SUPPLEMENTARY MATERIALS

Supplementary Methods

Detailed description of the models

The three models used in this study were developed as part of National Cancer Institute (NCI)'s Cancer Intervention and Surveillance Modeling Network (CISNET) Breast Working Group. The three models include model D (Dana Farber Cancer Institute) [1], model G-E (Georgetown University-Albert Einstein College of Medicine) [2], and model W-H (University of Wisconsin-Madison, Madison, Wisconsin, and Harvard Medical School, Boston, Massachusetts) [3]. The three models were independently developed to evaluate the impact of breast cancer control interventions on long-term trends in breast cancer incidence and mortality in the US. All three models have the ability to follow multiple birth cohorts over time and use common data on other-cause mortality, screening behavior, screening performance, breast cancer subtype distribution, treatment use, and treatment efficacy. The details of model inputs, assumptions, and structure are described extensively at the CISNET website (http://cisnet.cancer.gov/breast/profiles.html) and in prior publications [1-5].

The models start with estimates of overall breast cancer incidence and survival trends in the absence of screening or adjuvant treatment and then overlay data on screening use, screening accuracy, and reductions in mortality associated with adjuvant treatment for each molecular subtype to match observed U.S. population incidence and mortality over time. Models represent natural history of breast cancer using different structures. **Supplementary Table 1** compares the key assumptions used in the models.

As described in the main text, a major strength of CISNET models is that high-quality data are used as common input. Mammography utilization and performance, cancer stage distribution by mode of detection, and ER/HER2 joint distributions among diagnosed cancers are provided by NCI-funded Breast Cancer Surveillance Consortium (BCSC), a collaborative network of six breast imaging registries that have been collecting information from 291 radiology facilities since 1996 [5, 8, 9]. BCSC links imaging data to tumor registry and pathology data [9]. Breast cancer treatment patterns and effectiveness over time are informed by data from National Comprehensive Cancer Network, meta-analyses, and clinical trial results [5, 10-16], and death due to non-breast cancer reasons was estimated from the Centers for Disease Control and Prevention (CDC) Wide-ranging ONline Data for Epidemiologic Research (WONDER) database [17].

Among key common inputs of CISNET models, an important parameter for this analysis is the use of mammography screening over time. The mammography dissemination model was originally developed by Cronin et. al. [18, 19] using data from BCSC and National Health Information Survey and has since been updated to reflect the changes in screening modalities over time in the US [5]. The model captures trends in screening usage patterns including changes in frequency by age over time. We assume all screened women are categorized into three screening groups based on age: annual screeners are women with a mean interval between consecutive screening exams of <1.5 years, biennial screeners are women with a mean interval of 1.5-2.5 years, and irregular screeners are women with a mean interval of >2.5 years. Each screening group's time interval between subsequent mammograms is estimated using stratified survival analyses.

Briefly, model D (Dana-Farber Cancer Institute) is a stochastic model depicting the early detection process of screening and predicts breast cancer mortality as a function of disease natural history, detection, and treatment [1]. Model D is unique among CISNET breast cancer models in that it is entirely analytical. Model D models DCIS by including transitions from normal breast tissue to a pre-clinical undetectable DCIS state, and progression to a screen detectable DCIS or screen detectable invasive cancer state. Furthermore, model D represents recurrence of breast cancer.

Model G-E (Georgetown University-Albert Einstein College of Medicine) is a continuous-time, event-driven microsimulation utilizing a parallel universes approach is implemented in the C++ programming language and is specifically oriented toward estimating the impact of screening and adjuvant treatment innovations that have taken place since 1975 [2]. Life history in the absence of intervention is generated for each woman and the effects of screening and treatment are overlaid on this life history. Natural history is simulated phenomenologically relying on dates, stage, and age of clinical and screen detection, and recurrence of a tumor by molecular subtype. Model G-E can model the simultaneous, sequential, or interleaved use of multiple screening technologies having different detection characteristics.

Model W-H (University of Wisconsin-Madison and Harvard Medical School) is a discrete-event micro-simulation model that uses a systems engineering approach to replicate breast cancer epidemiology in the U.S. population over time [3]. The model, programmed in C++ with over 20,000 lines of code, runs on both Microsoft Windows and UNIX platforms. It was developed at the University of Wisconsin-Madison and has been continuously maintained and enhanced for over 20 years. Model W-H is a population-based model that simulates the lifetimes of individual women through the interaction of four main components: breast cancer natural history, detection, treatment and mortality. Each woman enters the model at age 20 and ages in 6 month cycle times. A unique feature of model W-H is that it accounts for the possibility that a fraction of tumors are of limited malignant potential and therefore does not pose a lethal threat.

Details of the parameter estimation for the pandemic scenarios

Scenario 2, modeling reduction in screening, was informed in part by data from Epic Health Research Network, which pooled data from 60 healthcare organizations representing 306 hospitals that span 28 states and cover 10 million patients. According to Epic Health Research Network data, breast cancer screening rates fell 63% during March 15- June 16, 2020, and were 29% lower in the week of June 16 compared to pre-pandemic screening rates in 2017, 2018, and 2019 [20]. Assuming that a 29% reduction in screening rates persisted through September, we estimated the overall reduction in screening rates for the six month period to be equal to 47%. A similar magnitude and duration of the drop and recovery of screening mammography volume has been observed within the BCSC. As a result, in Scenario 2, we assumed that there is a 50% reduction in screening rates.

Scenario 3, modeling delays in diagnosis of symptomatic cases, was informed in part by data from two registries within the BCSC, as illustrated in the following figure. Clinical indication for mammography exams in the BCSC is coded as 1) Screening; 2) Additional evaluation of a recent mammogram; 3) Short interval follow-up; and 4) Evaluation of a Breast Problem (symptomatic). The numbers of exams coded as 4) Evaluation of a Breast Problem (symptomatic) provides evidence regarding the number of women seeking diagnostic imaging for breast symptoms. We determined the monthly count of these exams for each month January through June 2020 and divided by the average monthly count prior to the pandemic.

Supplementary Table 2 shows how we modified the treatment input for the use of chemotherapy due to pandemic effect. As noted in the main text, our reduced treatment scenario reduced the use of chemotherapy only for women who are diagnosed in Stage I and Stage IIa with ER+/HER2- subtype. The rates of endocrine therapy were not modified from their base levels. In addition, the rate of reduction was 50% in women younger than 70 and 25% for women older than 70.

Supplementary Figures 2 shows how models replicated observed age-adjusted mortality rates as reported by the NCI's SEER database between 2010 and 2017. **Supplementary Figure 2** presents age-adjusted rates including women in ages between 30 and 84. **Supplementary Figures 3** and **4** presents base-case results obtained by models D and GE.

Details of the base-case and sensitivity analysis results

We present the complete base-case results for our exemplary model (model W-H) in **Supplementary Tables 3-7**. **Supplementary Figures 5** and **6** show cumulative excess breast cancer mortality according to model D and model GE over time when the pandemic-related disruptions last for 12 months. For all of the other sensitivity analyses, all of the results are generated by using only the exemplary model (model W-H) unless noted otherwise. The results of the sensitivity analyses are given in **Supplementary Tables 8-15**. For the sensitivity analysis on other-cause mortality, we used the recent publication by the Centers for Disease Control and Prevention (CDC) which reported a detailed age-specific impact of COVID-19 on mortality [21]. For example, it is reported that COVID-19 increased mortality rates by 12% for the 65-74 age group [21]. We used the rates reported by the CDC report and assumed that the increase in other-cause mortality would be the same in 2020 and 2021 due to pandemic and did this sensitivity analysis and reported the results in Supplementary Table 15.

