Online Supplement for “Combined DES/SD Model of Breast Cancer Screening for Older Women, II: Screening-and-Treatment Simulation”

JEREMY J. TEJADA¹

*SIMCON Solutions LLC,
5041 Lahoma St., Dallas, TX 75235, USA*

JULIE S. IVY²

RUSSELL E. KING³

JAMES R. WILSON⁴

MATTHEW J. BALLAN⁵

MICHAEL KAY⁶

*Edward P. Fitts Department of Industrial and Systems Engineering,
North Carolina State University,
Campus Box 7906, Raleigh, NC 27695-7906, USA*

KATHLEEN DIEHL⁷

*Department of Surgery, Division of Surgery Oncology,
University of Michigan Health Systems,
1500 East Medical Center Drive, Ann Arbor, MI 48109-5932, USA*

BONNIE C. YANKASKAS⁸

*Departments of Radiology and Epidemiology,
University of North Carolina at Chapel Hill,
107 Deerfield Trail, Chapel Hill, NC 27516-9510, USA*

¹ E-mail: jjtejada@simcon-solutions.com. Telephone: (512) 693-8280.

² Member, Institute of Industrial Engineers. E-mail: jsivy@ncsu.edu. Telephone: (919) 513-1683.

³ Fellow, Institute of Industrial Engineers. E-mail: king@ncsu.edu. Telephone: (919) 515-5186.

⁴ Fellow, Institute of Industrial Engineers, and corresponding author. E-mail: jwilson@ncsu.edu. Telephone: (919) 515-6415.

⁵ E-mail: mjballan@simcon-solutions.com. Telephone: (561) 706-1792.

⁶ Member, Institute of Industrial Engineers. E-mail: kay@ncsu.edu. Telephone: (919) 515-2008.

⁷ E-mail: kdiehl@med.umich.edu. Telephone: (734) 615-4823.

⁸ E-mail: bcy@med.unc.edu. Telephone: (919) 967-7182.

Online Supplement for “Combined DES/SD Model of Breast Cancer Screening for Older Women, II: Screening-and-Treatment Simulation”

This Online Supplement to the main article titled “Combined DES/SD Model of Breast Cancer Screening for Older Women, II: Screening-and-Treatment Simulation” contains more detailed discussions of the screening-and-treatment simulation, including all the equations governing the state variables (levels) and rates (flows) in the SD submodel.

A1. DES Submodel

When the screening-and-treatment simulation is invoked, a user interface is displayed that enables the user to select values for the primary design variables and run-control parameters using option buttons and drop-down menus as detailed in the Online Supplement and on pp. 184–196 of Tejada (2012). Following the user’s specification of the screening policy to be evaluated, women enter the screening-and-treatment simulation exactly as they entered the natural-history simulation. As discussed in Tejada *et al.* (2012), individual attributes and cancer histories associated with women entering the natural-history simulation are stored into a database in the order that those individuals enter the natural-history simulation. In the screening-and-treatment simulation, those individuals are then retrieved from the database in the same order and are reassigned their corresponding attributes and cancer histories so that they enter the screening-and-treatment simulation at the same points in simulated time that they entered the natural-history simulation. As elaborated in Section 4 of this article and in Chapter 4 of Tejada (2012), we perform 10 runs of the screening-and-treatment simulation for each screening policy to be evaluated; and we use the method of common random numbers (Kelton et al., 2010) to sharpen the comparisons between different screening policies. Thus, the same 10 randomly sampled populations used in the natural-history simulation are re-created in the screening-and-treatment simulation. This approach enables us to compute more precise point and confidence interval (CI) estimators for the mean differences in performance between selected screening policies.

After her attributes and breast cancer history are initialized at the time she joins the simulated population in the screening-and-treatment model, each woman enters the screening portion of the DES submodel. The screening submodel implements the selected screening policy, samples the probability of adherence to each screening appointment for each individual, and determines the type of screening, diagnostic, and work-up exams to perform on that individual as required. The method we used to

determine the probability of mammographic detection of breast cancer in the screening submodel is summarized below.

A1.1. Detection as a function of tumor size

The following figure displays the probability that a mammography exam will detect the presence of breast cancer in a woman as a function of tumor size at the time of her exam. For example, the probability of mammographic detection of breast cancer for a woman with a tumor size of 20 mm would be 0.90. For additional information about how tumor size and tumor growth rates were modeled in the simulation, the reader is referred to Tejada (2012).

Fig. 1. Graph of the Probability of Mammographic Detection as a Function of Tumor Size (Fryback *et al.*, 2006)

A1.2. Important variables in the DES submodel

A list and description of important global variables including their names, dimension (if array), type, and their initial values is given in Table 1.

Table 1. Global Variables Initialized at the Beginning of the Simulation Model

Variable Name	Type	Description	Initial
---------------	------	-------------	---------

			Value(s)
65OlderModel	Binary(0,1)	0 if ages 35 and older are considered 1 if ages 65 and older are considered	1
IncludeUSPopAge	Binary(0,1)	0 if BCSC database is used to determine age of initial population 1 if 2000 US Census is used to determine age of initial population	1
PopDist65[5]	Real	Given we are only considering women over 65, these conditional percentages represent the percentage of the population that is 65–70, 70–75, 75–80, 80–85, and 85+	0
PopDistAllAges[11]	Real	Given we are considering all women over 35, these conditional percentages represent the percent of the population that is 35–40, 40–45, 45–50, ..., and 85+	0
AllAgesSampleSize	Integer	Total number of women in the BCSC data set	1,007,660
65OlderSampleSize	Integer	Number of women in the BCSC data set who are at least 65 years old	250,509
WriteData	Binary(0,1)	0 if not writing data to files 1 if writing data to files	1
IncludedDistantEvents	Integer(0,1,2)	0 if not considering stage at diagnosis 1 if using the Michaelson metastasis / regional node model 2 if using the Plevritis stage at diagnosis model	2
SimLength	Integer	Length of the simulation in years	25
SimStartYear	Integer	Year the simulation begins	2012
InitialPopSize	Integer	Number of women in the initial population	20,582
CurrentPopSize	Integer	Number of women in currently in the simulation model	InitialPopSize
DeathsThisYear	Integer	Number of deaths that occurred in current model year	0
TotalDeaths	Integer	Total number of deaths at the end of the current model year	0
GrowthIndex	Integer	Value of 1 for the first year and increased by 1 each year; used as x -value in the linear model ($y=mx+b$) for the population growth percentage (PopGrowthRatePercent)	1
PopGrowthRatePercent	Real	The population growth percentage calculated according to the linear model: $\text{PopGrowthRatePercent} = (0.165) * (\text{GrowthIndex}) - 330.52$	0
NeededPopSize	Integer	The expected number of women that would needed to be added to the population for it to grow according to the linear model	0
GrowthThisYear	Integer	The actual population growth for the current year ~ $\text{Poisson}(\text{NeededPopSize})$	0
NumOfMamms	Integer	The number of mammograms given in the 25-year time horizon	0
SignalCouter	Integer	Specifies the signal number for the 25 signals that are used to ensure the data is written to the output file in the proper order	2012
TumorDensityB	Real	The density of breast cancer tumors (Cells/Cm^3)	238,732,414.6

A1.3. Fitting data for the percentage of digital mammograms

For the period 2001–2009, the BCSC provided data on both the number of mammograms given in a specified year, and the number of digital mammograms given in a specified year, and from this one can easily derive the percentage of digital mammograms for a specified year. Given that data is only available for the period 2001–2009, and our simulation runs through the year 2020, we developed a method for estimating the percentage of digital mammograms for the period 2010–2020. We choose to simply fit a polynomial function to the data, and we explored 2nd – 6th degree polynomials both from a visual perspective, and used R^2 and adjusted R^2 values to evaluate the goodness of fit. The adjusted R^2 values are important, because they remove the bias that is introduced by introducing extra terms. The adjusted R^2 values for 2nd – 6th degree polynomial fits are given in Table 2. Graphs of the fits for 3rd – 5th degree polynomials are presented in Fig. 2, Fig. 3, and Fig. 4 respectively. Upon examination of these figures and the associated adjusted R^2 values, we can see that a 4th degree polynomial function provides the best fit to the data

