SUPPLEMENTARY MATERIAL

Supplementary Methods

Sample Inclusion and Selection:

Identifying patients over multiple years of data: Patients in the Blue Cross Blue Shield (BCBS) database had up to two identifiers: a Member ID, which only identifies patients within health plans (which may change from year to year) and Master ID, which identifies patients even when they switch health plans. However, not all patients had a Master ID. For patients with a Master ID, we were able to identify women across the entire three-year study period. Women without a Master ID may appear under different Member IDs.

Identifying screening mammograms: We used a validated algorithm that reliably distinguishes screening from diagnostic mammograms to identify screening mammograms.[1] The algorithm first excludes claims for a mammogram with a Healthcare Common Procedure Coding System (HCPCS) code indicating a diagnostic exam. From among remaining exams, the algorithm then excludes mammograms performed within 9 months of a previous mammogram. Lastly, the algorithm excludes mammograms performed within 365 days of a breast cancer diagnosis, defined by ICD 9 or 10 codes (Supplementary Table 1).

In addition, we excluded women classified as having a screening mammogram but who met the following criteria (Table 1):

- Breast MRI or biopsy on the same day as a purported screening mammogram
- ICD-10 code indicating a personal history of cancer genetic syndrome
- Prior claims for prophylactic mastectomy

Definitions of Covariates and Outcomes:

Covariates: Model covariates were chosen based on two criteria: covariates must be plausible confounders and must be measurable in our dataset. In multivariable models, covariates included age, metro residence, hospital referral region (HRR) of residence, time since last mammogram, family history of breast cancer and screening ultrasound. Definitions of covariates are detailed here:

- *Metro location*: defined according to MSA boundaries using Office of Management and Budget Boundaries
- *HRR of residence:* defined according to participant zip code, using Dartmouth Health Atlas boundaries, 2015[2]
- *Time since last mammogram:* defined according to the time between index screen and last claim for a screening mammogram. We used a liberal definition and did not require the last mammogram to adhere to the algorithm used for the index mammogram, but rather considered time since last claim for any screening mammogram, using codes identified in Supplementary Table 1.
- *Family history of breast cancer*: defined according to ICD 9 or ICD 10 codes indicating a family history of breast cancer.
- *Screening breast ultrasound*: there is no HCPCS code specifically denoting screening breast ultrasound so we considered bilateral, whole breast ultrasounds to likely be screening exams.

Outcomes: We used HCPCS codes denoted in Supplementary Table 1 to define imagining outcomes (diagnostic mammography, diagnostic DBT, ultrasound, and MRI) and

biopsy. To identify incident breast cancers, we adapted an algorithm proposed by Fenton et al.[3] This algorithm begins with a screening mammogram and identifies subsequent claims with an associated ICD code indicating a breast neoplasm within 123 days. Incident cancers are identified if they are then followed by a claim for a breast procedure within 365 days. The algorithm also identifies claims for carcinoma in-situ and includes them as cancer diagnoses if they are followed by additional breast imaging within 82 days.

We extended this algorithm to identify cancers diagnosed between 4-12 months after the index mammogram to capture potential interval cancers. In this modification, we required that ICD9 or 10 codes occur between 4-12 months. Since in-situ carcinomas are unlikely to be interval cancers, we did not include that portion of the algorithm that identifies in-situ carcinomas.

Mammogram-Level Models:

We used two modeling approaches which included mammogram-level data. First, we used a logistic regression in which the primary predictor was the type of screening test (DBT vs 2D) and the outcome was recall, biopsy, MRI, or cancer diagnosis, all of which are binary outcomes. Because region of residence is a potential confounder, we included HRRs as fixed effects in this model (i.e., dummy variables).

We also fit a multilevel model as an alternate specification. In this model, mammograms were the lowest unit of analysis and were nested within HRRs, modeled as random effects. Models included the same covariates as the mammogram-level logistic regression, other than HRR fixed effects. Covariates were included as fixed effects at the mammogram level. Models

assumed an identity correlation structure. Results of this alternate specification are provided in Table 5.

HRR-Level analysis:

Conceptual Approach: Supplementary Figure 1 is a schematic depicting the way in which the area-level analysis is relatively robust to confounding. Prior to the introduction of DBT (Period 1), a mix of higher and lower risk women were screened using 2D mammography. After the introduction of DBT (Period 2), there may be differential referral to DBT and 2D based on level of risk. In a cross-sectional analysis, this differential referral would produce the appearance of different outcomes attributable to screening type. However, an area-level analysis, in which the outcome is measured for the entire screened population, would not reflect this differential referral. Likewise, because areas are observed longitudinally over time, we can also account for factors that may influence both DBT adoption and screening outcomes (such as regional differences in radiologist practice patterns or regional differences in baseline breast cancer rates). Observed differences in outcomes are more likely to be attributable to differences due to the screening test itself.