Supplementary References

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Supplementary Tables

Supplementary Table 1: Summary of key model features (Adopted from previous publications [5-7])[a]

Feature	Model		
	model D (Dana-Farber)	model G-E (Georgetown-Albert Einstein)	model W-H (Wisconsin-Harvard)
Type	Analytical	Simulation	Simulation
Natural history of breast cancer	State transition	State transition	Continuous tumor growth with some indolent and aggressive cases
Method of construction	Stochastic process, State transition	Time to event	Longitudinal, Stochastic process, State transition
Includes DCIS	Yes	Yes	Yes
Includes ER, HER2	Yes	Yes	Yes
SEER breast cancer data used for model calibration	Incidence	Incidence	Incidence and mortality
Screening benefit mechanism	Stage shift	Stage shift, age shift	Smaller tumor size, age shift
Treatment benefit mechanism	Hazard reduction	Hazard reduction	Cure fraction
Factors affecting treatment benefit	ER and HER2; age; year of and size at diagnosis	ER and HER2; age; year of and stage at diagnosis	ER and HER2; age; year of and stage at diagnosis

[a] Abbreviations: DCIS: Ductal carcinoma in situ; ER: estrogen receptor; HER2: human epidermal growth factor receptor 2; SEER: Surveillance, Epidemiology, and End Results

Supplementary Table 2. The distribution of chemotherapy use with and without pandemic for ER+/HER2- tumors by age group and stage

		No pandemic effect			Pandemic effect		
Age, y	Stage	NONE	Chemotherapy	Endocrine therapy	NONE	Chemotherapy	Endocrine therapy
<50	I	7.02%	35.35%	90.92%	7.54%	26.51%	90.92%
<50	IIa	3.94%	63.80%	93.19%	4.66%	47.85%	93.19%
50-69	I	6.96%	19.95%	91.76%	7.28%	14.96%	91.76%
50-69	IIa	1.64%	49.18%	94.45%	2.62%	36.89%	94.45%
70+	I	16.27%	4.87%	83.57%	16.35%	2.44%	83.57%
70+	IIa	10.40%	14.40%	86.40%	12.00%	7.20%	86.40%

Supplementary Table 3. Base-case age-adjusted mortality rates (Ages 30-84) for all scenarios in each year (model W-H only)[a]

Year	No pandemic	Delayed screening	Skipped screening	Hybrid delayed/ skipped screening	Delayed diagnosis	Reduced chemo treatment	Delayed screening & Delayed diagnosis	Skipped screening & Delayed diagnosis	Hybrid delayed/ skipped screening & Delayed diagnosis	Delayed screening & Delayed diagnosis & Reduced chemo treatment	Skipped screening & Delayed diagnosis & Reduced chemo treatment	Hybrid delayed/ skipped screening & Delayed diagnosis & Reduced chemo treatment
2020	30.91	30.98	31.06	31.02	31.08	30.91	31.17	31.24	31.20	31.17	31.24	31.20
2021	31.12	31.17	31.28	31.23	31.41	31.13	31.51	31.62	31.56	31.52	31.63	31.57
2022	31.12	31.14	31.28	31.21	31.39	31.17	31.44	31.58	31.51	31.48	31.62	31.55
2023	31.12	31.12	31.20	31.16	31.28	31.13	31.29	31.37	31.33	31.30	31.39	31.34
2024	31.44	31.48	31.61	31.54	31.56	31.46	31.60	31.74	31.67	31.62	31.76	31.69
2025	31.63	31.69	31.74	31.71	31.68	31.63	31.76	31.81	31.78	31.76	31.81	31.79
2026	32.03	32.14	32.20	32.17	32.09	32.04	32.20	32.26	32.23	32.21	32.27	32.24
2027	32.11	32.07	32.18	32.12	32.12	32.11	32.10	32.21	32.15	32.10	32.21	32.15
2028	32.05	32.12	32.11	32.12	32.05	32.05	32.13	32.12	32.12	32.13	32.12	32.12
2029	31.72	31.70	31.77	31.74	31.73	31.72	31.71	31.78	31.75	31.71	31.78	31.75
2030	32.60	32.61	32.53	32.57	32.61	32.60	32.62	32.54	32.58	32.62	32.54	32.58

[a] chemo = chemotherapy

Supplementary Table 4. Base-case raw number of breast cancer deaths (Ages 30-84) for all scenarios in each year (model W-H only)[a]

Year	No pandemic	Delayed screening	Skipped screening	Hybrid delayed/ skipped screening	Delayed diagnosis	Reduced chemo treatment	Delayed screening & Delayed diagnosis	Skipped screening & Delayed diagnosis	Hybrid delayed/ skipped screening & Delayed diagnosis	Delayed screening & Delayed diagnosis & Reduced chemo treatment	Skipped screening & Delayed diagnosis & Reduced chemo treatment	Hybrid delayed/ skipped screening & Delayed diagnosis & Reduced chemo treatment
2020	35,812	35,880	35,967	35,923	36,000	35,812	36,091	36,178	36,134	36,091	36,178	36,134
2021	36,851	36,910	37,049	36,979	37,192	36,870	37,302	37,440	37,371	37,314	37,452	37,383
2022	37,742	37,781	37,935	37,858	38,044	37,811	38,113	38,267	38,190	38,171	38,325	38,248
2023	38,277	38,269	38,356	38,313	38,467	38,288	38,471	38,558	38,514	38,482	38,570	38,526
2024	39,432	39,489	39,673	39,581	39,576	39,449	39,645	39,828	39,737	39,662	39,845	39,754
2025	40,471	40,550	40,639	40,595	40,530	40,477	40,638	40,726	40,682	40,643	40,732	40,688
2026	41,526	41,668	41,747	41,707	41,591	41,538	41,738	41,818	41,778	41,750	41,829	41,790
2027	42,718	42,625	42,803	42,714	42,730	42,724	42,654	42,833	42,744	42,660	42,839	42,750
2028	43,079	43,161	43,160	43,161	43,086	43,079	43,167	43,167	43,167	43,167	43,167	43,167
2029	43,196	43,139	43,249	43,194	43,208	43,202	43,151	43,261	43,206	43,151	43,261	43,206
2030	45,248	45,243	45,131	45,187	45,254	45,248	45,250	45,137	45,193	45,250	45,137	45,194

[a] chemo = chemotherapy

Supplementary Table 5. Base-case raw number of cumulative breast cancer deaths (Ages 30-84) for all scenarios in each year (model W-H only)[a]

