iframe=true&height=500&width=330&mo
dal=true", false);
        updateGraph.counter = 1;
     }
/*****************************************************************
STEP 1  collect user input
Acquire all the user inputs and assigns the appropriate j_primary and g-values to:
Age; Tumor Diameter; Nodal Status; # of Positive Nodes; ER Status; PR Status;
HERS Status; Histologic Type; Grade;
*****************************************************************************/

    age = document.form.ageInput.value*1;
    dia = document.form.diameter.value*1;
    nnum=document.form.nodenumber.value*1;
    erstatus =document.form.erstatus.value*1;
    prstatus =document.form.prstatus.value*1;
    her2 =document.form.her2status.value*1;
    histology =document.form.histology.value*1;
    grade =document.form.grade.value*1;

    endo=document.form.endotherapy.value*1;
    chemo=document.form.chemotherapy.value*1;

    //inlcude separate therapy calculations for user-specified therapies
    includeTherapyCalc = !document.form.therapy[1].checked;
   years_alive = document.form.years_alive.value*1;
/*****************************************************************
STEP 2 calculate yearly and cumulative cancer and total death rates
*****************************************************************************/
```

```
    /*****************************************************************
    Initizes empty arrays necessary for calculations
    * L_cancer_percentage: contains the distribution of breast cancer lethality for 15 years
    * L_cancer_death_yearly: describes to the total number of deaths due to breast cancer at a
single year
    * L_cancer_death_cumm: describes the cummulative number of deaths due to breast cancer for a
given year and all its previous years
    * L_noncancer_prob: contains the probability of survival from the nsvr data adjusted to
exclude the probability of dying from breast cancer as mentioned previously
    * L_noncancer_death_yearly: describes to the total number of deaths due to non-breast cancer
causes at a single year
    * L_noncancer_death_cumm: describes the cummulative number of deaths due to non-breast cancer
causes for a given year and all its previous years
    * L_overall_death_yearly: describes to the total number of deaths due to all causes at a
single year
    * L_overall_death_cumm: describes the cummulative number of deaths due to all causes for a
given year and all its previous years
    * remaining_percentage: describes the percentage of the initial population surviving to a
specific year
    * calc_num_surviving: calculated number of women with breast cancer surviving
    * calc_person_years_lived_between_years: calculated number of person years lived by women
with breast cancer between two consecutive years
    * calc_total_num_of_person_years_lived_above: caculated number of person years lived by women
with breast cancer above a certain age
    ******************************************************************************/
    var L_cancer_percentage=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_noncancer_prob=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_cancer_death_yearly=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_cancer_death_cumm=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_noncancer_death_yearly=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_noncancer_death_cumm=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_overall_death_yearly=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_overall_death_cumm=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var remaining_percentage=new Array(1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var cancer_death_hazard = new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);


    var L_cancer_percentage_therapy=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_noncancer_prob_therapy=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_cancer_death_yearly_therapy=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_cancer_death_cumm_therapy=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_noncancer_death_yearly_therapy=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_noncancer_death_cumm_therapy=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_overall_death_yearly_therapy=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var L_overall_death_cumm_therapy=new Array(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var remaining_percentage_therapy=new Array(1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0);
    var remaining_percentage_cancer_therapy = 1.0;

    endotherapyEffect=0; //Resets endotherapy effect before every calculation to no endotherapy
    chemotherapyEffect=0; //Resets endotherapy effect before every calculation to no chemotherapy
    totaltherapyEffect=0; //Resets total therapy effect before every calculation to no therapy

    nvsr_death_prob_yearly=nvsr_death_prob_yearly_female;
    nvsr_life_expect=nvsr_life_expect_female;


    Qn = 0.014751
    Qs=0.010054;
    j_primary=0.8057;
    Z=1; //initializes Z value
    R=0.07581; //initializes R value