Table 2. Adjusted R^2 values for Polynomial Fits to Percentage of Digital Mammogram Data

Order	Adjusted R^2
2	0.9865
3	0.9867
4	0.9976
5	0.9964
6	0.9965

Fig. 2. 3rd Degree Polynomial Fit to Percentage of Digital Mammograms

Fig. 3. 4th Degree Polynomial Fit to Percentage of Digital Mammograms

Fig. 4. 5th Degree Polynomial Fit to Percentage of Digital Mammograms

A2. SD Submodel: State Variable Details

Several SD state variables and some new individual characteristics are incorporated into the combined DES/SD model. The following section lists these state variables and individual characteristics, defines the units for each (if necessary), and defines the ranges of values for each. Comprehensive explanations of each of the user specified state variables in the SD submodel are provided first. Screenshots of the corresponding user interfaces displayed when inputting values for each of these variables are provided in the next section. We then expand upon each of the attributes directly and indirectly affecting each woman's adherence to her screening policy. Extensive discussions of these attributes were excluded from the corresponding paper for purposes of brevity and are instead reproduced here. Finally, we expand upon the adjustment factors developed for the intermediate state variable, breast cancer screening technology.

A2.1. SD input levels (4)

$NumOfFacilities(t) \in [5000, 15000]$, expressed as the total number of screening facilities nationwide;

$CapacityOfFacilities(t) \in [12250, 20000]$, the service rate of all the facilities expressed as the total number of mammograms per year;

$PublicAds(t) \in \{1, 2, 3\}$, the overall level of public advertising; and

$BCResearch(t) \in \{1, 2, 3\}$, the overall level of research on breast cancer.

A2.2. Other SD levels (5)

$DistanceToFacilities(t) \in [5, 25]$, the patient's travel distance from home to a screening facility, in miles;

$CongestionAtFacilities(t) \in [0, 100]$, the patient's expected waiting time before being screened, in minutes;

$ScreeningTechnology(t) \in [0, 1]$, the current level of screening technology, where 0="completely ineffective" and 1="perfect";

$TimeToGetResults(t) \in [5, 35]$, the delay between completion of screening and notifying the patient of the results, expressed in days; and

$AppointmentAvailability(t) \in [0, 1]$, the probability that the patient can make an appointment for screening.

A2.3. SD levels linked to individual attributes affecting adherence (3)

$Access(t) \in [0,1]$, the degree to which patients get an appointment and their degree of difficulty in getting there, where 0="almost no access" and 1="excellent access";
 $ScreenProcSat(t) \in [0,1]$, the patient's degree of satisfaction with the screening process, where 0="completely dissatisfied" and 1="completely satisfied"; and
 $PublicAwareness(t) \in [0,1]$, level of public awareness of the importance of breast cancer screening.

A2.4. Input characteristics from individuals from DES submodel (4)

$Age(t) \in [65,110]$, expressed in years;
 $InitialAge \in [65,95]$, expressed in years;
 $BMI \in \{1,2,3,4\}$, expressed as follows: category=1 if patient's BMI ≤ 25 ;
category=2 if patient's BMI $\in (25,30]$; category=3 if patient's BMI $\in (30,35]$;
and category=4 otherwise;
 $HouseSize \in \{0,1,2\}$, expressed as number of other members of the patient's household; and
 $ScreenTechSat(t) \in \{0,1\}$, level of satisfaction with screening technician, where
0="completely unsatisfactory" and 1="completely satisfactory."

A2.5. Individual characteristics directly linked to adherence (5)

$Comorbidity(t) \in \{0,1\}$, indicator of comorbid conditions where 0="no comorbid conditions," and 1="comorbid condition(s) present";
 $MammSat(t) \in \{0,1\}$, indicator of satisfaction with previous mammograms, where
0="dissatisfied" and 1="satisfied";
 $NumOfBarriers(t) \in \{0,1,2\}$, number of perceived barriers to screening;
 $IntentToAdhere(t) \in \{0,1\}$, indicator of patient's intent to adhere to screening, where
0="do not intend to adhere" and 1="do intend to adhere"; and
 $Last2Adherence(t) \in \{0,1,2\}$, number of times patient went to screening out of last two opportunities.

A2.6 Personal penalty factors (5)

The following random variables represent variation among individual women in the weights they place on various factors in determining, for example, their overall satisfaction with previous mammographic experiences, etc, as detailed in Section 4.2.2 below.

$$\text{ScreenTechPen} \sim \text{UNIFORM}(0.25, 1)$$

$$\text{ScreenProcPen} \sim \text{UNIFORM}(0.25, 1)$$

$$\text{ComorbidPen} \sim \text{UNIFORM}(0.25, 1)$$

$$\text{HouseSizePen} \sim \text{UNIFORM}(0.25, 1)$$

$$\text{AccessPen} \sim \text{UNIFORM}(0.25, 1)$$

A2.7 Other factors

The following auxiliary factors are explained in detail in the next sections.

$$\text{NumOfFacilitiesTrend}(t) \in \{-2, -1, 0, 1, 2\};$$

$$\text{CapacityOfFacilitiesTrend}(t) \in \{-2, -1, 0, 1, 2\};$$

$$\text{NumberOfMammograms}(t), \text{ the number of women who got a mammogram in year } t;$$

$$\text{DemandforScreening}(t), \text{ the total demand for mammograms in year } t;$$

$$\text{DemandPerFacility}(t), \text{ the average hourly demand per facility for mammograms in year } t;$$

$$\text{ArrivalRatePerFacility}(t) = \lambda(t), \text{ the average number of women needing a mammogram who arrive per hour at each facility during business hours in year } t;$$

$$\text{ServiceRatePerFacility}(t), \text{ the average number of mammograms that can potentially be completed per hour at each facility during business hours in year } t;$$

$$\text{MeanServiceTimePerFacility}(t) = E[S], \text{ the expected value of the duration (in hours) of each mammogram performed in year } t;$$

$$\text{VarianceServiceTime}(t) = \text{Var}[S], \text{ the variance of the duration of each mammogram (expressed in hr}^2\text{) performed in year } t;$$

$$\text{FalsePosPercent}(t) \in [0, 1], \text{ the fraction of mammograms given in year } t \text{ that can be expected to yield a false positive};$$

$$\text{FalsePosPercentAdj}(t) \in [0, 1], \text{ FalsePosPercent}(t) \text{ adjusted for changes in screening technology in year } t;$$

$FalseNegPercent(t) \in [0,1]$, the fraction of mammograms performed in year t that can be expected to yield a false negative;

$FalseNegPercentAdj(t) \in [0,1]$, $FalseNegPercent(t)$ adjusted for changes in screening technologies in year t ;

$TreatmentSurvivalAdj(t) \in [0,1.8]$, the number of years until breast cancer death for women who are treated, adjusted for the level of technology in year t ;

$StageFactor \in \{1, 2, 3\}$, represents the stage of breast cancer at diagnosis and is used to determine $TreatmentSurvivalAdj(t)$ for a woman in a given stage;

A2.8. User specified state variables

Four of the state variables in the SD submodel are user inputs. The user can adjust these state variables through the user interface and control them to an even greater extent via model logic. The number of screening facilities, $NumOfFacilities(t)$, is fixed for $t \in \{2001, \dots, 2011\}$; but the user can control the trend in the number of facilities (increasing, slightly increasing, constant, slightly decreasing, or decreasing) over the period 2012–2020. Similarly, the user can control future trends in the capacity of these screening facilities, $CapacityOfFacilities(t)$. The state variable for advertising for breast cancer screening, $PublicAds(t)$, can be assigned by the user for every $t \in \{2001, \dots, 2020\}$. The state variable for breast cancer research, $BCResearch(t)$, can also be assigned by the user for every $t \in \{2001, \dots, 2020\}$.