Year	No pandemic	Delayed screening	Skipped screening	Hybrid delayed/ skipped screening	Delayed diagnosis	Reduced chemo treatment	Delayed screening & Delayed diagnosis	Skipped screening & Delayed diagnosis	Hybrid delayed/ skipped screening & Delayed diagnosis	Delayed screening & Delayed diagnosis & Reduced chemo treatment	Skipped screening & Delayed diagnosis & Reduced chemo treatment	Hybrid delayed/ skipped screening & Delayed diagnosis & Reduced chemo treatment
2020	35,812	35,880	35,967	35,923	36,000	35,812	36,091	36,178	36,134	36,091	36,178	36,134
2021	72,664	72,790	73,015	72,903	73,191	72,682	73,393	73,617	73,505	73,405	73,629	73,517
2022	110,406	110,571	110,950	110,761	111,236	110,493	111,506	111,884	111,695	111,576	111,955	111,765
2023	148,682	148,840	149,307	149,073	149,703	148,781	149,976	150,443	150,210	150,058	150,524	150,291
2024	188,114	188,329	188,979	188,654	189,279	188,230	189,621	190,271	189,946	189,720	190,370	190,045
2025	228,585	228,880	229,618	229,249	229,809	228,707	230,259	230,998	230,628	230,363	231,102	230,732
2026	270,111	270,547	271,366	270,957	271,400	270,245	271,997	272,815	272,406	272,113	272,931	272,522
2027	312,829	313,172	314,169	313,671	314,129	312,969	314,652	315,648	315,150	314,773	315,770	315,272
2028	355,908	356,333	357,329	356,831	357,215	356,048	357,819	358,815	358,317	357,941	358,937	358,439
2029	399,104	399,472	400,578	400,025	400,423	399,250	400,970	402,076	401,523	401,092	402,198	401,645
2030	444,352	444,716	445,709	445,212	445,677	444,497	446,220	447,213	446,717	446,342	447,335	446,838

[a] chemo = chemotherapy

Supplementary Table 6. Base-case excess number of cumulative breast cancer deaths compared to Scenario 1 (Ages 30-84) for all scenarios in each year (model W-H only)[a]

Year	Delayed screening	Skipped screening	Hybrid delayed/ skipped screening	Delayed diagnosis	Reduced chemo treatment	Delayed screening & Delayed diagnosis	Skipped screening & Delayed diagnosis	Hybrid delayed/ skipped screening & Delayed diagnosis	Delayed screening & Delayed diagnosis & Reduced chemo treatment	Skipped screening & Delayed diagnosis & Reduced chemo treatment	Hybrid delayed/ skipped screening & Delayed diagnosis & Reduced chemo treatment
2020	68	154	111	187	0	279	365	322	279	365	322
2021	127	351	239	528	18	729	954	841	741	966	853
2022	166	545	355	830	88	1,100	1,479	1,289	1,170	1,549	1,360
2023	158	624	391	1,021	99	1,294	1,761	1,527	1,375	1,842	1,609
2024	215	865	540	1,165	116	1,507	2,157	1,832	1,606	2,256	1,931
2025	294	1,033	664	1,223	122	1,674	2,412	2,043	1,778	2,516	2,147
2026	436	1,254	845	1,288	133	1,886	2,704	2,295	2,001	2,820	2,410
2027	343	1,340	842	1,300	140	1,822	2,819	2,321	1,944	2,941	2,443
2028	425	1,421	923	1,307	140	1,910	2,907	2,409	2,032	3,029	2,531
2029	368	1,474	921	1,319	146	1,866	2,972	2,419	1,988	3,094	2,541
2030	364	1,357	860	1,325	146	1,868	2,861	2,365	1,990	2,983	2,487

[a] chemo = chemotherapy

Supplementary Table 7. Base-case % increase in excess number of cumulative breast cancer deaths compared to Scenario 1 (Ages 30-84) for all scenarios in each year (model W-H only)[a]

Year	Delayed screening	Skipped screening	Hybrid delayed/ skipped screening	Delayed diagnosis	Reduced chemo treatment	Delayed screening & Delayed diagnosis	Skipped screening & Delayed diagnosis	Hybrid delayed/ skipped screening & Delayed diagnosis	Delayed screening & Delayed diagnosis & Reduced chemo treatment	Skipped screening & Delayed diagnosis & Reduced chemo treatment	Hybrid delayed/ skipped screening & Delayed diagnosis & Reduced chemo treatment
2020	0.19%	0.43%	0.31%	0.52%	0.00%	0.78%	1.02%	0.90%	0.78%	1.02%	0.90%
2021	0.17%	0.48%	0.33%	0.73%	0.02%	1.00%	1.31%	1.16%	1.02%	1.33%	1.17%
2022	0.15%	0.49%	0.32%	0.75%	0.08%	1.00%	1.34%	1.17%	1.06%	1.40%	1.23%
2023	0.11%	0.42%	0.26%	0.69%	0.07%	0.87%	1.18%	1.03%	0.93%	1.24%	1.08%
2024	0.11%	0.46%	0.29%	0.62%	0.06%	0.80%	1.15%	0.97%	0.85%	1.20%	1.03%
2025	0.13%	0.45%	0.29%	0.54%	0.05%	0.73%	1.06%	0.89%	0.78%	1.10%	0.94%
2026	0.16%	0.46%	0.31%	0.48%	0.05%	0.70%	1.00%	0.85%	0.74%	1.04%	0.89%
2027	0.11%	0.43%	0.27%	0.42%	0.04%	0.58%	0.90%	0.74%	0.62%	0.94%	0.78%
2028	0.12%	0.40%	0.26%	0.37%	0.04%	0.54%	0.82%	0.68%	0.57%	0.85%	0.71%
2029	0.09%	0.37%	0.23%	0.33%	0.04%	0.47%	0.74%	0.61%	0.50%	0.78%	0.64%
2030	0.08%	0.31%	0.19%	0.30%	0.03%	0.42%	0.64%	0.53%	0.45%	0.67%	0.56%

[a] chemo = chemotherapy

Supplementary Table 8. Sensitivity analysis on the proportion of patients who reschedule their missed screening mammograms in 6 months[a]

Scenario	2022		2025		2030	
Scenario 1: No COVID-19 impact, median cumulative number of deaths	122,675		250,633		473,903	
	Hybrid delayed/skipped screening (Scenario 2c)		Disruptions in screening & diagnosis (Scenario 5c)		Disruptions in screening & diagnosis &treatment (Scenario 6c)	
% of women who reschedule their missed mammograms in 6 months	Excess number of deaths	% increase	Excess number of deaths	% increase	Excess number of deaths	% increase
0%	1,357	0.31%	2,329	0.52%	2,983	0.67%
10%	1,258	0.28%	2,230	0.50%	2,884	0.65%
20%	1,158	0.26%	2,130	0.48%	2,785	0.63%
30%	1,059	0.24%	2,031	0.46%	2,685	0.60%
40%	960	0.22%	1,932	0.43%	2,586	0.58%
50%	860	0.19%	1,832	0.41%	2,487	0.56%
60%	761	0.17%	1,733	0.39%	2,387	0.54%
70%	662	0.15%	1,634	0.37%	2,288	0.51%
80%	562	0.13%	1,535	0.35%	2,189	0.49%
90%	463	0.10%	1,435	0.32%	2,089	0.47%
100%	364	0.08%	1,336	0.30%	1,990	0.45%

[a] This tables presents median cumulative excess breast cancer mortality by 2022, 2025, and 2030 due to the COVID-19 pandemic effect for selected scenarios across the three models. The excess mortality is expressed in terms of both the number of breast cancer deaths and % increase compared to cumulative number of breast cancer deaths without pandemic effect

Supplementary Table 9. Sensitivity analysis on the rate of reduction in screening rates (reduced screening is 25% compared to 50% for the base case)[a]