HRR-level modeling: For our HRR-level analysis, we measured the relationship between DBT use and outcomes on the population level. Our primary predictor was the proportion of screening mammograms that used DBT within an HRR. Outcomes were calculated as number per 1000 screening mammograms in the HRR in which we observed claims for the outcome. Each HRR was observed at 6-month intervals over 3 years (i.e., 6 observations per HRR).

We used linear regression to evaluate the relationship between population level DBT use and population level outcomes. The model included HRR fixed effects to estimate within-HRR effects and year fixed effects to control for period effects,. Models used robust standard errors clustered at the HRR level. Models were weighted by HRR screened population size, which we assumed to be generally constant over time. We evaluated the residuals of this model for normality and found that for each outcome, residuals were largely normal. Results were expressed as marginal effects assuming that 1% of the population uses DBT or 99% of the population uses DBT.

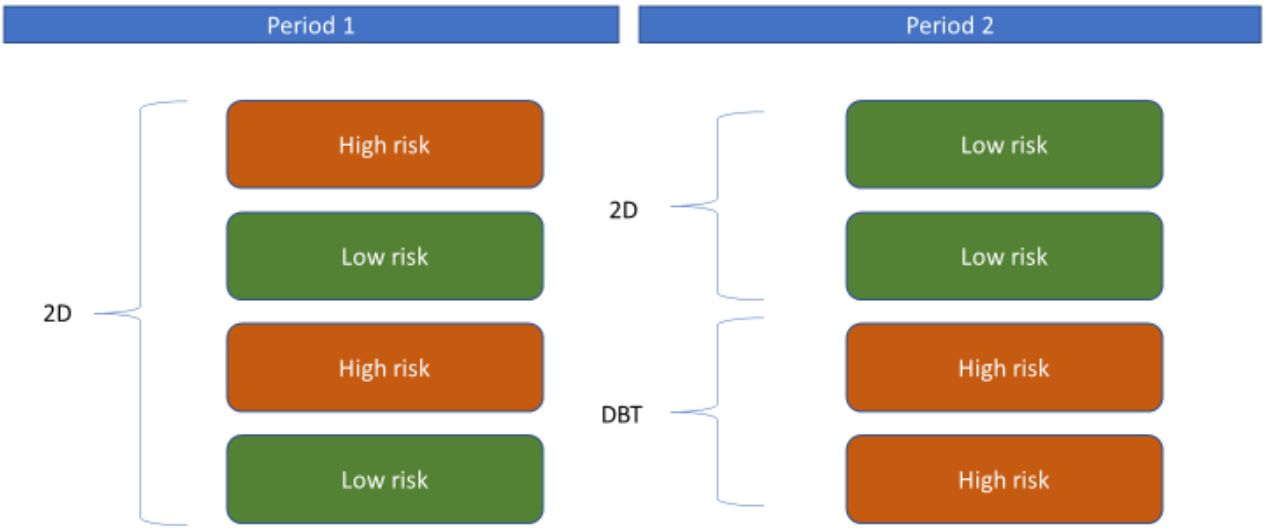
Supplementary Table 1: HCPCS and ICD9 and 10 Definitions:

Description	Codes (CPT/HCPCS unless otherwise noted)
Screening mammography	77057, 77067, G0202, +GG (+77063 DBT)
Diagnostic mammography	G0204, G0206, 77055, 77056, 77065, 77066, +77051 (add-on); DBT indicated by 77061, 77062 as part of main procedure or +G0279 (add-on)
Breast ultrasound, diagnostic	76641 (without 50 modifier), 76642
Breast ultrasound, screening	76641 (+50 bilateral procedure modifier code)
Breast MRI	77058, 77059, C8903-C8908
Breast biopsy	19000, 19001, 19100, 19101, 19102, 19103, 19081, 19082, 19083, 19084, 19085, 19086, 19110, 19112, 19120, 19125, 19126
Diagnosis code-based exclusion/covariates	
Breast cancer or personal history of disease (exclusion)	ICD-9 Diagnosis Codes: 174.*, 233.0, V10.3 ICD-10 Diagnosis Code: C50.*; D05.*, Z85.3*, Z86.000
Genetic susceptibility to breast cancer (exclusion)	ICD-9 Diagnosis Code: V84.01; ICD-10 Diagnosis Code: Z15.01
Visit diagnosis of prophylactic mastectomy (exclusion)	ICD-9 Diagnosis Code: V50.41; ICD-10 Diagnosis Code: Z40.01
Family History of Breast Cancer (covariate)	ICD-9 Diagnosis Code: V16.3; ICD-10 Diagnosis Code: Z80.3
Breast procedure codes for identifying incident cancers	
Invasive Breast Cancer Diagnosis	ICD-9 Diagnosis Codes: 174.*; ICD-10 Diagnosis Code: C50.*
In situ breast cancer diagnosis	ICD-9 Diagnosis Codes: 233.0; ICD-10 Diagnosis Code: D05.*
Breast directed surgery (CPT)	19110, 19120, 19125, 19126, 19160, 19162, 19180, 19182, 19200, 19220, 19240, 19301, 19302,19303, 19304, 19305, 19306, 19307