A2.8.1. Number of screening facilities trend

The number of breast cancer screening facilities present in the US, $NumOfFacilities(t)$, directly impacts the average distance each woman must travel to get screened as well as the congestion at each facility. As the number of facilities decreases, the distance to each facility will increase and the congestion will increase (unless the capacity of each facility increases). Breast cancer screening facilities must register with the FDA, and we were able to obtain data on the approximate number of facilities in 2001 from the BCSC and in 2012 by querying the FDA website. There were approximately 10,125 registered facilities in 2001 and there were approximately 8,444 registered at the start of 2012. However, the number of women in the US population is increasing, the average age is increasing, and public awareness regarding the importance of mammography has increased since 2001. All these facts lead to the conclusion that the demand has likely been increasing, while the number of facilities has been decreasing. Our breast cancer experts have suggested that this phenomenon has been caused by smaller facilities shutting down and

joining other facilities, and the average capacity of registered facilities has increased, thus allowing the country's screening capacity to keep up with demand.

We assumed the number of facilities decreased linearly from 2001 to 2012, and the user does not have control over the number of facilities during this time period. However, beginning in 2013, the user is allowed to choose one of the following five settings to govern how the number of facilities will change from 2013 to 2020: decreasing, slightly decreasing, constant (default), slightly increasing, and increasing. The state-variable $NumOfFacilitiesTrend(t)$ is defined according to Equation (1):

$$NumOfFacilitiesTrend(t) \equiv \begin{cases} -2, & \text{if decreasing,} \\ -1, & \text{if slightly decreasing,} \\ 0, & \text{if constant (default),} \\ 1, & \text{if slightly increasing,} \\ 2, & \text{if increasing.} \end{cases} \quad (1)$$

For the period 2013 to 2020, the number of facilities at time t can be computed as a function of the number of facilities at time $t-1$ and the trend in the number of facilities at time $t-1$ according to Equation (2):

$$NumOfFacilities(t) = NumOfFacilities(t-1) + 50 * NumOfFacilitiesTrend(t-1). \quad (2)$$

Based on the data, it would be reasonable to believe either -1 or 0 will reflect the actual future trend, but it may be interesting to explore how other options affect the results. The default value of $NumOfFacilitiesTrend(t)$ is 0 , that is, the number of facilities will remain constant during the period 2013–2020. However, the default value for the state-variable $CapacityOfFacilitiesTrend(t)$ is 1 , that is, the capacity of screening facilities is slightly increasing during this period. It is known that demand for screening will increase, so we naturally assumed that the overall capacity for screening would at least slightly increase during the period 2013–2020.

A2.8.2. Average capacity of screening facilities trend

The average capacity of screening facilities, $CapacityOfFacilities(t)$, is defined in terms of the average number of mammograms per year that facilities can provide; and this can easily be translated into an hourly arrival rate with some basic assumptions. Demand has likely increased with the size and age of the US female population, and the number of facilities has decreased. Thus, the average capacity of screening facilities must be at least slightly increasing in order to maintain a reasonable level of service.

We assumed the average capacity of screening facilities increased from 2001–2012, and the user does not have control over the number of facilities during this time period. However beginning in 2013, the user is allowed to choose one of the following five settings to govern how the average capacity of facilities will change from 2013–2020: decreasing, slightly decreasing, constant (default), slightly increasing, and increasing. The state-variable $CapacityOfFacilitiesTrend(t)$ is defined according to Equation (3):

$$CapacityOfFacilitiesTrend(t) \equiv \begin{cases} -2, & \text{if decreasing,} \\ -1, & \text{if slightly decreasing,} \\ 0, & \text{if constant,} \\ 1, & \text{if slightly increasing, (default)} \\ 2, & \text{if increasing.} \end{cases} \quad (3)$$

For the period 2013–2020, the capacity of facilities at time t can be computed as a function of the capacity of facilities at time $t - 1$ and the trend in the capacity of facilities at time $t - 1$ according to Equation (4),

$$CapacityOfFacilities(t) = CapacityOfFacilities(t - 1) + 0.1 * CapacityOfFacilitiesTrend(t - 1). \quad (4)$$

Based on the assumed past trend, it would be reasonable to believe that a value of either 1 or 2 in Equation (3) will reflect the actual future trend, but it may be interesting to explore how other options affect the results. The default value of $CapacityOfFacilitiesTrend(t)$ is 1, that is, the capacity of facilities will slightly increase during the period 2013–2020.

A2.8.3. Public advertising for breast cancer screening

Public advertisements for breast cancer screening influences breast cancer awareness in the population. The value of the SD state variable public advertising for breast cancer can be set by the user and can be constant or have some criterion for changing. We define the value of this state variable, $PublicAds(t)$, as either low, medium, or high according to Equation (5):

$$PublicAds(t) \equiv \begin{cases} 1, & \text{if low,} \\ 2, & \text{if medium (default),} \\ 3, & \text{if high.} \end{cases} \quad (5)$$

Currently, the value of the public advertising state variable is set to medium for both the past time periods and the future. However, the user does have control over the values for both of these periods. So the impact of increasing or decreasing the value of the public advertising state variable can be observed for the given time period by changing the input values for this state variable. It is difficult to quantify the value of public advertising. One might think of using the number of local TV/radio ads or the total amount of money raised through charitable organizations, but it is difficult to find data on these quantities. Thus, we chose to go with a more subjective low-medium-high scale for this input.

A2.8.4. Breast cancer research

Breast cancer research also influences breast cancer awareness in the population. Like the public advertising state variable, the value of the breast cancer research state variable can be set by the user and can be constant or have some criterion for changing. We define the value of the breast cancer research state variable, $BCResearch(t)$, as either low, medium, or high according to Equation (6):

$$BCResearch(t) \equiv \begin{cases} 1, & \text{if low,} \\ 2, & \text{if medium (default),} \\ 3, & \text{if high.} \end{cases} \quad (6)$$

Currently, the value of the breast cancer research state variable is set to medium for both the past time periods and the future. However, the user does have control over the values for both of these periods. So the impact of increasing or decreasing the value of the breast cancer research state variable can be observed for the given time period by changing the input values for this variable. It is difficult to quantify breast cancer research. One might think of using the number of papers published or estimating the total research expenditures on breast cancer research, but it is difficult to find data on these quantities, so again we chose to go with a more subjective low-medium-high scale for this input.

A2.9. Attributes indirectly affecting adherence

A2.9.1. Age

The minimum age in the model is 65, and the maximum possible age is 110, a function of the breast cancer-adjusted life tables. The maximum initial age was limited to 95, a function of the BCSC risk-estimation data set.

A2.9.2. Body mass index (*BMI*)

The variable *BMI* is assigned at the beginning of the natural history model and is used in the Barlow risk model. However, the risk model allows for the possibility of *BMI* being unknown; but *BMI* is needed to determine comorbidity (see the next section). For women who have unknown *BMI*, the BCSC data from 2009, the latest available year, is used to assign *BMI*, which is defined in the following way:

$$BMI \equiv \begin{cases} 1, & \text{if the individual's body mass index} \leq 25, \\ 2, & \text{if } 25 < \text{the individual's body mass index} \leq 30, \\ 3, & \text{if } 30 < \text{the individual's body mass index} \leq 35, \\ 4, & \text{if the individual's body mass index} > 35. \end{cases} \quad (7)$$

The BCSC data yield the following probability distribution of *BMI* for a randomly sampled individual in the population of women of age 65+:

$$\Pr\{\text{Value of } BMI \text{ assigned} = j\} = \begin{cases} 0.480, & \text{if } j = 1, \\ 0.281, & \text{if } j = 2, \\ 0.140, & \text{if } j = 3, \\ 0.099, & \text{if } j = 4. \end{cases} \quad (8)$$

Based on the BCSC data for the distribution of body mass index in the population of older US women, we see that the assigned values of 1, 2, 3, and 4 for the attribute *BMI* for an individual woman correspond respectively to the following ranges of the individual's body mass index: [0, 25]; (25, 30]; (30, 35]; and (35, ∞).