Scenario	2022		2025		2030	
Scenario 1: No COVID-19 impact, cumulative number of deaths	110,406		228,585		473,903	
	Excess number of deaths	% increase	Excess number of deaths	% increase	Excess number of deaths	% increase
Delayed screening (Scenario 2a)	118	0.11%	221	0.10%	293	0.07%
Skipped screening (Scenario 2b)	257	0.23%	551	0.24%	714	0.16%
Hybrid delayed/skipped screening (Scenario 2c)	187	0.17%	386	0.17%	504	0.11%
Delayed diagnosis (Scenario 3)	830	0.75%	1,223	0.54%	1,325	0.30%
Reduced chemotherapy treatment (Scenario 4)	88	0.08%	122	0.05%	146	0.03%
Disruptions in screening & diagnosis (Scenario 5c)	503	0.46%	769	0.34%	861	0.19%
Disruptions in screening & diagnosis &treatment (Scenario 6c)	1,157	1.05%	1,818	0.80%	2,067	0.47%

[a] This table presents the cumulative excess breast cancer mortality due to pandemic effect by 2022, 2025, and 2030 for selected scenarios for the exemplary model. The excess mortality is expressed in terms of both the number of breast cancer deaths and % increase compared to cumulative number of breast cancer deaths without pandemic effect

Supplementary Table 10. Sensitivity analysis on the rate of reduction in screening rates (reduced screening is 75% compared to 50% for the base case)[a]

Scenario	2022		2025		2030	
Scenario 1: No COVID-19 impact, cumulative number of deaths	110,406		228,585		473,903	
	Excess number of deaths	% increase	Excess number of deaths	% increase	Excess number of deaths	% increase
Delayed screening (Scenario 2a)	227	0.21%	188	0.08%	369	0.08%
Skipped screening (Scenario 2b)	776	0.70%	1,520	0.66%	1,925	0.43%
Hybrid delayed/skipped screening (Scenario 2c)	501	0.45%	854	0.37%	1,147	0.26%
Delayed diagnosis (Scenario 3)	830	0.75%	1,223	0.54%	1,325	0.30%
Reduced chemotherapy treatment (Scenario 4)	88	0.08%	122	0.05%	146	0.03%
Disruptions in screening & diagnosis (Scenario 5c)	609	0.55%	833	0.36%	992	0.22%
Disruptions in screening & diagnosis &treatment (Scenario 6c)	1,545	1.40%	2,412	1.06%	2,860	0.64%

[a] This table presents the cumulative excess breast cancer mortality due to pandemic effect by 2022, 2025, and 2030 for selected scenarios for the exemplary model. The excess mortality is expressed in terms of both the number of breast cancer deaths and % increase compared to cumulative number of breast cancer deaths without pandemic effect

Supplementary Table 11. Sensitivity analysis on the proportion of the clinical detected cases that are delayed (15% of cases are delayed compared to 25% for the base case)[a]

Scenario	2022		2025		2030	
Scenario 1: No COVID-19 impact, cumulative number of deaths	110,406		228,585		473,903	
	Excess number of deaths	% increase	Excess number of deaths	% increase	Excess number of deaths	% increase
Delayed screening (Scenario 2a)	166	0.15%	294	0.13%	364	0.08%
Skipped screening (Scenario 2b)	545	0.49%	1,033	0.45%	1,357	0.31%
Hybrid delayed/skipped screening (Scenario 2c)	355	0.32%	664	0.29%	860	0.19%
Delayed diagnosis (Scenario 3)	488	0.44%	697	0.30%	758	0.17%
Reduced chemotherapy treatment (Scenario 4)	88	0.08%	122	0.05%	146	0.03%
Disruptions in screening & diagnosis (Scenario 5c)	900	0.82%	1,447	0.63%	1,711	0.38%
Disruptions in screening & diagnosis &treatment (Scenario 6c)	970	0.88%	1,551	0.68%	1,832	0.41%

[a] This table presents the cumulative excess breast cancer mortality due to pandemic effect by 2022, 2025, and 2030 for selected scenarios for the exemplary model. The excess mortality is expressed in terms of both the number of breast cancer deaths and % increase compared to cumulative number of breast cancer deaths without pandemic effect

Supplementary Table 12. Sensitivity analysis on the proportion of the clinical detected cases that are delayed (40% of cases are delayed compared to 25% for the base case)[a]

Scenario	2022		2025		2030	
Scenario 1: No COVID-19 impact, cumulative number of deaths	110,406		228,585		473,903	
	Excess number of deaths	% increase	Excess number of deaths	% increase	Excess number of deaths	% increase
Delayed screening (Scenario 2a)	166	0.15%	294	0.13%	364	0.08%
Skipped screening (Scenario 2b)	545	0.49%	1,033	0.45%	1,357	0.31%
Hybrid delayed/skipped screening (Scenario 2c)	355	0.32%	664	0.29%	860	0.19%
Delayed diagnosis (Scenario 3)	1,369	1.24%	1,994	0.87%	2,225	0.50%
Reduced chemotherapy treatment (Scenario 4)	88	0.08%	122	0.05%	146	0.03%
Disruptions in screening & diagnosis (Scenario 5c)	837	0.76%	1,246	0.54%	1,417	0.32%
Disruptions in screening & diagnosis &treatment (Scenario 6c)	1,646	1.49%	2,556	1.12%	2,969	0.67%

[a] This table presents the cumulative excess breast cancer mortality due to pandemic effect by 2022, 2025, and 2030 for selected scenarios for the exemplary model. The excess mortality is expressed in terms of both the number of breast cancer deaths and % increase compared to cumulative number of breast cancer deaths without pandemic effect

Supplementary Table 13. Sensitivity analysis on the rate of reduction in chemotherapy use (12.5% of women aged<70 and 25% of women aged>70 compared to 25% of women aged<70 and 50% of women aged>70 for the base case)[a]

Scenario	**2022**		**2025**		**2030**	
Scenario 1: No COVID-19 impact, cumulative number of deaths	110,406		228,585		473,903	
	Excess number of deaths	% increase	Excess number of deaths	% increase	Excess number of deaths	% increase
Delayed screening (Scenario 2a)	166	0.15%	294	0.13%	364	0.08%
Skipped screening (Scenario 2b)	545	0.49%	1,033	0.45%	1,357	0.31%
Hybrid delayed/skipped screening (Scenario 2c)	355	0.32%	664	0.29%	860	0.19%
Delayed diagnosis (Scenario 3)	830	0.75%	1,223	0.54%	1,325	0.30%
Reduced chemotherapy treatment (Scenario 4)	46	0.04%	69	0.03%	87	0.02%
Disruptions in screening & diagnosis (Scenario 5c)	1,289	1.17%	2,043	0.89%	2,365	0.53%
Disruptions in screening & diagnosis &treatment (Scenario 6c)	1,324	1.20%	2,100	0.92%	2,433	0.55%

[a] This table presents the cumulative excess breast cancer mortality due to pandemic effect by 2022, 2025, and 2030 for selected scenarios for the exemplary model. The excess mortality is expressed in terms of both the number of breast cancer deaths and % increase compared to cumulative number of breast cancer deaths without pandemic effect

Supplementary Table 14. Sensitivity analysis on the rate of reduction in chemotherapy use (50% of women aged<70 and 75% of women aged>70 compared to 25% of women aged<70 and 50% of women aged>70 for the base case)[a]

