Appendix 1 (as supplied by the authors): Supplementary tables

Table S1: Resource Utilization (RU) and Cost Input Parameters

Variables	Definitions and Descriptions	Costs (2012CAN$)	Resource Utilization (RU)
Screening and Diagnosis			
Breast Cancer Screening program	RU: Assume all women eligible would be screened- Cost: Includes mammography and radiology based on the Ontario Health Insurance Plan (OHIP) (1)	$183.00 per screen	100% of women eligible for screening
Non-invasive Workup	RU: Assume all women with a positive mammogram Cost: Includes mammography, radiology, physician clinic visit based on OHIP (1)	$445.95 per work-up	100% of women who have a positive screening exam
Invasive Work-up-Needle Biopsy	RU: Of the women who get a non-invasive workup, 14.7% subsequently receive an invasive procedure based on the Ontario Breast Screening Program (OBSP) (2) Cost: Physician clinic visit, needle biopsy procedure and pathology based on OHIP (1)	$745.46 per work-up	82.1% of women who receive an invasive work-up.
Invasive Work-up-Excisional	RU: Of the women who get a non-invasive workup, 14.7% receive an invasive procedure based on OBSP (2); Cost: physician clinic visits, excision, pathology based on OHIP (1)	$1,652.44 per work-up	17.8% of women who receive an invasive work-up.
Treatment			
Chemotherapy	RU: Proportion of women receiving chemotherapy; Cost: Mean value of 1st, 2nd and 3rd generation chemotherapies based on expert opinion, Cancer Care Ontario (CCO) (3), and Sunnybrook Pharmacy Department (4).	$7,376.10 per course	Women receiving chemotherapy with invasive cancer-see details below Women receiving chemotherapy with DCIS=0%-see details below
Herceptin	RU: Incidence of Herceptin-assume all women who are HER2+ received Herceptin; Cost: Assume that treatment Costs are based on 8 cycles; Includes chemotherapy costs recommended for Herceptin (paclitaxel); includes health care personnel costs and physician clinic visits associated with administration. Based on ASCO	$29,709 per course	14% with invasive cancer 0% with DCIS

	abstract (5), CCO (3), and Sunnybrook Pharmacy Department (4)		
Tamoxifen	RU: Assume utilization of tamoxifen for appropriate population over 10-year time horizon. Cost: Annual cost (excludes markup+dispensing)+physician clinic visit 4 times per year. Based on the Ontario Drug Benefit Formulary (ODBF) (6)	$383.40 per annum	100% for invasive cancer based in eligible women 100% for DCIS in eligible women
Aromatase Inhibitors (AI)	RU: Assume utilization of AI for appropriate population over 10 year time horizon; Cost: annual cost of letrozole (excludes markup and dispensing) + physician clinic visits 4 times per year. Based on the ODBF (6).	$822.40 per annum	100% for invasive cancer in eligible women 0% for DCIS
Treatment Cost per Appropriate Cohort			
ER+, <50 years, DCIS, annual cost	RU: Tamoxifen only (over 10 year time horizon); Cost: tamoxifen only based on the ODBF (36)	$383.40	100%
ER+, <50 years, Invasive, annual cost	RU: Tamoxifen (over 10 year time horizon)+Chemotherapy; Cost: tamoxifen (over 10 year time horizon)+Chemotherapy based on the ODBF (6), CCO (3), Sunnybrook Pharmacy Department (4) and expert opinion.	$7,759.50	100%
ER+, <50 years, Invasive, annual cost with Herceptin	RU: Tamoxifen (over 10 year time horizon)+Chemotherapy+Herceptin; Cost: tamoxifen (over 10 year time horizon)+Chemotherapy+Herceptin. Based on the ODBF (6), CCO (3), Sunnybrook Pharmacy Department (4), and expert opinion	$37,462.50	100%
ER+, >=50 years, DCIS, annual cost	RU: Tamoxifen (over 10 year time horizon)+only; Cost: tamoxifen only based on ODBF (4)	$383.40	100% of women in this cohort received this regimen
ER+, >=50 years, Invasive, annual cost	RU: Chemotherapy+Aromatase Inhibitor (AI) (over 10 year time horizon); Cost: chemotherapy+AI (over 10 year time horizon). Based on ODBF (34), CCO (3), Sunnybrook Pharmacy Department (4), and expert opinion	$8,198.50	100% of women in this cohort received this regimen
ER+, >= 50 years, Invasive,	RU: Chemotherapy+AI (over 10 year time horizon)+Herceptin; Cost: Chemotherapy +AI (over 10	$37,901.50	100% of women in this cohort received this regimen