    /*****************************************************************
    * If nodal status is unknown, j_primary is set to 1
    ******************************************************************************/
    if (document.form.nodesKnown.value *1 == 0) {
        j_primary=1;
        nnum=0;
    } else {
        nnum=nnum;
    }
```

```
/*****************************************************************
 STEP 2.a      The program loads the g parameters determined by the user input, and computes the
product of all of them
*****************************************************************************/
  g_parameter = 1; //Resets g_parameter before every calculation

    /*****************************************************************
    * Multiply g-parameter with g-value based on age
    *****************************************************************************/
    if(age == 0) {
        g_parameter=g_parameter*1; //if user age is 0 then g-value is 1
       } else if(age >= 21 && age <= 30) {
         g_parameter=g_parameter*1.2545;     //if user age is 21-30 then g-value is 1.2545
       } else if(age >= 31 && age <= 40) {
          g_parameter=g_parameter*1.1267;  //if user age is 31-40 then g-value is 1.1267
       } else if(age >= 41 && age <= 50) {
          g_parameter=g_parameter*0.8661;  //if user age is 41-50 then g-value is 0.8661
       } else if(age >= 51 && age <= 60) {
          g_parameter=g_parameter*1.0190;  //if user age is 51-60 then g-value is 1.0190
       } else if(age >= 61 && age <= 70) {
          g_parameter=g_parameter*1.0172;  //if user age is 61-70 then g-value is 1.0172
       } else if(age >= 71 && age <= 80) {
          g_parameter=g_parameter*1.0201;  //if user age is 71-80 then g-value is 1.0201
       } else if(age >= 81 && age <= 90) {
          g_parameter=g_parameter*1.1646;  //if user age is 81-90 then g-value is 1.1646
       } else if(age >= 91 && age <= 100) {
          g_parameter=g_parameter*1.32845;  //if user age is 91-100 then g-value is 1.32845
       } else {
          g_parameter=g_parameter*1; //if user age is <=20 or >=101 then g-value is 1
       }

    /*****************************************************************
    * Multiply g-parameter with g-value based on ER/PR status
    *****************************************************************************/
    switch (erstatus) {

        case 1: //ER status Positive
               if(prstatus==1) { //PR Positive
                              //if ER is POSITIVE and PR is POSITIVE then g-value is  0.91545
                              g_parameter=g_parameter* 0.91545;
               } else if(prstatus==2) { //PR Negative
                              //if ER is POSITIVE and PR is NEGATIVE then g-value is 1.13885
                              g_parameter=g_parameter*1.13885;
               }
        break;
        case 2: //ER status Negative
               if(prstatus==1) { //PR Positive
                              //if ER is NEGATIVE and PR is POSITIVE then g-value is 1.0462
                              g_parameter=g_parameter*1.0462;
               } else if(prstatus==2) { //PR Negative
                              //if ER is NEGATIVE and PR is NEGATIVE then g-value is 1.1902
                              g_parameter=g_parameter*1.1902;
               }
        break;
    }  //end Switch for erpr

    /*****************************************************************
    * Multiply g-parameter with g-value based on HER2 status
    *****************************************************************************/
    switch (her2) {
        case 0:
               //if HER2 is UNKNOWN then g-value is 1
               g_parameter=g_parameter*1;
        break;
        case 1:
               //if HER2 is POSITIVE then g-value is 1.515
               g_parameter=g_parameter*1;
        break;
        case 2:
               //if HER2 is NEGATIVE then g-value is 0.9662
```