Scenario	2022		2025		2030	
Scenario 1: No COVID-19 impact, cumulative number of deaths	110,406		228,585		473,903	
	Excess number of deaths	% increase	Excess number of deaths	% increase	Excess number of deaths	% increase
Delayed screening (Scenario 2a)	166	0.15%	294	0.13%	364	0.08%
Skipped screening (Scenario 2b)	545	0.49%	1,033	0.45%	1,357	0.31%
Hybrid delayed/skipped screening (Scenario 2c)	355	0.32%	664	0.29%	860	0.19%
Delayed diagnosis (Scenario 3)	830	0.75%	1,223	0.54%	1,325	0.30%
Reduced chemotherapy treatment (Scenario 4)	140	0.13%	215	0.09%	262	0.06%
Disruptions in screening & diagnosis (Scenario 5c)	1,289	1.17%	2,043	0.89%	2,365	0.53%
Disruptions in screening & diagnosis &treatment (Scenario 6c)	1,394	1.26%	2,217	0.97%	2,580	0.58%

[a] This table presents the cumulative excess breast cancer mortality due to pandemic effect by 2022, 2025, and 2030 for selected scenarios for the exemplary model. The excess mortality is expressed in terms of both the number of breast cancer deaths and % increase compared to cumulative number of breast cancer deaths without pandemic effect

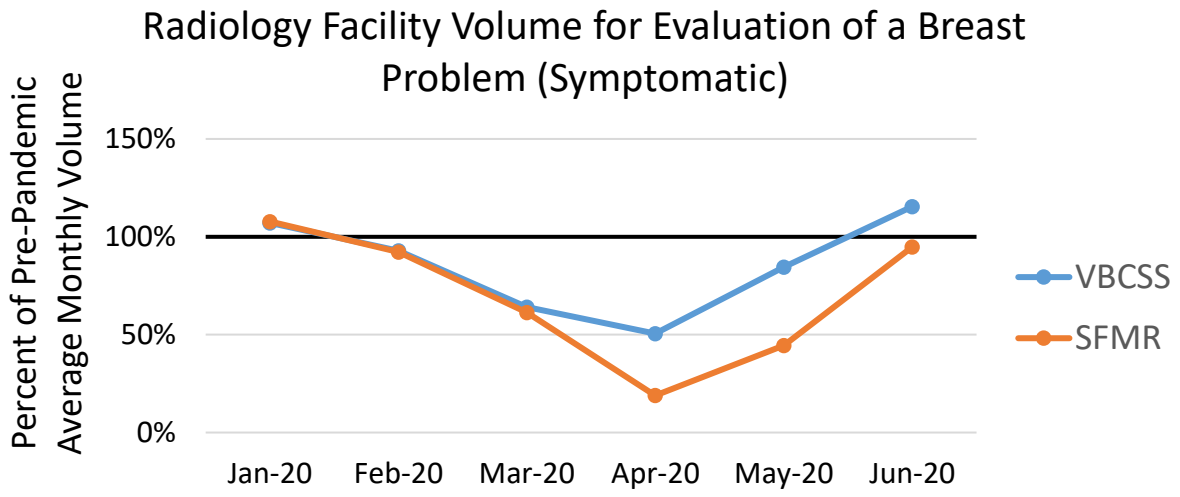
Supplementary Table 15. Sensitivity analysis on the impact of COVID-19 on other-cause mortality[a]

Scenario	**2022**		**2025**		**2030**	
Scenario 1: No COVID-19 impact, cumulative number of deaths	110,242		228,319		444,058	
	Excess number of deaths	% increase	Excess number of deaths	% increase	Excess number of deaths	% increase
Delayed screening (Scenario 2a)	189	0.17%	220	0.10%	198	0.04%
Skipped screening (Scenario 2b)	655	0.59%	1,121	0.49%	1,320	0.30%
Hybrid delayed/skipped screening (Scenario 2c)	422	0.38%	670	0.29%	759	0.17%
Delayed diagnosis (Scenario 3)	837	0.76%	1,225	0.54%	1,327	0.30%
Reduced chemotherapy treatment (Scenario 4)	88	0.08%	122	0.05%	146	0.03%
Disruptions in screening & diagnosis (Scenario 5c)	1,369	1.24%	2,086	0.91%	2,300	0.52%
Disruptions in screening & diagnosis &treatment (Scenario 6c)	1,440	1.31%	2,185	0.96%	2,417	0.54%

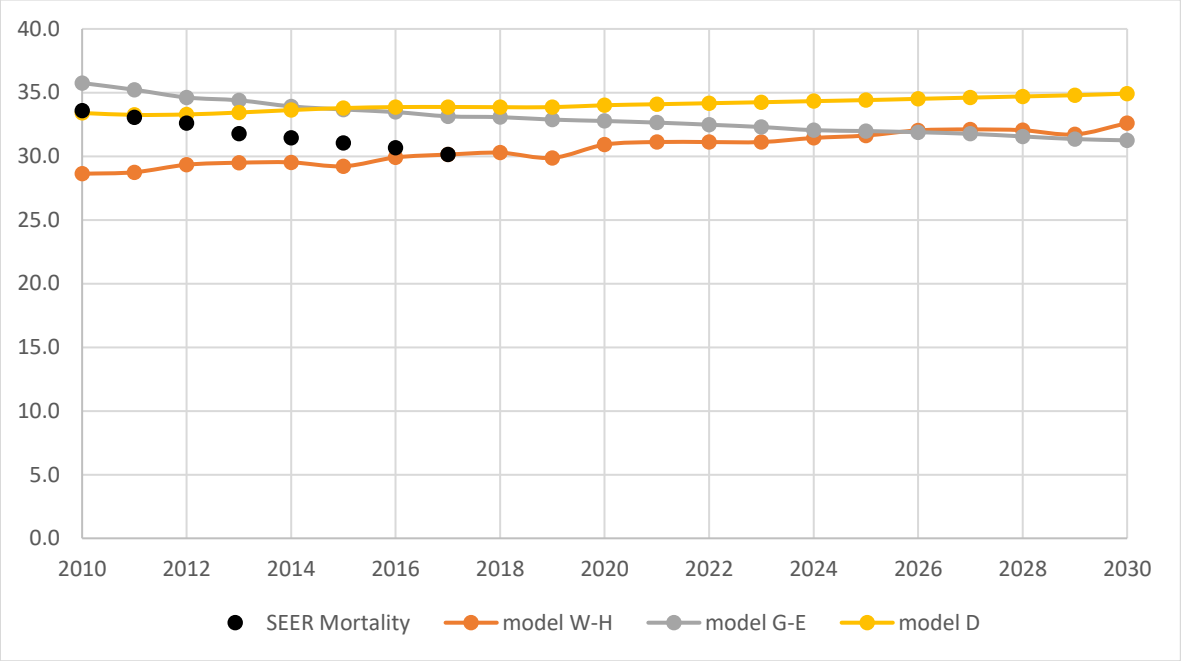
[a] This table presents the cumulative excess breast cancer mortality due to pandemic effect by 2022, 2025, and 2030 for selected scenarios for the exemplary model. The excess mortality is expressed in terms of both the number of breast cancer deaths and % increase compared to cumulative number of breast cancer deaths without pandemic effect. Scenario 1 in this table also considers a higher other-cause mortality therefore number of deaths due to breast cancer is different than that in the base case for this scenario.