Supplementary Table 2: Odds Ratios from Mammogram-Level Model

	Recall				Biopsy				Cancer detection, 0-4 months				Cancer detection, 5-12 months			
Type of Screen	OR	99% CI		p	OR	99% CI		p	OR	99% CI		p	OR	99% CI		p
2D	ref															
DBT	0.98	0.97	0.99	<.001	1.29	1.27	1.32	<.001	1.29	1.24	1.34	<.001	1.14	1.03	1.28	0.002
Age																
40-44	ref															
45-49	0.86	0.86	0.87	<.001	0.98	0.95	1.00	0.015	1.45	1.36	1.55	<.001	1.16	0.99	1.36	0.018
50-54	0.72	0.71	0.73	<.001	0.91	0.89	0.93	<.001	1.72	1.62	1.83	<.001	1.09	0.93	1.28	0.16
55-59	0.60	0.59	0.60	<.001	0.79	0.77	0.81	<.001	1.94	1.82	2.06	<.001	1.01	0.86	1.18	0.92
60-64	0.56	0.56	0.57	<.001	0.81	0.79	0.83	<.001	2.40	2.26	2.55	<.001	1.16	0.99	1.36	0.013
MSA status																
nonmetro	ref															
metro	1.03	1.02	1.04	<.001	1.05	1.02	1.08	<.001	1.05	0.98	1.12	0.050	0.99	0.85	1.15	0.89
Timing of index mammogram																
1/1/15-6/30/15	ref															
7/1/15-12/31/15	0.96	0.95	0.97	<.001	0.96	0.93	0.99	<.001	1.00	0.95	1.06	0.95	0.92	0.80	1.07	0.18
1/1/16-6/30/16	1.00	0.99	1.01	0.36	0.97	0.94	1.00	0.004	1.03	0.98	1.09	0.15	0.89	0.76	1.04	0.047
7/1/16-12/31/16	0.97	0.96	0.98	<.001	0.95	0.92	0.97	<.001	1.03	0.97	1.08	0.19	0.87	0.75	1.01	0.016
1/1/17-6/30/17	0.99	0.98	1.00	0.036	0.94	0.92	0.97	<.001	0.99	0.93	1.04	0.54	0.78	0.66	0.91	<.001
7/1/17-12/31/17	0.98	0.97	0.99	<.001	0.91	0.89	0.94	<.001	0.99	0.94	1.04	0.64	0.79	0.68	0.93	<.001
Months since last mammogram																
9-12	ref															
12-24	0.95	0.93	0.97	<.001	1.02	0.96	1.09	0.32	1.06	0.94	1.19	0.23	0.86	0.64	1.15	0.17
>24	1.22	1.19	1.25	<.001	1.54	1.45	1.64	<.001	1.64	1.44	1.85	<.001	0.91	0.66	1.26	0.46
Not observed	1.40	1.37	1.43	<.001	1.82	1.71	1.93	<.001	1.71	1.52	1.92	<.001	0.98	0.73	1.31	0.84
Family History of breast cancer																
No	ref															
Yes	1.18	1.16	1.19	<.001	1.19	1.15	1.22	<.001	1.20	1.14	1.27	<.001	2.18	1.91	2.49	<.001
Received Screening Ultrasound																
No	ref															
Yes	4.73	4.61	4.86	<.001	3.97	3.76	4.19	<.001	3.76	3.35	4.21	<.001	2.06	1.42	3.00	<.001

Supplementary Figure 1: Conceptual diagram for the area-level analysis



In Period 1, a mixture of high and low risk women are screened with 2D mammography. In period 2, low risk women are screened with 2D and high risk women are screened with DBT. This differential screening would produce a biased estimate of the effectiveness of DBT for screening compared to 2D. However, population-level screening outcomes would not be impacted by this differential sorting.

References:

1. Fenton JJ, Zhu W, Balch S, Smith-Bindman R, Fishman P, Hubbard RA. Distinguishing screening from diagnostic mammograms using Medicare claims data. *Med Care*. 2014;52(7):e44-51. doi:10.1097/MLR.0b013e318269e0f5
2. The Dartmouth Atlas of Health Care. http://www.dartmouthatlas.org/tools/downloads.aspx?tab=39
3. Fenton JJ, Onega T, Zhu W, et al. Validation of a Medicare Claims-based Algorithm for Identifying Breast Cancers Detected at Screening Mammography. *Med Care*. 2016;54(3):e15-22. doi:10.1097/MLR.0b013e3182a303d7