A2.9.3. Number of other members in household

The number of other members in each woman's household, *HouseSize*, is assigned upon entering the screening-and-treatment model. It is defined as follows:

$$HouseSize \equiv \begin{cases} 0, & \text{if no other members in household,} \\ 1, & \text{if one other member in household,} \\ 2, & \text{if two or more other members in household.} \end{cases} \quad (9)$$

For a randomly sampled individual in the population of older US women, *HouseSize* is assigned according to the following distribution using data from Gierisch, et al. (2010):

$$\Pr\{HouseSize \text{ for an individual} = k\} = \begin{cases} 0.109, & \text{if } k = 0, \\ 0.527, & \text{if } k = 1, \\ 0.364, & \text{if } k = 2. \end{cases} \quad (10)$$

A2.9.4. Satisfaction with screening technician

The attribute $ScreenTechSat(t)$ is assigned to each woman following screening appointments. Its value represents a woman's satisfaction with the screening technician during her most recent screening appointment. The screening technician handles women's breasts, which can be uncomfortable for some women. Furthermore, women vary in their willingness to engage in conversation during screening and it may be difficult for the technician to gauge this, further leading to discomfort. This factor is an attempt to take into account these types of human interactions that take place during screening exams. According to discussions with several women and breast cancer experts, screening technicians are not typically the same for all screening appointments. Thus, the uniform distribution on the unit interval $[0, 1]$ was used to assign values to this attribute, where one corresponds to the highest level of satisfaction and zero corresponds to the lowest.

A2.10. Attributes directly affecting adherence

A2.10.1. Comorbidity

The comorbidity attribute is defined in Equation (11) below. When each woman enters the model, there is a probability that she already has comorbidities present. If comorbidities are present, then it is assumed that they are not cured and persist for the duration of the woman's life. For women without comorbidities, each year there is some probability that comorbidities will become present. To describe this process, we use a two-state Markov chain as defined by Equation (12), with an initial distribution defined by Equation (13):

$$Comorbidity(t) \equiv \begin{cases} 0, & \text{if comorbid condition(s) are not present} \\ 1, & \text{if comorbid condition(s) are present} \end{cases} \quad (11)$$

where: (i) the 2×2 matrix $\mathbf{P}_{co}$ of one-step transition probabilities with (i, j) element

$\Pr\{Comorbidity(t+1) = j \mid Comorbidity(t) = i\}$ has the form

$$\mathbf{P}_{co} = \begin{matrix} & \begin{matrix} 0 & 1 \end{matrix} \\ \begin{matrix} 0 \\ 1 \end{matrix} & \begin{bmatrix} 1 - P_{co}(t) & P_{co}(t) \\ 0 & 1 \end{bmatrix} \end{matrix}, \quad (12)$$

and the variable $P_{co}(t)$ is given in Table 3 as a function of age and body-mass index; and (ii) the 2×1 vector $\boldsymbol{\pi}_{co}$ of initial probabilities with the j^{th} element $\Pr\{Comorbidity(0) = j\}$ has the form

$$\pi_{CO} = \begin{bmatrix} 0 & 1 \\ 1 - \pi_{CO} & \pi_{CO} \end{bmatrix}, \quad (13)$$

and the variable π_{CO} is also given in Table 3 as a function of age and body-mass index. The relevant state transition probabilities and initial state probability distribution for each woman are a function of age and body mass index (BMI). Table 3 describes the relationship between age, BMI, and the two relevant probabilities. Piecewise linear functions are used to compute the probabilities not explicitly stated in Table 3.

Table 3. Relationship Between Comorbidity, Age, and BMI

Age/BMI	BMI = 1		BMI = 2		BMI = 3		BMI = 4	
Age	π_{CO}	$P_{CO}(t)$	π_{CO}	$P_{CO}(t)$	π_{CO}	$P_{CO}(t)$	π_{CO}	$P_{CO}(t)$
65	.15	0.0100	.20	0.0133	.25	0.0167	.30	0.0200
85	.35	0.0200	.40	0.0267	.45	0.0333	.50	0.0400
95	.45	0.0300	.45	0.0400	.55	0.0500	.60	0.0600
100	-	0.0500	-	0.0667	-	0.0833	-	0.1000
110	-	0.1000	-	0.1333	-	0.1666	-	0.2000

For each woman in the sample, her associated Markov chain governs changes in her attribute $Comorbidity(t)$. Her age will increase over time, but her *BMI* category will stay the same. The probability $P_{CO}(t)$ of acquiring comorbid conditions at time t increases with age and *BMI*.

A2.10.2. Satisfaction with mammography

When a woman enters the model, an initial distribution, π_{SAT} , will be used to determine her satisfaction with previous mammographic experiences. This distribution is given in Equation (15). The probabilities were derived from data in Gierisch *et al.* (2010).

$$MammSat(t) \equiv \begin{cases} 0, & \text{if somewhat satisfied, dissatisfied, or very dissatisfied,} \\ 1, & \text{if satisfied or very satisfied,} \end{cases} \quad (14)$$

$$\pi_{SAT} = \begin{bmatrix} 0 & 1 & 0 & 1 \\ 1 - \pi_{SAT} & \pi_{SAT} \end{bmatrix} = \begin{bmatrix} 0.111 & 0.889 \end{bmatrix}. \quad (15)$$

After each woman attends her first screening, her probability of being satisfied with the overall screening experience, $P_{SAT}(t)$, is a function of her experience with the technician on that visit and her satisfaction

with the screening process. Each time a woman goes for screening, a value of $ScreenTechSat(t)$ is sampled from the uniform distribution on the unit interval $[0, 1]$.

It is important to account for the fact that individual women may be heavily influenced by some factors and slightly influenced by others, and this may vary greatly from woman to woman. To account for this, two personal penalty factors, $ScreenTechPen$ and $ScreenProcPen$, are used as weights that describe how much emphasis each individual woman places on that factor. These penalty factors are both sampled from the uniform distribution with minimum 0.25 and maximum 1. Finally, the probability of being satisfied with the overall screening experience for each woman can be computed using Equation (16):

$$P_{SAT}(t) = 1 - (ScreenTechPen) * (1 - ScreenTechSat(t)) * (0.5) - (ScreenProcPen) * (1 - ScreenProcSat(t)) * (0.5), \quad (16)$$

$$MammSat(t) = \begin{cases} 0, & \text{with probability } 1 - P_{SAT}(t), \\ 1, & \text{with probability } P_{SAT}(t). \end{cases} \quad (17)$$

A2.10.3. Perceived number of barriers to screening

The number of perceived barriers to screening is defined in Equation (18).

$$NumofBarriers(t) \equiv \begin{cases} 0, & \text{if the woman has 0 perceived barriers,} \\ 1, & \text{if the woman has 1 perceived barrier,} \\ 2, & \text{if the woman has 2+ perceived barriers.} \end{cases} \quad (18)$$

We consider three possible barriers: health status, the number of other members in the household, and access to screening; weighted according to the penalty factors $ComorbidPen$, $HouseSizePen$, and $AccessPen$ respectively, to account for the fact that some women may be influenced by some of these factors more than others. Each penalty factor was sampled from the uniform distribution with minimum 0.25 and maximum 1. The perceived number of barriers to screening for each woman can be computed according to Equation (19). This is translated into the three states $\{0, 1, 2\}$ using the established thresholds in Equation (20):

$$NumofBarriers(t) = (ComorbidPen) * (Comorbidity(t) == 1) + (HouseSizePen) * (HouseSize == 0)(1) + (HouseSizePen) * (HouseSize == 1)(0.5) + (AccessPen) * (1 - Access(t)), \quad (19)$$

where

$$NumofBarriers(t) = \begin{cases} 0, & 0 \leq NumofBarriers(t) \leq 0.75, \\ 1, & 0.75 < NumofBarriers(t) \leq 1.75, \\ 2, & NumofBarriers(t) > 1.75. \end{cases} \quad (20)$$