Supplementary Figures

Supplementary Figure 1. Radiology facility mammography volume for evaluation of a breast problem during January – June 2020 at selected facilities participating in the Vermont Breast Cancer Surveillance System (VBCSS) and San Francisco Mammography Registry (SFMR).

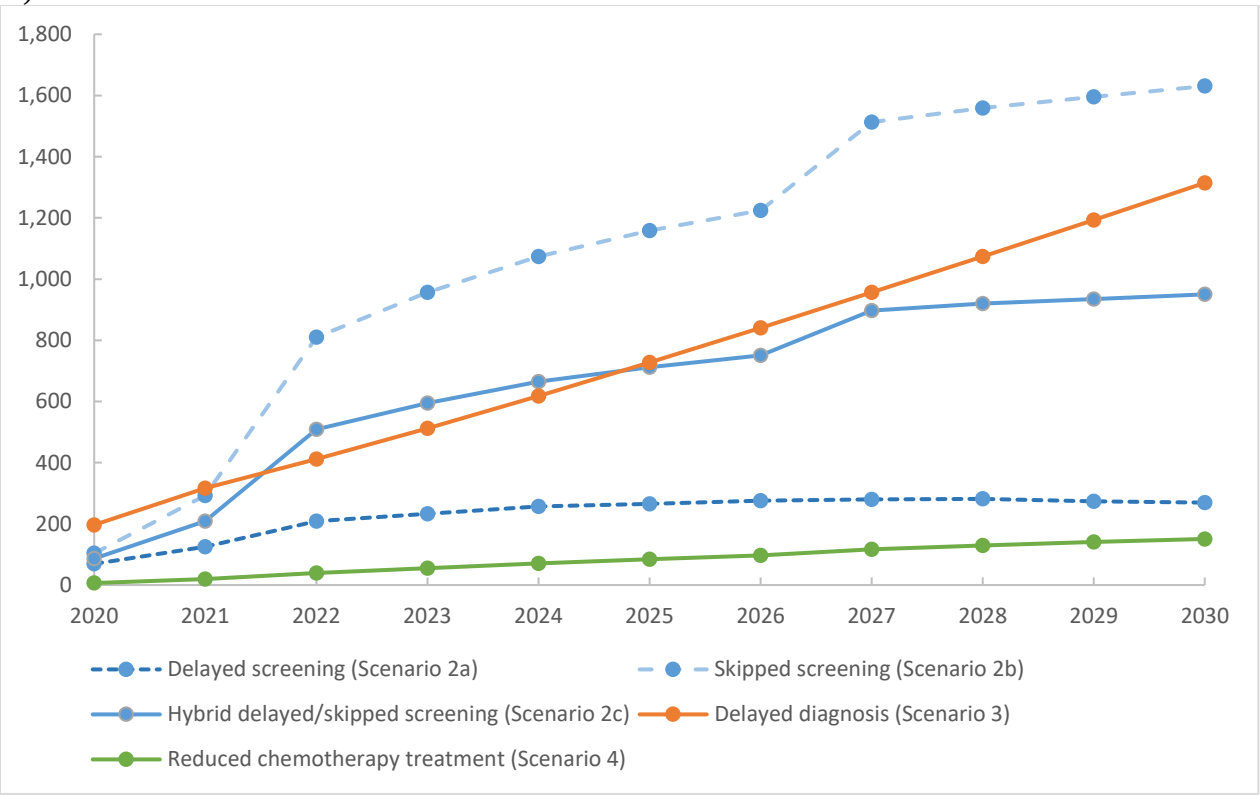


Supplementary Figure 2. Age-adjusted (30-84 years old) mortality over time with comparison to SEER data for no pandemic scenario (Scenario 1)

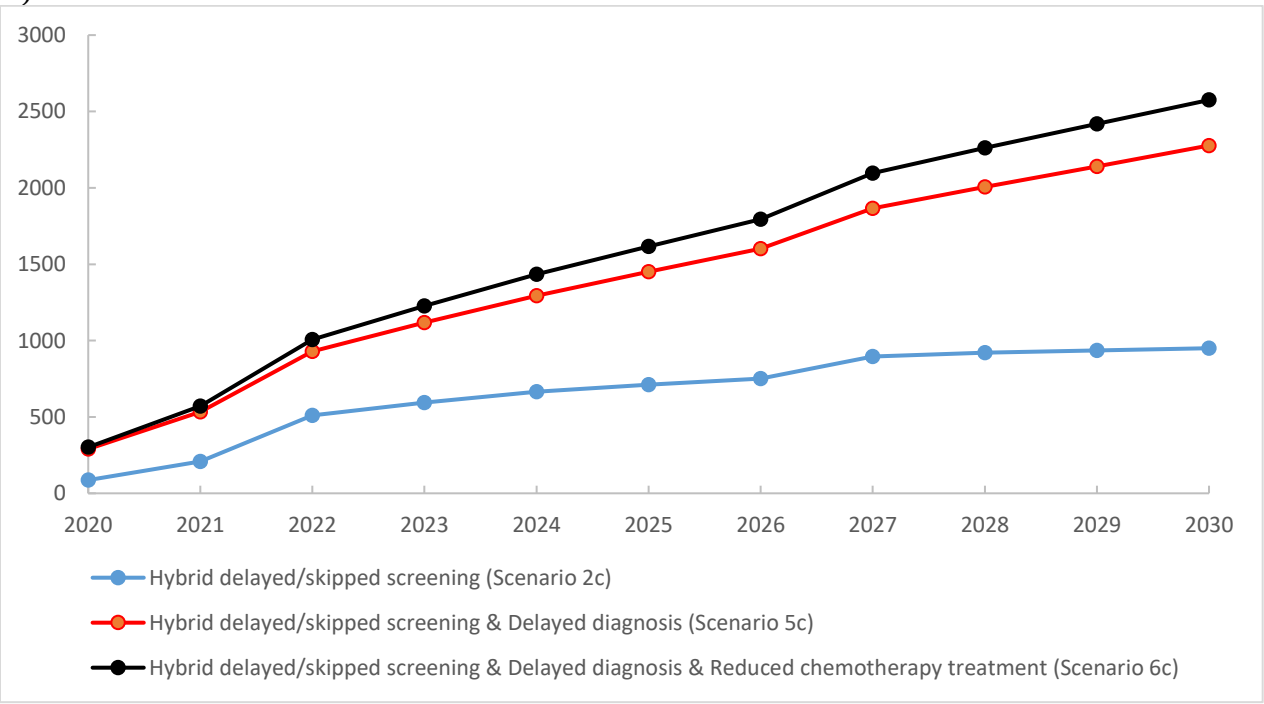


Supplementary Figure 3. Cumulative excess breast cancer mortality according to model D over time. Panel A presents the number of cumulative excessive deaths when each disruption is modeled separately and Panel B presents the number of excessive deaths when disruptions are combined.