```
            g_parameter=g_parameter*1;
    break;
}  //end switch for HER2

/*********************************************************************
* Multiply g-parameter with g-value based on histology status
*********************************************************************/
switch (histology) {
    case 0:
            //if HISTOLOGY is UNKNOWN then g-value is 1
            g_parameter=g_parameter*1;
    break;
       case 1:
            //if HISTOLOGY is DUCTAL then g-value is 1.0573
            g_parameter=g_parameter*1.0573;
    break;
    case 2:
            //if HISTOLOGY is LOBULAR then g-value is 0.9032
            g_parameter=g_parameter*0.9032;
    break;
    case 3:
            //if HISTOLOGY is DUCTALandLOBULAR then g-value is 0.8573
            g_parameter=g_parameter*0.8573;
    break;
    case 4:
            //if HISTOLOGY is MUCINOUS then g-value is 0.4646
            g_parameter=g_parameter*0.4646;
    break;
       case 5:
            //if HISTOLOGY is MEDULLARY then g-value is 0.5995
            g_parameter=g_parameter*0.5995;
    break;
    case 6:
            //if HISTOLOGY is TUBULAR then g-value is 0.2752
            g_parameter=g_parameter*0.2752;
    break;
    case 7:
            //if HISTOLOGY is COMEDO then g-value is 0.8645
            g_parameter=g_parameter*0.8645;
    break;
    case 8:
            //if HISTOLOGY is SCIRRHOUS then g-value is 1.6314
            g_parameter=g_parameter*1.6314;
    break;
    case 9:
            //if HISTOLOGY is INFLAMMATORY then g-value is 3.3130
            g_parameter=g_parameter*3.3130;
    break;
    case 10:
            //if HISTOLOGY is PAGETS then g-value is 1.4535
            g_parameter=g_parameter*1.4535;
    break;
    case 11:
            //if HISTOLOGY is PAPILLARY then g-value is 0.5414
            g_parameter=g_parameter*0.5414;
    break;
    case 12:
            //if HISTOLOGY is CRIBIFORM then g-value is 0.9636
            g_parameter=g_parameter*0.9636;
    break;
    case 13:
            //if HISTOLOGY is APOCRINE then g-value is 0.8505
            g_parameter=g_parameter*0.8505;
    break;
    case 14:
            //if HISTOLOGY is PHYLLODES then g-value is 0.14972
            g_parameter=g_parameter*0.14972;
    break;
}  //end Switch for histology

/*****************************************************************
```

```
    * Multiply g-parameter with g-value based on grade
    ************************************************************************/
    switch (grade) {
        case 0:
               //if GRADE is UNKNOWN then g-value is 1
               g_parameter=g_parameter*1;
        break;
        case 1:
               //if GRADE is 1 then g-value is 0.4324
               g_parameter=g_parameter*0.4324;
        break;
        case 2:
               //if GRADE is 2 then g-value is 0.8570
               g_parameter=g_parameter*0.8570;
        break;
        case 3:
               //if GRADE is 3 then g-value is 1.1224
               g_parameter=g_parameter*1.1224;
        break;
        case 4:
               //if GRADE is UNDIFFERENTIATED then g-value is 1.26495
               g_parameter=g_parameter*1.26495;
        break;
    } //end Switch for grade


/*********************************************************************
*  STEP 2.b    The program calculates the 15-year Kaplan-Meier cancer death rate, L, using the
SNAP method and the product of the g parameters
* Calculates lethality of primary breast cancer tumor (L_primary), lethality of nodes (L_nodes),
and 15-year Kaplan Meier cancer * specific death rate (L_cancer_KM)
*********************************************************************/
    L_primary = 1 - Math.exp(-Qn*g_parameter*j_primary*Math.pow(dia*10,Z));
    L_nodes = 1 - Math.exp(-nnum*R);
    L_cancer_KM = L_primary + L_nodes - (L_primary*L_nodes);

    distribution_index =  Math.max(6, Math.floor(L_cancer_KM * 10));