A2.10.4. Intention to adhere to screening policy

Intention to adhere to the screening policy is defined in Equation (21). Upon entering the simulation model, an initial distribution, π_{INT} , will be used to determine each woman's intention to adhere to the screening policy. This distribution is given below. The probabilities were derived from data in Gierisch *et al.* (2010).

$$IntentToAdhere(t) = \begin{cases} 0, & \text{if woman does not intend to adhere,} \\ 1, & \text{if woman intends to adhere,} \end{cases} \quad (21)$$

$$\pi_{INT} = \begin{bmatrix} 0 & 1 & 0 & 1 \\ 1 - \pi_{INT} & \pi_{INT} \end{bmatrix} = \begin{bmatrix} 0.082 & 0.918 \end{bmatrix}. \quad (22)$$

After each woman attends her first screening, the probability that she intends to adhere to the screening policy, $P_{INT}(t)$, is a function of her screening experience satisfaction, her perception of the number of barriers to screening, and public awareness of breast cancer. The intent to adhere for each woman is computed according to Equations (23) and (24):

$$P_{INT}(t) = \frac{MammSat(t) + (3 - NumOfBarriers(t)) + PublicAwareness(t)}{5}, \quad (23)$$

$$IntentToAdhere(t) = \begin{cases} 0, & \text{with probability } 1 - P_{INT}(t), \\ 1, & \text{with probability } P_{INT}(t). \end{cases} \quad (24)$$

A2.10.5. Number of times adherent to screening policy

Each individual woman is assigned the attribute $Last2Adherence(t)$, which indicates how many screening appointments she actually attended out of the last two suggested by her screening policy. Possible values are zero, one, or two; and the definition is given in Equation (25):

$$Last2Adherence(t) = \begin{cases} 0, & \text{if she adhered 0 times out of the last 2 opportunities,} \\ 1, & \text{if she adhered 1 times out of the last 2 opportunities,} \\ 2, & \text{if she adhered 2 times out of the last 2 opportunities.} \end{cases} \quad (25)$$

A2.11. Intermediate state variables

State variables that are not inputs specified by the user and are not directly linked to adherence are considered to be intermediate state variables. They may be functions of user inputs or other intermediate state variables. In turn, they may influence hybrid state variables that alter DES logic, or they may influence primary state variables that directly affect adherence. The average distance to a screening facility is a function of the number of facilities present in the United States. The average level of congestion at screening facilities is a function of the demand for screening, the number of facilities, and the average capacity of those facilities. The state variable for breast cancer screening technology is a function of the state variable for breast cancer research, and it directly affects the hybrid state variables for false positives and false negatives in the DES logic through various adjustment factors. The average time to get results, in days, is a function of the state variable for technology and the average level of congestion. Finally, appointment availability is a function of the congestion at screening facilities. Note that all of the aforementioned intermediate state variables are discussed in the corresponding article, “Combined DES/SD Model of Breast Cancer Screening for Older Women, II: Screening-and-Treatment Simulation,” however only the breast cancer screening technology state variable is included here because its corresponding adjustment factors were excluded from the original article for brevity. The definition of the breast cancer screening technology state variable is reproduced here for context.

A2.11.1. Breast cancer screening technology

The state variable (stock) for screening technology, $ScreeningTechnology(t)$, can take on values between 0 and 1, with 0 representing extremely poor technology, 0.4 representing technology in 2001, and 1 representing the most advanced technology that is achievable by the year 2020.

$$ScreeningTechnology(t) = ScreeningTechnology(t-1) + \frac{BCResearch(t-1)}{100}. \quad (26)$$

Screening technology is assumed to have an impact on the percentage of false negative screening exams and false positive screening and diagnostic exams. We assumed that increases in technology would cause false positives to increase, as seen over the last 10 years, and false negatives to decrease. We also assumed a minimum adjustment of 0% and a maximum adjustment of 5% for both false positives and false negatives. Please refer to Table 4, Table 5, and Table 6 of the corresponding article (Tejada, 2013b) for the base values of $FalsePosPercent$ and $FalseNegPercent$ for both screening and diagnostic exams.

A2.11.1.1. Adjustment factors

We now introduce two adjustment factors, $FalsePosPercentAdj(t)$ and $FalseNegPercentAdj(t)$, that will be used in the DES submodel and define them mathematically:

$$FalsePosPercentAdj(t) \equiv \begin{cases} 0, & \text{if } 0 \leq ScreeningTechnology(t) \leq 0.4, \\ 5/6, & \text{if } 0.4 < ScreeningTechnology(t) \leq 0.5, \\ 10/6, & \text{if } 0.5 < ScreeningTechnology(t) \leq 0.6, \\ 15/6, & \text{if } 0.6 < ScreeningTechnology(t) \leq 0.7, \\ 20/6, & \text{if } 0.7 < ScreeningTechnology(t) \leq 0.8, \\ 25/6, & \text{if } 0.8 < ScreeningTechnology(t) \leq 0.9, \\ 30/6, & \text{if } 0.9 < ScreeningTechnology(t) \leq 1.0, \end{cases} \quad (27)$$

$$FalseNegPercentAdj(t) \equiv \begin{cases} 0, & \text{if } 0 \leq ScreeningTechnology(t) \leq 0.4, \\ -5/6, & \text{if } 0.4 < ScreeningTechnology(t) \leq 0.5, \\ -10/6, & \text{if } 0.5 < ScreeningTechnology(t) \leq 0.6, \\ -15/6, & \text{if } 0.6 < ScreeningTechnology(t) \leq 0.7, \\ -20/6, & \text{if } 0.7 < ScreeningTechnology(t) \leq 0.8, \\ -25/6, & \text{if } 0.8 < ScreeningTechnology(t) \leq 0.9, \\ -30/6, & \text{if } 0.9 < ScreeningTechnology(t) \leq 1.0, \end{cases} \quad (28)$$

$$FalsePosPercent(t) = FalsePosPercent + FalsePosPercentAdj(t), \quad (29)$$

$$FalseNegPercent(t) = FalseNegPercent + FalseNegPercentAdj(t). \quad (30)$$

The state of technology is also assumed to affect survival after treatment. As technology improves, survival after treatment will improve. Thus, we introduce an adjustment factor, $TreatmentSurvivalAdj(t)$, that describes the increase in survival, in years, as a function of the state of technology. We define another adjustment factor, $StageFactor$, which acts as a multiplier for $TreatmentSurvivalAdj(t)$ based on the stage of cancer at diagnosis. There will be less improvement in survival for distant cancer than there would be for localized cancer, so $StageFactor$ is defined as follows:

$$StageFactor \equiv \begin{cases} 1, & \text{if cancer stage at diagnosis is distant,} \\ 2, & \text{if cancer stage at diagnosis is regional,} \\ 3, & \text{if cancer stage at diagnosis is local,} \end{cases} \quad (31)$$

$$TreatmentSurvivalAdj(t) = (ScreeningTechnology(t) - 0.4) * StageFactor. \quad (32)$$

A3. Gierisch Logistic Regression Equation for Nonadherence

Let p_{NAD} denote the probability of nonadherence to the current screening appointment given the values of the categorical variables $\{x_1, x_2, \dots, x_{12}\}$ for a specific woman. In terms of the logit function, $\text{Logit}(x) \equiv \ln[x/(1-x)]$ for $x \in (0,1)$, we exploit the findings of Gierisch *et al.* (2010) to conclude that $\text{Logit}(p_{\text{NAD}})$ has a linear regression on $\{x_1, x_2, \dots, x_{12}\}$,

$$L_{\text{NAD}} = \text{Logit}(p_{\text{NAD}}) = \ln\left(\frac{p_{\text{NAD}}}{1-p_{\text{NAD}}}\right) = \beta_0 + \sum_{j=1}^{12} \beta_j x_j.$$