annual cost with Herceptin	year time horizon)+Herceptin. Based on ODBF (6), CCO (3), Sunnybrook Pharmacy Department (4), and expert opinion		
ER-, <50 years, DCIS, annual cost	No drug therapy. Based on expert opinion.	$0	100% of women in this cohort received this regimen
ER-, < 50 , Invasive, annual cost	RU: Chemotherapy; Cost: Chemotherapy. Based on ODBF(6), CCO (3), Sunnybrook Pharmacy Department (4), and expert opinion	$7,376.10	100% of women in this cohort received this regimen
ER-, < 50 years, Invasive, annual cost with Herceptin	RU: Chemotherapy+Herceptin; Cost: Chemotherapy+Herceptin Based on ODBF (6), CCO (3), Sunnybrook Pharmacy Department (4), and expert opinion.	$37,079.10	100% of women in this cohort received this regimen
ER-, >=50 years, DCIS, annual cost	No drug therapy. Based on expert opinion	$0	100% of women in this cohort received this regimen
ER-, >=50 years, Invasive, annual cost	RU: chemotherapy; Cost: chemotherapy. Based on ODBF (6), CCO (3), Sunnybrook Pharmacy Department (4), and expert opinion. Source: Cancer Care Ontario, expert opinion	$7,376.10	100% of women in this cohort received this regimen
ER-, >=50 years, Invasive, annual cost with Herceptin	RU: Chemotherapy+Herceptin; Cost: Chemotherapy+Herceptin Based on ODBF (6), CCO (3), Sunnybrook Pharmacy Department (4), and expert opinion.	$37,079.10	100% of women in this cohort received this regimen
Procedures			
Radiation for invasive cancer	RU: Proportion of women with breast cancer who received radiation therapy. Based on Mittmann et al (7). Cost: 25 fractions * $138 (1996) or 188.39 (2012). Based on Bank of Canada (8), Earle et al (9), and OHIP (1).	$5,014.05 per radiation	67%
Surgery for invasive cancer	RU: Proportion of women with breast cancer receiving surgery based on Mittmann et al (10)	Costs stratified by lumpectomy and mastectomy	90%
Surgery-lumpectomy for invasive cancer	RU: Proportion of all women receiving surgery; Cost: OCCI 2012. Based on Ontario Case Cost Initiative (OCCI) (11).	$4,937.06 per surgery	63% The joint report by the Canadian Institute for Health Information (CIHI) and the Canadian Partnership Against Cancer show the annual rates for the two treatments vary widely from one province to another.
Surgery-	RU: Proportion of all women	$6,956.77 per surgery	37%

mastectomy for invasive cancer	receiving surgery Cost: OCCI 2012. Based on OCCI (11).		The joint report by the Canadian Institute for Health Information (CIHI) and the Canadian Partnership Against Cancer show the annual rates for the two treatments vary widely from one province to another.
Radiation for DCIS	RU: Proportion of women with DCIS who received radiation therapy Cost: 25 fractions * $138 (1996) or 188.39 (2012). Based on Bank of Canada (8), Earle et al (9), and OHIP (1)	$5,014.05 per radiation	50%
Surgery-lumpectomy for DCIS	RU: Proportion of DCIS women receiving surgery. Based on expert opinion; Cost: OCCI 2012. Based on OCCI (11), Canadian Institute for Health Information (CIHI) (12) and expert opinion	$4,937.06 per surgery	67%
Surgery-mastectomy for DCIS	RU: Proportion of all DCIS receiving surgery Cost: OCCI 2012. Based on OCCI (11), CIHI Report (12), and expert opinion	$6,956.77 per surgery	33%

Table S2: Values for Univariate Sensitivity Analyses

Variable	Base Case Value	Sensitivity Analysis Value	Source and Comments
Percent of women eligible for screening who missed screening	0%	50%	In Ontario, 60% of women over age 50 participate in regular screening, but about 43% do this through the organized program. The retention rate for women continuing screening after a previous screen is approximately 85% (12)
Detection sensitivity for mammography	Model calibrated as per empirical data (13, 14)	100%	Ideal
Herceptin	100% of HER2+ women (14% of invasive cancers)	0%	Assumption applied to all women in model
Treatment	Surgery, radiation, chemo, hormonal	Surgery, radiation only	Assumption applied to all women in model
Health Preference values	Values	+/- 25%	

Appendix to: Mittmann N, Stout NK, Tosteson ANA, et al. Cost-effectiveness of mammography policies from a publicly funded health care system perspective. *CMAJ Open* 2018. DOI:10.9778/cmajo.20170106.