/*********************************************************************
* STEPs 2.c, 2.d, & 2.e calculate cancer death rate in each of the 15 years following diagnosis
* Calculates yearly lethalities due to breast cancer and other causes
*********************************************************************/
        cumulative_cancer_death = 0;
        lethality_survived = 0;
        for (i=1; i<=15; i++) {
            //STEP 2.c calculates cancer death rate by multiplying 15yr KM cancer death rate by
expected BRCA yearly lethality
            //cancer-specific hazard = chance of cancer death / cancer-specific survival to that
point
            cancer_death_hazard[i] = L_cancer_distribution[distribution_index][i-1]*L_cancer_KM /
(1-cumulative_cancer_death);
            if (document.form.recur_evid[1].checked ==true && years_alive > 0) { // no evidence
of recurrence
                //Reduce the death distribution in the years immediately following the evidence
of no recurrence
                cancer_death_hazard[i] = L_cancer_distribution[distribution_index][i-1] /
Math.max(1, 3-(i-years_alive));
            }
            cumulative_cancer_death = cumulative_cancer_death +
L_cancer_distribution[distribution_index][i-1] * L_cancer_KM;

                    if (i > years_alive) {
                L_cancer_KM_cond =  L_cancer_KM * (1- lethality_survived) / (1 -
(lethality_survived * L_cancer_KM));
                L_cancer_death_yearly[i]=remaining_percentage[i-1] * cancer_death_hazard[i];
                L_noncancer_prob[i]=nvsr_death_prob_yearly[i+age];

            } else {
```

```
                lethality_survived = lethality_survived +
L_cancer_distribution[distribution_index][i-1];
                L_cancer_death_yearly[i]=0;
                L_noncancer_prob[i]=0;
            }
            //STEP 2.d calculates non-BRCA death rate by multiplying the fraction of patients not
dying of cancer by the yearly risk of death due to non-cancer causes for the given age

            L_noncancer_death_yearly[i]=(remaining_percentage[i-1] - L_cancer_death_yearly[i])
*L_noncancer_prob[i];
            //STEP 2.e calculates overall death rate by adding breast cancer deaths to non-breast
cancer deaths
            L_overall_death_yearly[i]=L_cancer_death_yearly[i]+L_noncancer_death_yearly[i];
               remaining_percentage[i]=remaining_percentage[i-1]-L_overall_death_yearly[i];


        }

/*********************************************************************
* STEP 2.f  Calculate 15 values for cumulative breast cancer, non-breast cancer, and total death
rates by summing the respective yearly values computed in the steps above.
*********************************************************************/

    for(i=1;i<=15;i++) {
        L_cancer_death_cumm[i]=L_cancer_death_cumm[i-1]+L_cancer_death_yearly[i];
        L_noncancer_death_cumm[i]=L_noncancer_death_cumm[i-1]+L_noncancer_death_yearly[i];
        L_overall_death_cumm[i]=L_overall_death_cumm[i-1]+L_overall_death_yearly[i];
    }

/*********************************************************************
* STEP 3   Calculate the mean number of years of life left that can be expected for the cancer
patient
*********************************************************************/

/*********************************************************************
* STEP 3.a   Calculate the life expectancy for the cancer patient by multiplying the chance of
dying in each of the years 1-15 by the number of years survived to that point.  Then add the NVSR
life expectancy for people 15 years older than the patient's current age, multiplied by the
patients chance of surviving 15 years.
*********************************************************************/
    calc_life_expectation = 0;
    for (i=1; i<=15; i++){
        calc_life_expectation = calc_life_expectation + L_overall_death_yearly[i] * (i-0.5);
    }
    calc_life_expectation = calc_life_expectation + (1 - L_overall_death_cumm[15]) *
(nvsr_life_expect[age + 15] +15)

/*********************************************************************
* STEP 3.b   The program calculates the expected years of life lost due to cancer, by subtracting
the calculated life expectancy (step 3.a) from the NVSR-given life expectancy for the specified
age.
*********************************************************************/

    expect_years_life_lost = nvsr_life_expect[age] - calc_life_expectation;