From Equation (19), we see that

$$p_{\text{NAD}} = \frac{\exp(L_{\text{NAD}})}{1 + \exp(L_{\text{NAD}})} = \frac{1}{1 + \exp(-L_{\text{NAD}})}.$$

Finally we obtain the desired estimate of p_{AD} , the probability of adherence, from the relation $p_{\text{AD}} = 1 - p_{\text{NAD}}$. The estimates of the regression coefficients are given in Table 4 below:

Table 4. Regression Coefficients for Gierisch Logistic Regression Equation

β_0	-1.6852	β_5	0.9783	β_9	0.1398
β_1	0.5188	β_6	-0.1744	β_{10}	0.2624
β_2	0.3577	β_7	-0.3488	β_{11}	0.3716
β_3	0.3001	β_8	0.0000	β_{12}	0.4700
β_4	0.3920				

A4. User Interface

The user interface was designed to make alternative screening policies very easy to implement in the integrated screening model. One of the goals of this research was to ensure that this model, or some form of it, could be understood by clinical experts and government policy makers. Because we own the rights to this model, we are able to share its abilities and results with whomever we please. With the appropriate Arena software (or access to it via a web applet of some sort), the user can simply click the run button, and a series of prompts are displayed that allow the user to choose several options related to the screening policies for both the past and future periods. Default values for the period 2001–2011 are suggested to users, and they are encouraged to choose those values unless they have a valid reason not to. In addition to a user interface for screening policies, one of the forms in the user interface allows the user to select values for the SD input variables, such as the trend in the number of screening facilities. Again default values are suggested, but users are allowed to change these values if they want to explore alternative

scenarios. These prompts were designed in Microsoft Visual Basic, which has an editor embedded within Arena.

Upon clicking the run button the message box in Figure 5 appears with the following statement: "Unless you have communicated with the programmer, please select the default values for all prompts which have a default value. This will ensure the correct inputs are used for the past period 2001–2011, and accurate results are obtained for the future period 2012–2020."

Fig. 5. User Message Box Appearing Before the User Interface Launches

After clicking the OK button, the user is given the form in Figure 6, which gives the user the opportunity to choose the screening interval for the period 2001–2011. The default value is one year, and this default value was chosen using our validation technique presented in [Tejada \(2012\)](#). The only reason for choosing a different value would be if the user wanted to determine what would have happened from 2001–2011 if a different screening policy had been chosen, but this has limited value since the population starts out cancer free, and it takes five to ten years (depending on the statistic examined) for most of the important performance measures to reach steady-state. If the user closes this box without making a selection, the value of the screening interval defaults to one year.

Fig. 6. User Interface Prompt for Screening Interval during the Period 2001-2011

Following a selection by clicking the OK button (or by closing the prompt), the dialogue box in Figure 7 is shown regardless of the previous selection. The user is allowed to choose whether the stopping age is a deterministic value that stops screening for every woman, or is assigned according to a distribution so that each woman has her own individual stopping age. For the period 2001–2011, there was no definitive stopping age, so it makes sense to use a stochastic distribution to assign a stopping age to each woman individually. Thus, stochastic is the default for this prompt, and the user is encouraged to select this value.

Fig. 7. User Interface Prompt for Type of Screening Stopping Age during the Period 2001-2011

If “deterministic” is selected for the type of stopping age, then the prompt in Figure 8 will appear which instructs the user to select a deterministic stopping age. If “stochastic” is chosen as the type of stopping age, then the prompt in Figure 9 will appear which instructs the user to select the mode of a beta distribution for the stopping age with a minimum of 65 and a maximum of 100. The default is a stochastic stopping age with a mode of 75 years; because this was shown to best match the data for that time period (see the next section).

FormStop1A

Select a Deterministic Stopping Age for the Period 2001-2011:

☐ 70
☐ 75
☐ 80
☒ 85
☐ 90
☐ 95
☐ 100

OK

Fig. 8. User Interface Prompt for Deterministic Screening Stopping Age during the Period 2001–2011

FormStop1B

Select the Mode for a Beta Distribution for Screening Stopping Age for the period 2001-2011:
(Min=65, Max=105)

☐ 70
☒ 75 (Default)
☐ 80
☐ 85
☐ 90
☐ 95
☐ 100

OK

Fig. 9. User Interface Prompt for Stochastic Screening Stopping Age during the Period 2001–2011

This concludes the prompts, which govern the screening policy for the period 2001–2011. The next series of prompts governs the screening policy for the period 2012–2020. First, the user is presented with the prompt in Figure 10, which allows the user to select one of three different types of screening policies: interval-based screening, risk-based screening, and factor based screening. The next prompt depends on the type of screening policy selected.

Fig. 10. User Interface Prompt for the Type of Screening Policy during the Period 2001–2011

If the user selects “interval screening” as the policy type, then the same screening interval will be used for all women; and the prompt in Figure 11 will appear, allowing the user to choose the screening interval. After the user selects the screening interval, the stopping age options will appear.

If the user selects “risk-based screening” as the policy type, then the user is allowed to choose different screening intervals for high-risk and low-risk women. The user also chooses the definition of “high-risk.” In the natural history model, we used the Barlow risk model to estimate the one-year risk of being diagnosed with cancer. We recorded individual observations, and then determined the 95th, 90th, 85th, and 80th percentiles of the data, which represent the top 5%, 10%, 15%, and 20% of women in terms of annual risk. Figure 12 appears first, and prompts the user to select a screening interval for high-risk women and whether high risk corresponds to the top 5%, 10%, 15%, and 20% of women in terms of annual risk. Figure 13 then appears and prompts the user to select the screening interval for low-risk women. After the user selects the screening interval for low-risk women, the stopping age options will appear.

If the user selects factor-based screening, then the prompt in Figure 14 will appear. The eleven risk factors are listed along the left side, and there is box next to each factor. Selecting the box next to a factor means the screening intervals that the user selects for different values of that factor will be taken into account when determining the screening interval used for each woman. The user is allowed to select screening intervals of one, two, three, four, or five years for each value of every factor. If the user selects multiple factors, then each woman will be assigned the appropriate screening interval for each factor, and the smallest interval of that group is actually used. This is a rather conservative approach. Another

approach could be to average the numbers and round up and/or round down, and this may be considered in future work. After the user clicks the OK button, the stopping age options will appear.

FormInterval

Select the Screening Interval
for the Period 2012-2020:

☒ 1 Year

☐ 2 Years

☐ 3 Years

☐ 4 Years

☐ 5 Years

☐ No Mammography

OK

Fig. 11. User Interface Prompt for Screening Interval for the Period 2012–2020

Form Risk High

Select the Screening Interval for High Risk women for the Period 2012-2020:

☒ 1 Year
☐ 2 Years
☐ 3 Years
☐ 4 Years
☐ 5 Years
☐ No Mammography

Select the Cutoff Percentage for High Risk (Top X% in terms of 1-Year Risk are High Risk):

Top 5%
 Top 10%
 Top 15%
 Top 20%

OK

Fig. 12. User Interface Prompt for Screening Interval for High Risk Women for the Period 2012–2020

FormRiskLow

Select the Screening Interval for Low Risk women for the Period 2012-2020:

☒ 1 Year
☐ 2 Years
☐ 3 Years
☐ 4 Years
☐ 5 Years
☐ No Mammography

OK

Fig. 13. User Interface Prompt for Screening Interval for Low Risk Women for the Period 2012–2020

FormFactorBased

Please Select The Factors on Which the Screening Interval Should be Based (You must choose at least 1):

Note: If you select multiple factors, each woman will be assigned a screening interval for each factor. The minimum of those screening intervals will be used.

Example: Assume the screening interval for women 65-69 is 2 years and for white women it is every year. Then a 68 year old white woman would have a screening interval of 1 year (The minimum of every 1 and every 2 years).