A)

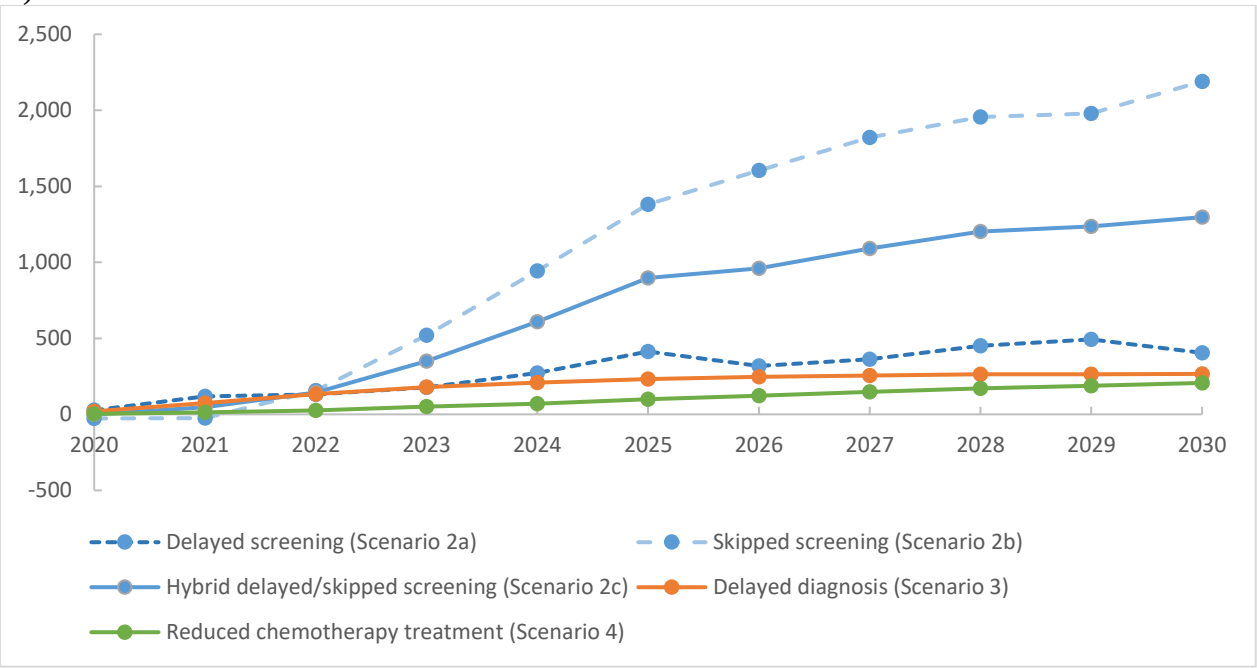


B)

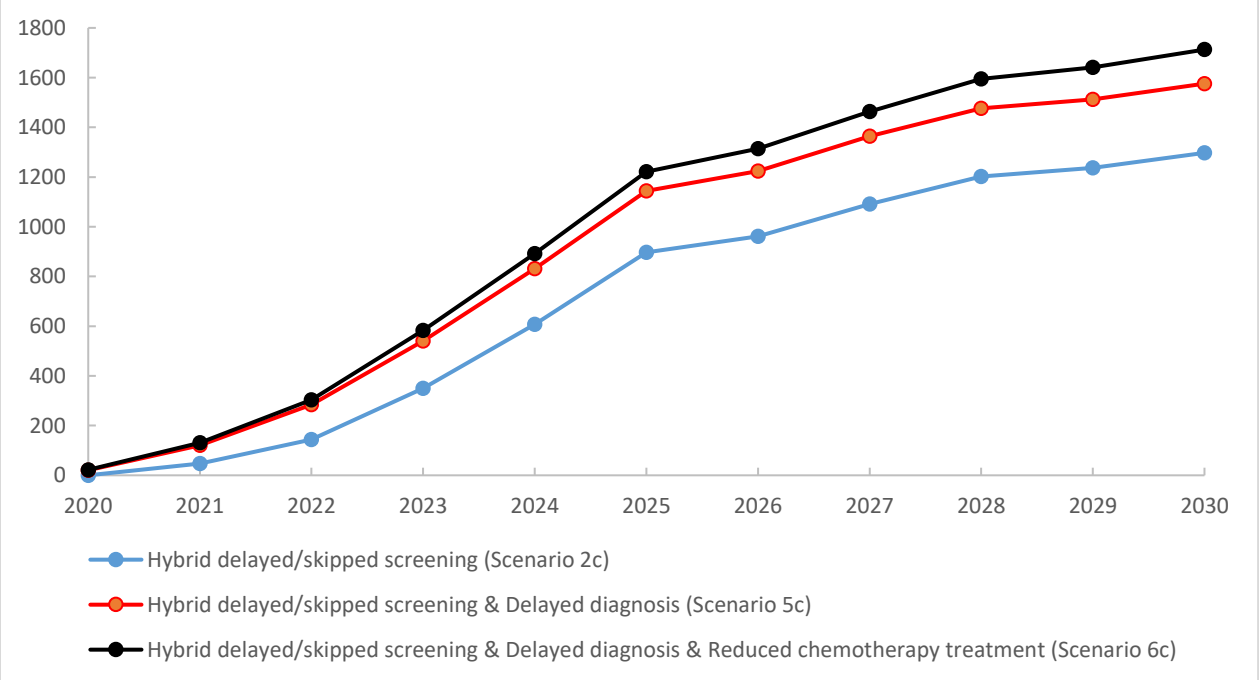


Supplementary Figure 4. Cumulative excess breast cancer mortality according to model GE over time. Panel A presents the number of cumulative excessive deaths when each disruption is modeled separately and Panel B presents the number of excessive deaths when disruptions are combined.

A)

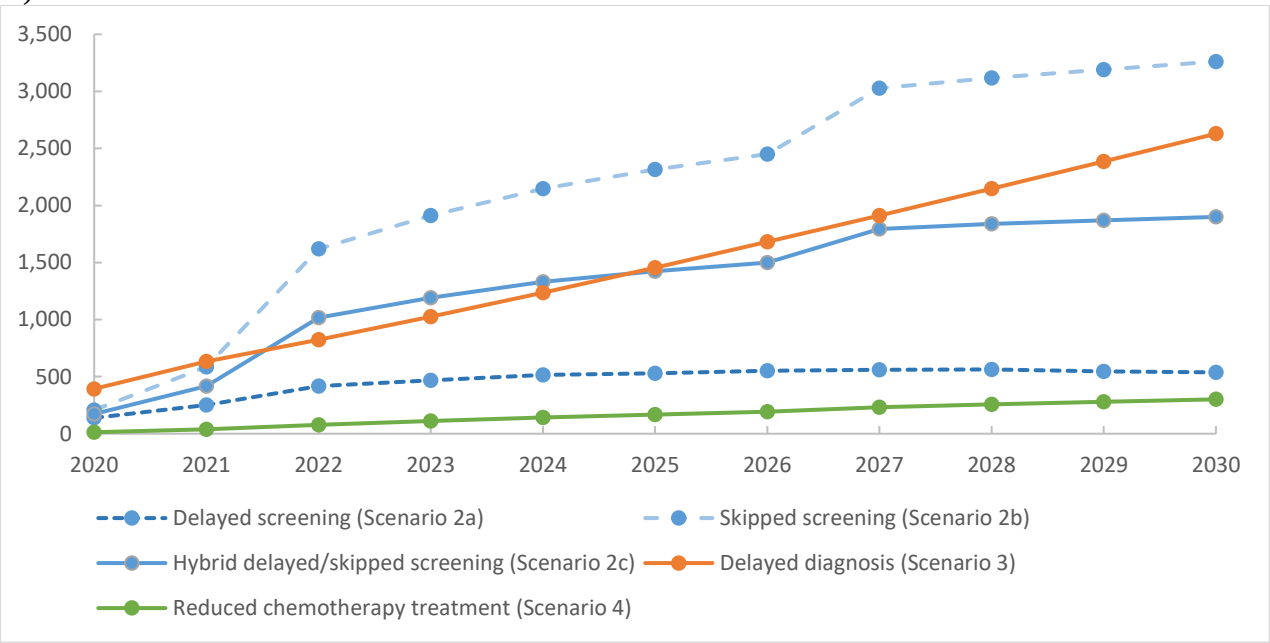


B)