 /*************************************************
STEP 4  Calculate death rates with a specific therapy type
*************************************************/
/*************************************************
STEP 4.a  Calculate the "risk-reduction" value based on the combination of therapies entered by
the user and the information collected in steps 1.c and 1.d, consistent with the assumptions of
Adjuvant!Online
*************************************************/
    /*********************************************************************
    * The following code gives the effect of endocrine (hormonal) therapy.
    *********************************************************************/
    if (endo==0) {
        endotherapyEffect=0;
    } else {
    switch(erstatus) {
```

```
    case 0: //If ER unknown
            if(age<50){
                    endotherapyEffect=0.20;
            } else if(age >=50 && age < 60) {
                    endotherapyEffect=0.21;
            } else {
                    endotherapyEffect=0.23;
            }
    break;
    case 1: //If ER+
            if(age<50){
                    endotherapyEffect=0.32;
            } else if(age >=50 && age < 60) {
                    endotherapyEffect=0.32;
            } else {
                    endotherapyEffect=0.32;
            }
    break;
    case 2: //If ER-
            if(age<50){
                    endotherapyEffect=0;
            } else if(age >=50 && age < 60) {
                    endotherapyEffect=0;
            } else {
                    endotherapyEffect=0;
            }
    break;
} //end switch
} //end if for endo

/*********************************************************************
* The following code gives the effect of chemotherapy.
*********************************************************************/

switch (chemo) {
    case 0: //no chemo
            chemotherapyEffect=0;
    break;
    case 1: //CMF
            switch(erstatus) {
                    case 0: //If ER unknown
                            if(age<50){
                                    chemotherapyEffect=0.30;
                            } else if(age >=50 && age < 60) {
                                    chemotherapyEffect=0.18;
                            } else {
                                    chemotherapyEffect=0.10;
                            }
                    break;
                    case 1: //If ER+
                            if(age<50){
                                    chemotherapyEffect=0.30;
                            } else if(age >=50 && age < 60) {
                                    chemotherapyEffect=0.16;
                            } else {
                                    chemotherapyEffect=0.08;
                            }
                    break;
                    case 2: //If ER-
                            if(age<50){
                                    chemotherapyEffect=0.30;
                            } else if(age >=50 && age < 60) {
                                    chemotherapyEffect=0.22;
                            } else {
                                    chemotherapyEffect=0.15;
                            }
                    break;
            } //end switch er
    break;

    case 2: //Anthra
```

```
        switch(erstatus) {
                case 0: //If ER unknown
                        if(age<50){
                                chemotherapyEffect=0.41;
                        } else if(age >=50 && age < 60) {
                                chemotherapyEffect=0.31;
                        } else {
                                chemotherapyEffect=0.24;
                        }
                break;
                case 1: //If ER+
                        if(age<50){
                                chemotherapyEffect=0.41;
                        } else if(age >=50 && age < 60) {
                                chemotherapyEffect=0.29;
                        } else {
                                chemotherapyEffect=0.23;
                        }
                break;
                case 2: //If ER-
                        if(age<50){
                                chemotherapyEffect=0.41;
                        } else if(age >=50 && age < 60) {
                                chemotherapyEffect=0.34;
                        } else {
                                chemotherapyEffect=0.29;
                        }
                break;
        } //end switch er
break;

case 3: //1st gen
        switch(erstatus) {
                case 0: //If ER unknown
                        if(age<50){
                                chemotherapyEffect=0.30;
                        } else if(age >=50 && age < 60) {
                                chemotherapyEffect=0.18;
                        } else {
                                chemotherapyEffect=0.10;
                        }
                break;
                case 1: //If ER+
                        if(age<50){
                                chemotherapyEffect=0.30;
                        } else if(age >=50 && age < 60) {
                                chemotherapyEffect=0.16;
                        } else {
                                chemotherapyEffect=0.08;
                        }
                break;
                case 2: //If ER-
                        if(age<50){
                                chemotherapyEffect=0.30;
                        } else if(age >=50 && age < 60) {
                                chemotherapyEffect=0.22;
                        } else {
                                chemotherapyEffect=0.15;
                        }
                break;
        } //end switch er
break;

case 4: //2nd gen
        switch(erstatus) {
                case 0: //If ER unknown
                        if(age<50){
                                chemotherapyEffect=0.44;
                        } else if(age >=50 && age < 60) {
                                chemotherapyEffect=0.34;
                        } else {
```