☒ Age	65-69 1 Year	70-74 1 Year	75-79 1 Year	80+ 1 Year		
☐ Ethnicity	Hispanic 1 Year	Non-Hispanic 1 Year	Unknown 1 Year			
☐ Race	White 1 Year	Asian 1 Year	Black 1 Year	Native American 1 Year	Other 1 Year	Unknown 1 Year
☐ BI-RADS Breast Density	1 - Mostly Fat 1 Year	2 - Scattered Densities 1 Year	3 - Heterogenously Dense 1 Year	4 - Extremely Dense 1 Year	Unknown 1 Year	1 Year 2 Years 3 Years 4 Years 5 Years No Screening
☐ BMI (kg/m^2)	<25 1 Year	25-30 1 Year	30-35 1 Year	35+ 1 Year	Unknown 1 Year	
☐ Age at First Birth	<30 1 Year	30+ 1 Year	No Children 1 Year	Unknown 1 Year		
☐ # of First Degree Relatives with Breast Cancer	0 1 Year	1 1 Year	2+ 1 Year	Unknown 1 Year		
☐ Hormone Therapy Use	Yes 1 Year	No 1 Year	Unknown 1 Year			
☐ Menopause	Natural 1 Year	Surgical 1 Year	Unknown 1 Year			
☐ Result of Last Mammogram	Negative 1 Year	Positive 1 Year	Unknown 1 Year			
☐ Previous Breast Procedure	Yes 1 Year	No 1 Year	Unknown 1 Year			

OK

Fig. 14. User Interface Prompt for Factor-Based Screening Intervals for the Period 2012–2020

The prompts for the type of stopping age (deterministic or stochastic) and then the appropriate prompts that follow are the same for the period 2012–2020 as they were for the period 2001–2011. The prompt in Figure 15 is shown first, prompting the user to select either a deterministic or stochastic stopping age. A stochastic stopping age was appropriate for the past when there was no actual policy; but for future periods, we would like to set a strict cutoff age at which people are no longer screened. Thus a deterministic stopping age is the default for the period 2012–2020. If the user selects a deterministic stopping age, then the prompt in Figure 16 appears and allows the user to select a deterministic stopping age; and if the user selects a stochastic stopping age, then the prompt in Figure 17 appears and allows the user to select the mode of a Beta distribution for the stopping age.

Form Stop 2

Deterministic or Stochastic
(Beta Distributed) Screening
Stopping Ages for the Period
2012-2020:

☒ Deterministic (Default)

☐ Stochastic

OK

Fig. 15. User Interface Prompt for Type of Screening Stopping Age for the Period 2011-2020

FormStop2A

Select a Deterministic
Stopping Age for the
Period 2012-2020:

☐ 70

☐ 75

☐ 80

☒ 85

☐ 90

☐ 95

☐ 100

OK

Fig. 16. User Interface Prompt for Deterministic Screening Stopping Age for the Period 2012–2020

FormStop2B

Select the Mode for a Beta Distribution for Screening Stopping Age for the period 2011-2020:
(Min=65, Max=105)

☐ 70
☐ 75
☐ 80
☒ 85
☐ 90
☐ 95
☐ 100

OK

Fig. 17. User Interface Prompt for Stochastic Screening Stopping Age for the Period 2012–2020

After the user selects a stopping age or mode for the stopping age and clicks the OK button, the message box in Figure 18 will appear with the following text: "Unless you have communicated with the programmer, please select default values for the Breast Cancer Research and Advertising for the period 2001–2011."

Arena

Unless you have communicated with the programmer, please select default values for both Breast Cancer Research and Advertising for the period 2001-2011.

OK

Fig. 18. User Message Box Appearing Before SD Input Prompt

After the user clicks the OK button on the message box, the final prompt in Figure 19 appears, allowing the user to select the inputs for the SD submodel. The user is allowed to select the trend in the number of breast cancer screening facilities and the trend in the capacity of those facilities. The user is also allowed to define the value of the public advertising state variable and the value of the breast cancer research state variable for the periods 2001–2011 and 2012–2020 separately. After the user clicks the OK button on this form, the model executes using the input values selected by the user. Extensive output reports are

generated, with results for each of the 10 populations individually, and another report is generated that aggregates those results into 95% confidence intervals.

FormSDLevels

Select the Level of Breast Cancer Research for the Periods 2001-2011 and 2012-2020:

2001-2011 2012-2020

2 - Med 2 - Med

Select the Trend in the Number of Breast Cancer Screening Facilities for the Period 2012-2020:

0 Constant

Select the Level of Breast Cancer Public Advertising for the Periods 2001-2011 and 2012-2020:

2001-2011 2012-2020

2 - Med 2 - Med

Select the Trend in the Capacity of Breast Cancer Screening Facilities for the Period 2012-2020:

1 Slightly Increasing

OK

Fig. 19. User Interface Prompt for SD Input Levels

A5. Costing Submodel: Distributions Fitted to Costing Data

The costing submodel keeps track of all of the costs within the integrated screening model. There are four major types of costs: the cost of screening exams, the cost of diagnostic exams, the cost of work-up exams, and the cost of treatment. These costs are added up and used to compute the cost-effectiveness of each alternative screening policy. Our costing data is derived from two sources. The primary source is the Medicare reimbursement database (US Department of Health and Human Services, 2012), which gives the costs of many procedures according to geographic location. Inputting these costs to the **Stat::Fit** distribution-fitting software (Geer Mountain Software Corporation, 2012), we obtained adequate fits for each of the available data sets. For procedures with no available data, we used the costs listed in Tosteson *et al.* (2008).

A5.1. Distribution for cost of film screening mammogram

- Best Distribution: Lognormal
- Lognormal Distribution Parameters: $\mu = 2.34$, $\sigma = 0.618$, $Min (Offset) = 71.0$
- Moments of the Fitted Lognormal Distribution
 - $\mu = 83.6$, $\sigma^2 = 73.4$, $\gamma_1 = 2.36$, $\gamma_2 = 11.3$
- Moments of the Data
 - $\mu = 83.3$, $\sigma^2 = 51.7$, $\gamma_1 = 1.29$, $\gamma_2 = 0.81$
- Anderson-Darling p-value = 0.0855
- Kolmogorov Smirnov p-value = 0.126

Fig. 20. Cost of Film Screening Mammogram Fitted Lognormal CDF vs. Empirical CDF

Fig. 21. Cost of Film Screening Mammogram Fitted Lognormal PDF vs. Empirical PDF

Fig. 22. Cost of Film Screening Mammogram P-P Plot of Lognormal Fit

A5.2. Distribution for cost of digital screening mammogram

- Best Distribution: Lognormal
- Lognormal Distribution Parameters: $\mu = 2.97$, $\sigma = 0.678$, $\text{Min (Offset)} = 121.0$
- Moments of the Fitted Lognormal Distribution
 - $\mu = 146.0$, $\sigma^2 = 349.7$, $\gamma_1 = 2.74$, $\gamma_2 = 15.8$
- Moments of the Data
 - $\mu = 144.37$, $\sigma^2 = 199.5$, $\gamma_1 = 1.35$, $\gamma_2 = 1.09$
- Anderson-Darling p-value = 0.0529
- Kolmogorov Smirnov p-value = 0.077

Fig. 23. Cost of Digital Screening Mammogram Fitted Lognormal CDF vs. Empirical CDF

Fig. 24. Cost of Digital Screening Mammogram Fitted Lognormal PDF vs. Empirical PDF

Fig. 25. Cost of Digital Screening Mammogram P-P Plot of Lognormal Fit

A.5.3. Distribution for cost of film diagnostic mammogram

- Best Distribution: Lognormal
- Lognormal Distribution Parameters: $\mu = 2.49$, $\sigma = 0.548$, $\text{Min (Offset)} = 75.0$
- Moments of the Fitted Lognormal Distribution
 - $\mu = 89.0$, $\sigma^2 = 68.72$, $\gamma_1 = 1.98$, $\gamma_2 = 7.72$
- Moments of the Data
 - $\mu = 88.9$, $\sigma^2 = 61.16$, $\gamma_1 = 1.29$, $\gamma_2 = 0.85$
- Anderson-Darling p-value = 0.115
- Kolmogorov Smirnov p-value = 0.0945

