Appendix E1

Supplemental Analysis to Account for Correlations between Women

To account for correlations between women who had more than one mammogram, we performed a similar analysis with one randomly selected mammogram per individual woman. This analysis reveals that in women 40–49, usual care screening detected 33 cancers while incurring 1223 false positive mammograms and 229 benign biopsies. Age-based screening detected more cancers than risk-based screening (22/33 versus 8/33; $P < .001$), while prompting more false positive mammograms (574/1223 versus 130/1223; $P < .0001$), and benign biopsies (99/229 versus 19/229; $P < .0001$).

Supplemental Analysis to Include Baseline Mammograms

In all breast cancer screening programs, a contributor to higher false positive rate in younger women is a higher proportion of baseline examinations, which tend to have higher recall rate. In this manuscript, both hypothetical scenarios include a lower proportion of baseline mammograms than would be expected in actual practice because younger women are less likely to be eligible for hypothetical screening scenarios and thus, their baseline mammograms are excluded. To determine if this bias, introduced by our observational study design, influences the conclusions we draw, we performed a secondary analysis, which included all baseline mammograms in the hypothetical scenarios.

Including all baseline mammograms in women 40–49, age-based screening ≥ 45 detected more cancers than risk-based screening (40/50 versus 22/50; $P = .001$) while prompting more false positive mammograms (1245/1787 versus 599/1787; $P < .001$), and more benign biopsies (274/384 versus 164/384; $P < .001$) (Table E1). This supplemental analysis emulates a reasonable clinical scenario. Risk based screening may well include a baseline mammogram after 40 in order to use breast density in the risk calculation to guide future screening.

Table E1: Short-term outcomes for mammograms in women 40–49 years of age including all baseline mammograms

	Usual Care 40–49 n = 20,539[a]	Age-based ≥ 45 n = 12,876[b]	Risk-based ≥ 40–49 n = 4375[b]
Baseline mammograms	2073 (10.1%)	2073 (16.1%)	2073 (47.4%)
Primary outcomes[c]			
Cancers detected by mammography	50 (0.24%)	40 (0.31%)	22 (0.50%)
False positive mammograms	1787 (8.7%)	1245 (9.7%)	599 (13.7%)
Benign biopsy	384 (1.9%)	274 (2.1%)	164 (3.7%)
Comparison to age-based ≥ 40			
Cancers not detected		10	28
Mammograms not performed		7663	16,164
False positive mammograms avoided		542	1188
Benign biopsies avoided		110	220

[a] Observed screening outcomes.

[b] Hypothetical screening strategies in women 40–49 including all baseline mammograms.

[c] Percentages in parentheses are over N in each column.