```
                                        chemotherapyEffect=0.28;
                                }
                        break;
                        case 1: //If ER+
                                if(age<50){
                                        chemotherapyEffect=0.44;
                                } else if(age >=50 && age < 60) {
                                        chemotherapyEffect=0.33;
                                } else {
                                        chemotherapyEffect=0.26;
                                }
                        break;
                        case 2: //If ER-
                                if(age<50){
                                        chemotherapyEffect=0.44;
                                } else if(age >=50 && age < 60) {
                                        chemotherapyEffect=0.38;
                                } else {
                                        chemotherapyEffect=0.32;
                                }
                        break;
        } //end switch er
        break;
        case 5: //3rd gen
                switch(erstatus) {
                        case 0: //If ER unknown
                                if(age<50){
                                        chemotherapyEffect=0.55;
                                } else if(age >=50 && age < 60) {
                                        chemotherapyEffect=0.47;
                                } else {
                                        chemotherapyEffect=0.42;
                                }
                        break;
                        case 1: //If ER+
                                if(age<50){
                                        chemotherapyEffect=0.55;
                                } else if(age >=50 && age < 60) {
                                        chemotherapyEffect=0.45;
                                } else {
                                        chemotherapyEffect=0.40;
                                }
                        break;
                        case 2: //If ER-
                                if(age<50){
                                        chemotherapyEffect=0.55;
                                } else if(age >=50 && age < 60) {
                                        chemotherapyEffect=0.49;
                                } else {
                                        chemotherapyEffect=0.45;
                                }
                        break;
                } //end switch er
        break;
    } //end switch for chemo

    /*****************************************************
    * Combine effect of endocrine therapy and chemotherapy
    *****************************************************/
    if (document.form.therapy[0].checked) {
        totaltherapyEffect = endotherapyEffect + chemotherapyEffect - (endotherapyEffect *
chemotherapyEffect);
      //  L_cancer_KM_therapy=Math.round(L_cancer_KM*(1-totaltherapyEffect)*1000)/1000;
        L_cancer_KM_therapy=L_cancer_KM*(1-totaltherapyEffect);
    } else if (document.form.therapy[1].checked) {
        L_primary = 1 - Math.exp(-Qs*g_parameter*j_primary*Math.pow(dia*10,Z));
        L_nodes = 1 - Math.exp(-nnum*R);
        L_cancer_KM_therapy = L_primary + L_nodes - (L_primary*L_nodes);
    } else { //no therapy selected
        L_cancer_KM_therapy = L_cancer_KM;
        totaltherapyEffect = 0;
```

```
    }
    distribution_index = Math.max(6, Math.floor(L_cancer_KM_therapy * 10)); ;



    /*********************************************************************
    * STEP 4.b calculates 15 values for the breast cancer death rate with therapy in each of the
15 years after diagnosis by multiplying the 15-year Kaplan-Meier cancer death rate, L,
(calculated in step 1) by the "risk-reduction" value computed above, and by the fraction of the
total lethality which can be expected in each year(the 15-part step function described in step
2.a that captures the breast carcinoma hazard function).
    *********************************************************************/
        cumulative_cancer_death = 0;
        lethality_survived = 0;
       for (i=1; i<=15; i++) {
           // calculates cancer death rate by multiplying 15yr KM cancer death rate by expected
BRCA yearly lethality
          //cancer-specific hazard = chance of cancer death / cancer-specific survival to that
point
           cancer_death_hazard[i] = L_cancer_distribution[distribution_index][i-
1]*L_cancer_KM_therapy / (1-cumulative_cancer_death);
           if (document.form.recur_evid[1].checked ==true && years_alive > 0) { // years
survived since diagnosis with no evidence of recurrence
               //Reduce the death distribution in the years immediately following the evidence
of no recurrence
               cancer_death_hazard[i] = cancer_death_hazard[i] / Math.max(1, 3-(i-years_alive));
           }
           cumulative_cancer_death = cumulative_cancer_death +
L_cancer_distribution[distribution_index][i-1] * L_cancer_KM_therapy;