Fig. 26. Cost of Film Diagnostic Mammogram Fitted Lognormal CDF vs. Empirical CDF

Fig. 27. Cost of Film Diagnostic Mammogram Fitted Lognormal PDF vs. Empirical PDF

Fig. 28. Cost of Film Diagnostic Mammogram P-P Plot of Lognormal Fit

A.5.4. Distribution for cost of digital diagnostic mammogram

- Best Distribution: Lognormal
- Lognormal Distribution Parameters: $\mu = 2.96$, $\sigma = 0.584$, $Min (Offset) = 114.0$
- Moments of the Fitted Lognormal Distribution
 - $\mu = 137.0$, $\sigma^2 = 213.2$, $\gamma_1 = 2.17$, $\gamma_2 = 9.40$
- Moments of the Data
 - $\mu = 136.6$, $\sigma^2 = 175.4$, $\gamma_1 = 1.35$, $\gamma_2 = 1.07$
- Anderson-Darling p-value = 0.124
- Kolmogorov Smirnov p-value = 0.201

Fig. 29. Cost of Digital Diagnostic Mammogram Fitted Lognormal CDF vs. Empirical CDF

Fig. 30. Cost of Digital Diagnostic Mammogram Fitted Lognormal PDF vs. Empirical PDF

Fig. 31. Cost of Digital Diagnostic Mammogram P-P Plot of Lognormal Fit

A.5.5. Distribution for cost of diagnostic ultrasound

- Best Distribution: Lognormal
- Lognormal Distribution Parameters: $\mu = 2.62$, $\sigma = 0.62$, $Min (Offset) = 83.0$
- Moments of the Fitted Lognormal Distribution
 - $\mu = 99.6$, $\sigma^2 = 130.0$, $\gamma_1 = 2.37$, $\gamma_2 = 11.5$
- Moments of the Data
 - $\mu = 99.2$, $\sigma^2 = 89.8$, $\gamma_1 = 1.31$, $\gamma_2 = 0.97$
- Anderson-Darling p-value = 0.0922
- Kolmogorov Smirnov p-value = 0.155

Fig. 32. Cost of Diagnostic Ultrasound Fitted Lognormal CDF vs. Empirical CDF

Fig. 33. Cost of Diagnostic Ultrasound Fitted Lognormal PDF vs. Empirical PDF

Fig. 34. Cost of Diagnostic Ultrasound P-P Plot of Lognormal Fit

A.5.6. Distribution for cost of core needle biopsy (ultrasound guided)

- Best Distribution: Pearson 6
- Pearson 6 Distribution Parameters: $\beta = 4872.7$, $p = 3.04$, $q = 115.4$, $\text{Min (Offset)} = 706.0$
- Moments of the Fitted Pearson 6 Distribution
 - $\mu = 836.0$, $\sigma^2 = 5715.4$, $\gamma_1 = 1.21$, $\gamma_2 = 2.26$
- Moments of the Data
 - $\mu = 839.4$, $\sigma^2 = 6212.6$, $\gamma_1 = 1.29$, $\gamma_2 = 0.877$
- Anderson-Darling p-value = 0.0510
- Kolmogorov Smirnov p-value = 0.0875

Fig. 35. Cost of CNB (Ultrasound Guided) Fitted Pearson 6 CDF vs. Empirical CDF

Fig. 36. Cost of CNB (Ultrasound Guided) Fitted Pearson 6 PDF vs. Empirical PDF

Fig. 37. Cost of CNB (Ultrasound Guided) P-P Plot of Pearson 6 Fit

A.5.7. Distribution for cost of fine needle aspiration (FNA)

- Best Distribution: Pearson 6
- Pearson 6 Distribution Parameters: $\beta = 739.5$, $p = 3.03$, $q = 29.2$, $\text{Min (Offset)} = 457.0$
- Moments of the Fitted Pearson 6 Distribution
 - $\mu = 536.0$, $\sigma^2 = 2391.2$, $\gamma_1 = 1.40$, $\gamma_2 = 3.31$
- Moments of the Data
 - $\mu = 536.9$, $\sigma^2 = 2325.8$, $\gamma_1 = 1.31$, $\gamma_2 = 0.916$
- Anderson-Darling p-value = 0.0523
- Kolmogorov Smirnov p-value = 0.0827

Fig. 38. Cost of FNA Fitted Pearson 6 CDF vs. Empirical CDF

Fig. 39. Cost of FNA Fitted Pearson 6 PDF vs. Empirical PDF

Fig. 40. Cost of FNA P-P Plot of Pearson 6 Fit

References

- Barlow, W. E. et al., 2006. Prospective Breast Cancer Risk Prediction Model for Women Undergoing Screening Mammography. *Journal of the National Cancer Institute*, 6 September, 98(17), pp. 1204-1214.
- Breast Cancer Surveillance Consortium (BCSC), 2009. *Performance Measures for 1,960,150 Screening Mammography Examinations from 2002 to 2006 by Age*. [Online]
Available at: http://breastscreening.cancer.gov/data/performance/screening/2009/perf_age.html
[Accessed 7 December 2011].
- Fryback, D. G. et al., 2006. The Wisconsin Breast Cancer Epidemiology Model. *Journal of the National Cancer Institute Monographs*, Volume 36, pp. 37-47.
- Geer Mountain Software Corporation, 2012. *Stat::Fit Distribution Fitting Software*. [Online]
Available at: <http://www.geerms.com/>
[Accessed 15 January 2011].
- Gierisch, J. M., Earp, J. A., Brewer, N. T. & Rimer, B. K., 2010. Longitudinal Predictors of Nonadherence to Maintenance of Mammography. *Cancer Epidemiology, Biomarkers & Prevention*, 30 March, Volume 19, pp. 1103-1111.
- Kelton, W.D., Sadowski, R.P. and Swets, N.B. (2010) *Simulation with Arena*, fifth edition. McGraw-Hill, New York, NY.
- Tejada, J. J., 2012. *An Integrated Discrete-Event/System Dynamics Simulation Model of Breast Cancer Screening for Older US Women*. [Online]
Available at: <http://repository.lib.ncsu.edu/ir/bitstream/1840.16/7935/1/etd.pdf>
[Accessed 2012 1 July].
- Tejada, J. J. et al., 2013a. Combined DES/SD Model of Breast Cancer Screening for Older Women, I: Natural History Simulation. *Submitted to IIE Transactions, In Review*.
- Tejada, J. J. et al., 2013b. Combined DES/SD Model of Breast Cancer Screening for Older Women, II: Screening-and-Treatment Simulation. *Submitted to IIE Transactions, In Review*.
- Tejada, J. J. et al., 2013c. Calibration, Validation, and Analysis of a Combined DES/SD Model of Breast Cancer Screening for Older Women. *Working paper*.
- Tosteson, A. N. et al., 2008. Cost-Effectiveness of Digital Mammography Breast Cancer Screening. *Annals of Internal Medicine*, Volume 148, pp. 1-10.
- U.S. Department of Health and Human Services, 2012. *Physician Fee Schedule Search*. [Online]
Available at: <http://www.cms.gov/apps/physician-fee-schedule/search/search-criteria.aspx>
[Accessed 10 May 2011].

Data collection for this work was supported by the National Cancer Institute-funded Breast Cancer Surveillance Consortium co-operative agreement (U01CA63740, U01CA86076, U01CA86082, U01CA63736, U01CA70013, U01CA69976, U01CA63731, U01CA70040). The collection of cancer data used in this study was supported in part by several state public health departments and cancer registries throughout the U.S. For a full description of these sources, please see: <http://www.breastscreening.cancer.gov/work/acknowledgement.html>.