Table S3: Marginal Cost-effectiveness and Cost-utility of Different Screening Scenarios (discount=1.5%) from the Health System perspective compared to No Screening. Values in Columns 2—6 and 8 are per 1000 Women.

Screening Scenario	Modeled Overall Health System Cost	Modeled LY	Modeled QALY	Health System Incremental Cost	Incremental LY	MCER ($/LYG)	Incremental QALY	MCUR ($/QALY)
No Screening	$1,965,899	30,602	24,998					
Triennial 50-69	$3,368,225	30,648	25,036	$1,402,326	46	$30,536	38	$36,981
Triennial 50-74	$3,642,494	30,653	25,039	$1,676,595	51	$33,026	42	$40,193
Biennial 50-69	$3,835,726	30,662	25,048	$1,869,827	61	$30,879	50	$37,265
Biennial 50-74	$4,217,275	30,669	25,053	$2,251,376	67	$33,715	55	$40,851
Annual 50-69	$5,250,458	30,688	25,069	$3,284,559	86	$38,366	72	$45,855
Annual 40-49	$4,310,198	30,639	25,030	$2,344,299	37	$63,167	32	$73,414
Annual 50-74	$5,789,126	30,694	25,075	$3,823,227	93	$41,313	77	$49,587
Annual 40-49, Biennial 50-69	$6,072,758	30,697	25,078	$4,106,859	95	$43,419	80	$51,442
Annual 40-49, Biennial 50-74	$6,444,999	30,703	25,083	$4,479,099	101	$44,221	85	$52,603
Annual 40-69	$7,516,630	30,721	25,098	$5,550,731	119	$46,705	100	$55,386
Annual 40-74	$8,051,766	30,727	25,103	$6,085,867	125	$48,718	105	$57,938

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Table S4: Univariate sensitivity analysis -marginal: Health system perspective- screening scenarios compared to No Screening where the outcomes are cost per life year gained (LYG) and cost per quality adjusted life year (QALY) (discount=1.5%).

Screening Scenario	Basecase	No Treatment	50% Missed Screens	100% Sensitivity	No Herceptin	Utilities +25%	Utilities - 25%
Marginal Cost Effectiveness Ratios relative to no screening							
No Screening							
Triennial 50-69	$30,536	$110,230	$27,950	$23,082	$27,805		
Triennial 50-74	$33,026	$116,482	$30,899	$25,258	$30,372		
Biennial 50-69	$30,879	$147,828	$27,799	$22,509	$28,331		
Biennial 50-74	$33,715	$144,336	$30,823	$24,931	$31,025		
Annual 50-69	$38,366	$183,315	$31,047	$29,224	$36,544		
Annual 40-49	$63,167	$870,149	$51,162	$65,828	$56,557		
Annual 50-74	$41,313	$197,039	$34,192	$20,854	$39,533		
Annual 40-49, Biennial 50-69	$43,419	$268,022	$36,801	$31,387	$40,072		
Annual 40-49, Biennial 50-74	$44,221	$260,950	$38,069	$32,310	$40,828		
Annual 40-69	$46,705	$267,191	$37,596	$34,880	$43,894		
Annual 40-74	$48,718	$289,120	$39,324	$36,370	$45,798		
Marginal Cost Utility Ratios							
No Screening							
Triennial 50-69	$36,981	$165,119	$33,327	$27,487	$33,035	$29,585	$46,227
Triennial 50-74	$40,193	$179,359	$36,920	$30,283	$36,243	$32,154	$50,241
Biennial 50-69	$37,265	$207,737	$32,768	$26,606	$33,498	$29,812	$46,581
Biennial 50-74	$40,851	$205,444	$36,442	$29,581	$36,848	$32,681	$51,064
Annual 50-69	$45,855	$247,211	$36,556	$34,224	$42,836	$36,684	$57,318

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Annual 40-49	$73,414	$1,248,787	$58,199	$75,173	$64,669	$58,731	$91,767
Annual 50-74	$49,587	$276,755	$40,447	$24,491	$46,545	$39,669	$61,983
Annual 40-49, Biennial 50-69	$51,442	$373,350	$42,949	$36,529	$46,656	$41,153	$64,302
Annual 40-49, Biennial 50-74	$52,603	$371,187	$44,603	$37,739	$47,731	$42,082	$65,753
Annual 40-69	$55,386	$370,904	$43,883	$40,491	$51,114	$44,309	$69,232
Annual 40-74	$57,938	$415,165	$46,069	$42,313	$53,467	$46,351	$72,423

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Table S5: Incremental cost-effectiveness analysis. Shaded rows indicate weakly dominated (W. Dom) scenarios which have been removed in the lower part of the table.