                  if (i > years_alive) {
               L_cancer_KM_cond_therapy =  L_cancer_KM_therapy * (1- lethality_survived) / (1 -
(lethality_survived * L_cancer_KM_therapy));
               L_cancer_death_yearly_therapy[i]=remaining_percentage[i-1] *
cancer_death_hazard[i];
               L_noncancer_prob[i]=nvsr_death_prob_yearly[i+age];

           } else {
               lethality_survived = lethality_survived +
L_cancer_distribution[distribution_index][i-1];
               L_cancer_death_yearly_therapy[i]=0;
               L_noncancer_prob[i]=0;
           }
           // calculates non-BRCA death rate by multiplying the fraction of patients not dying
of cancer by the yearly risk of death due to non-cancer causes for the given age

           L_noncancer_death_yearly_therapy[i]=(remaining_percentage[i-1] -
L_cancer_death_yearly_therapy[i]) *L_noncancer_prob[i];
           //calculates overall death rate by adding breast cancer deaths to non-breast cancer
deaths

L_overall_death_yearly_therapy[i]=L_cancer_death_yearly_therapy[i]+L_noncancer_death_yearly_thera
py[i];
             remaining_percentage[i]=remaining_percentage[i-1]-
L_overall_death_yearly_therapy[i];


       }
    /*********************************************************************
    * STEP 4.c & 4d   Calculate 15 values for the cumulative breast cancer death rate and
cumulative overall death rate in each of the 15 years after diagnosis by summing the respective
yearly risks of cancer death, with therapy, (step 2) from the time of diagnosis.
    *********************************************************************/
        for(i=1;i<=15;i++) {
           L_cancer_death_cumm_therapy[i]=L_cancer_death_cumm_therapy[i-
1]+L_cancer_death_yearly_therapy[i];
           L_noncancer_death_cumm_therapy[i]=L_noncancer_death_cumm_therapy[i-
1]+L_noncancer_death_yearly_therapy[i];
           L_overall_death_cumm_therapy[i]=L_overall_death_cumm_therapy[i-
1]+L_overall_death_yearly_therapy[i];
```

```
        }      //end of lethality summation

    /*********************************************************************
    * STEP 5 Calculates the life expectancy gained from therapy
    *********************************************************************/
    /*********************************************************************
    * STEP 5.a   Calculate the life expectancy for the cancer patient by multiplying the chance
of dying in each of the years 1-15 by the number of years survived to that point.  Then add the
NVSR life expectancy for people 15 years older than the patient's current age, multiplied by the
patients chance of surviving 15 years.
    *********************************************************************************/
        calc_life_expectation_therapy = 0;
        for (i=1; i<=15; i++){
            calc_life_expectation_therapy = calc_life_expectation_therapy +
L_overall_death_yearly_therapy[i] * (i-0.5);
        }
        calc_life_expectation_therapy = calc_life_expectation_therapy + (1 -
L_overall_death_cumm_therapy[15]) * (nvsr_life_expect[age + 15] +15)

    /*********************************************************************
    * STEP 5.b   calculates the life expectancy gained from therapy by subtracting the mean life
expectancy with therapy (step 2.e) from the mean life expectancy for the cancer patient (step 3).
    *********************************************************************************/

        expect_years_life_lost_therapy = nvsr_life_expect[age] - calc_life_expectation_therapy;

        expect_life_saved_years=Math.max(expect_years_life_lost - expect_years_life_lost_therapy,
0);
        expect_life_saved_days=expect_life_saved_years*365.25;