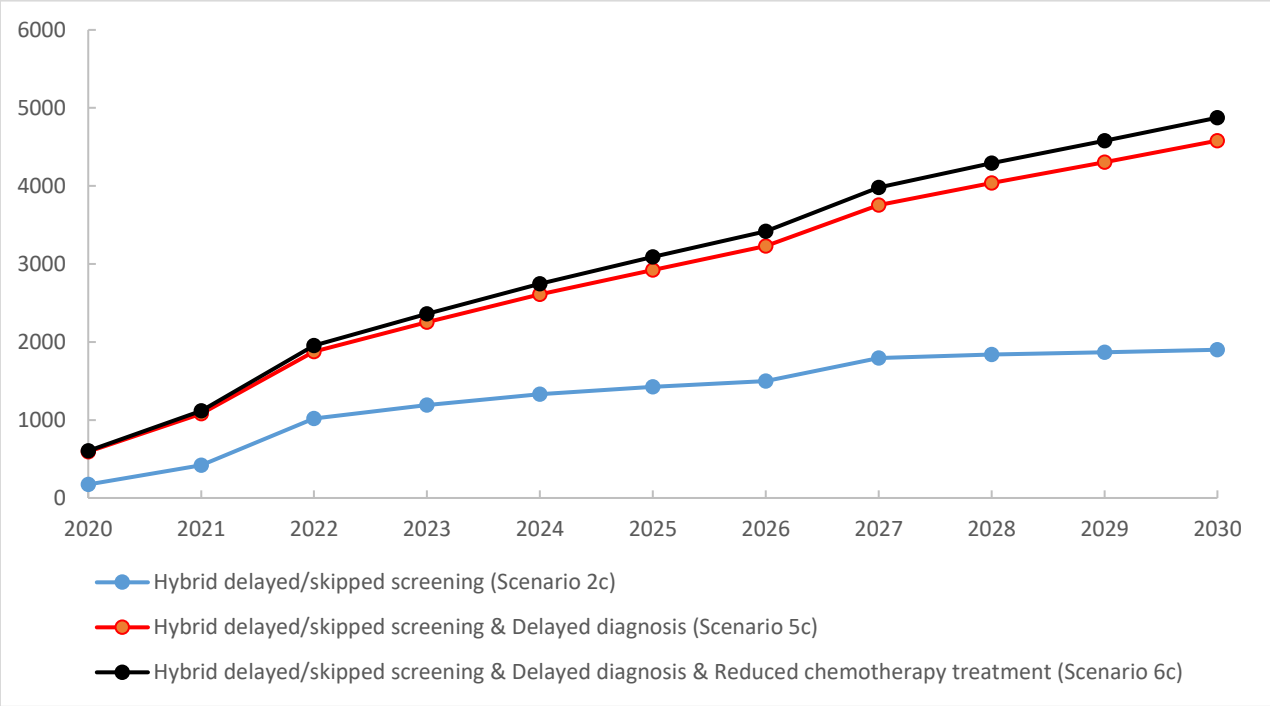


Supplementary Figure 5. Cumulative excess breast cancer mortality according to model D over time when the pandemic-related disruptions last for 12 months. Panel A presents the number of cumulative excessive deaths when each disruption is modeled separately and Panel B presents the number of excessive deaths when disruptions are combined.

A)

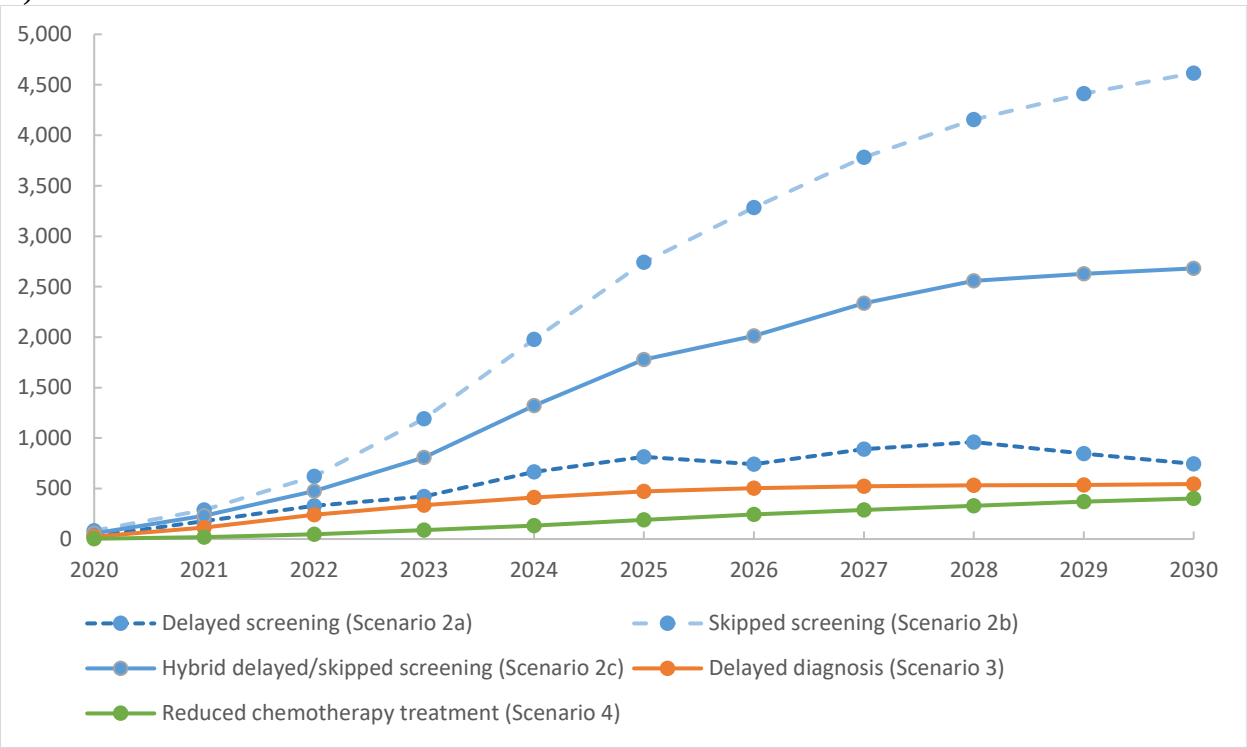


B)



Supplementary Figure 6. Cumulative excess breast cancer mortality according to model GE over time when the pandemic-related disruptions last for 12 months. Panel A presents the number of cumulative excessive deaths when each disruption is modeled separately and Panel B presents the number of excessive deaths when disruptions are combined.

A)



B)