Screening Scenario	Modeled Overall Health System Cost	Modeled LY	Modeled QALY	Health System Incremental Cost	Incremental LY	ICER ($/LYG)	Incremental QALY	ICUR ($/QALY)
No Screening	$1,965,899	30,602	24,998					
Triennial 50-69	$3,368,225	30,648	25,036	$1,402,326	46	$30,536	38	$36,981
Triennial 50-74	$3,642,494	30,653	25,039	$274,269		W. Dom		W. Dom
Biennial 50-69	$3,835,726	30,662	25,048	$467,501	15	$31,958	12	$38,142
Biennial 50-74	$4,217,275	30,669	25,053	$381,549		W. Dom		Dom
Annual 50-69	$5,250,458	30,688	25,069	$1,414,732	25	$56,460	21	$65,944
Annual 50-74	$5,789,126	30,694	25,075	$538,668		W. Dom		W. Dom
Annual 40-49, Biennial 50-69	$6,072,758	30,697	25,078	$283,631		W. Dom		W. Dom
Annual 40-49, Biennial 50-74	$6,444,999	30,703	25,083	$372,241		W. Dom		W. Dom
Annual 40-69	$7,516,630	30,721	25,098	$2,266,172	33	$68,164	29	$79,266
Annual 40-74	$8,051,766	30,727	25,103	$535,136	6	$88,088	5	$110,994

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Table S6: ICUR and ICER for changes in screening frequency and age to start screening

Screening Scenario	Modeled Overall Health System Cost	Modeled LY	Modeled QALY	Health System Incremental Cost	Incremental LY	ICER ($/LYG)	Incremental QALY	ICUR ($/QALY)
Increasing Screening Frequency								
Triennial 50-74	$3,642,494	30,653	25,039					
Biennial 50-74	$4,217,275	30,669	25,053	$574,781	16	$35,899	13	$42,900
Annual 50-74	$5,789,126	30,694	25,075	$1,571,851	26	$61,006	22	$71,481
Screening Younger Women								
Annual 50-74	$5,789,126	30,694	25,075					
Annual 40-74	$8,051,766	30,727	25,103	$2,262,640	32	$69,882	28	$80,986
Annual 50-69	$5,250,458	30,688	25,069					
Annual 40-69	$7,516,630	30,721	25,098	$2,266,172	33	$68,184	29	$79,266
Biennial 50-74	$4,217,275	30,669	25,053					
Annual 40-49, Biennial 50-74	$6,444,999	30,703	25,083	$2,227,723	35	$64,551	30	$74,164

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Table S7: Effect of changing the screening scenario from the baseline of biennial screening from 50-74. The upper part of the table considers scenarios where screening is increased from the baseline. In the lower part screening has been decreased from the baseline and the ICERS and ICURS express dollars saved per LY or QALY lost. Shaded rows indicate weakly dominated (W. Dom) scenarios.

Screening Scenario	Modeled Overall Health System Cost	Modeled LY	Modeled QALY	Health System Incremental Cost	Incremental LY	ICER ($/LY)	Incremental QALY	ICUR ($/QALY)
Increasing								
Digital Biennial 50-74	$4,217,275	30,669	25,053					
Digital Annual 50-69	$5,250,458	30,688	25,069	$1,033,183	19	$54,862	17	$62,549
Digital Annual 50-74	$5,789,126	30,694	25,075			W. Dom		
Digital Annual 40-49, Biennial 50-69	$6,072,758	30,697	25,078			W. Dom		
Digital Annual 40-49, Biennial 50-74	$6,444,999	30,703	25,083			W. Dom		
Digital Annual 40-69	$7,516,630	30,721	25,098	$2,266,172	33	$68,184	29	$79,266
Digital Annual 40-74	$8,051,766	30,727	25,103	$535,136	6	$88,088	5	$110,994
Decreasing								
Digital Biennial 50-74	$4,217,275	30,669	25,053					
Digital Biennial 50-69	$3,835,726	30,662	25,048	$381,549	6	$61,296	5	$ 77,307.62
Digital Triennial 50-74	$3,642,494	30,653	25,039			W. Dom		W. Dom
Digital Triennial 50-69	$3,368,225	30,648	25,036	$467,501	15	$31,958	12	$38,142
No Screening	$1,965,899	30,602	24,998	$1,402,326	46	$30,536	38	$36,981

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