/*****************************
* Throws alert messages if age is 0 or over 100
*****************************/
    alertText = "";
    if (age==0){
       alertText = alertText + "Note: Calculations do not incorporate non-breast-cancer risk.
<br><br> ";
    } else if (age>85){
                alertText = alertText + "Note: Calculations end at age 100 due to the lack of
viable data for people over the age of 100.<br><br>";
    }

/*****************************
* Throws alert messages if tumor size or nodes exceeds values for which we have validated the
calculator
*****************************/
    if (dia>5 || nnum>10) {
       alertText = alertText + "Note: The tumor size and/or number of positive nodes entered
exceeds the values against which the calculator has been validated, 50mm and 10 nodes
respectively. <br><br>";
    }


/*********************************************************************
* STEP 6a Displays results on the website
*********************************************************************/

document.getElementById("death_reduction").firstChild.nodeValue= Math.max(Math.round((1 -
L_cancer_KM_cond_therapy / L_cancer_KM_cond)*100) , 0);
document.getElementById("life_expect").firstChild.nodeValue=Math.round(nvsr_life_expect[age]*10)/
10;
document.getElementById("expect_life_lost").firstChild.nodeValue=Math.round(expect_years_life_los
t*10)/10;
document.getElementById("life_expect_with_cancer").firstChild.nodeValue=Math.round(calc_life_expe
ctation*10)/10;
document.getElementById("expect_saved_years").firstChild.nodeValue=Math.round(expect_life_saved_y
ears*10)/10;
document.getElementById("expect_saved_days").firstChild.nodeValue=Math.round(expect_life_saved_da
ys);
document.getElementById("l_km").firstChild.nodeValue=Math.round(L_cancer_KM_cond_therapy*1000)/10
;
```

```
document.getElementById("l_expected").firstChild.nodeValue=Math.round(L_cancer_death_cumm_therapy
[15]*1000)/10;
document.getElementById("ageText").firstChild.nodeValue=age;
if (years_alive > 0) {
    document.getElementById("yllText").firstChild.nodeValue="The remaining chance of cancer
death";
    document.getElementById("therapyBenefitRow").style.visibility="collapse";
    //document.getElementById("therapyDeathRow").style.visibility="collapse";
} else {
    document.getElementById("yllText").firstChild.nodeValue="Without therapy, cancer";
    document.getElementById("therapyBenefitRow").style.visibility="visible";
    //document.getElementById("therapyDeathRow").style.visibility="visible";
}
/*******************************
* STEP 6b  graphs the risk curves for cancer in the user-specified mode. For the outcome
calculator, the program displays the life expectancy (step 3.a), the life expectancy lost to
cancer (step 3.d), and the 15-year Kaplan-Meier cancer-specific death rate (step 1). For the
treatment calculator, the program displays these values, as well as the risk reduction value from
therapy (step 1) and the life expectancy gained from therapy (step 5.d).
*******************************/
if (includeTherapyCalc) {
   plotGraph(new Array(L_cancer_death_cumm,L_noncancer_death_cumm ,L_overall_death_cumm ,
L_cancer_death_cumm_therapy, L_noncancer_death_cumm_therapy, L_overall_death_cumm_therapy),
document.getElementById('display_options').value, null, true);
} else {
   plotGraph(new Array(L_cancer_death_cumm_therapy,L_noncancer_death_cumm_therapy
,L_overall_death_cumm_therapy), document.getElementById('display_options').value, null, false);
}

/*******************************************************
* STEP 6c  Display staging information
*********************************************************************/
tnm_stage = getTNM_Stage();
document.getElementById("tnm").firstChild.nodeValue= tnm_stage[0];
document.getElementById("stageNum").firstChild.nodeValue = tnm_stage[1];


}//end of run function
```

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