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SUPPLEMENTAL DATA

Cardiovascular versus breast cancer mortality in men with breast cancer: An age-stratified SEER competing-risk study

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Full article is available at the following link: Cardiovascular versus breast cancer mortality in men with breast cancer: An age-stratified SEER competing-risk study

Table S1. Missingness and data availability summary, non-metastatic cohort (*n* = 6702)

Variable / item	*n*	%	Handling
Race: Unknown	43	0.6	Explicit category (retained in models)
Race: Other	389	5.8	Explicit category
Grade: missing/unknown	2083	31.1	Variable omitted from all models
Age, marital status, summary stage	0	0.0	Complete
Excluded before primary cohort: distant disease	707	—	Analyzed separately (all-stage)
Excluded before primary cohort: unstageable	142	—	Excluded
Receptor/subtype available (of 4309 diagnosed 2010–2022)	4005	92.9	Subtype analysis subset

Table 1 consolidates "Other/Unknown race" (*n*=432) for brevity, while the regression tables maintain "Other race" and "Unknown race" as distinct categories, aligning with an explicit-category approach to missing data.

Table S2. Overall cumulative incidence (%) and numbers at risk

Cause / time	1y	3y	5y	10y	15y
Breast cancer	1.4	5.1	9.1	16.0	20.1
Cardiovascular	1.2	3.6	5.8	10.8	15.2
Other causes	1.6	5.5	9.0	17.5	24.8
No. at risk	6010	4781	3652	1782	676

Table S3. Restricted cardiovascular endpoint: Sensitivity analysis

Age group	Endpoint	Sustained crossover	CV−BC diff 5y	CV−BC diff 10y
70–79	Full CV (665 events)	13.6 y (exploratory)	−1.6 pp	−2.5 pp
70–79	Heart-only (541 events)	None within 15 y	−2.6 pp	−4.9 pp
≥80	Full CV (665 events)	From diagnosis	+4.6 pp	+14.6 pp
≥80	Heart-only (541 events)	3.0 y	+1.3 pp	+10.1 pp

The restricted endpoint counts deaths coded solely as diseases of the heart (541 of 665 cardiovascular deaths); the remaining 124 deaths (cerebrovascular disease, hypertension without heart disease, atherosclerosis, aortic aneurysm and dissection, and other arterial diseases) were reclassified as other-cause deaths. The crossover in men aged 80 years or older persisted, whereas the 70–79-year crossover did not occur within the follow-up period, supporting a cautious, exploratory interpretation of that finding. **Abbreviations**: BC, breast cancer; CV, cardiovascular; diff, difference; pp, percentage points.

Table S4. Period-specific cause-specific HRs (retain surv ≥ 0; events reconcile to 665)

Age (ref 60–69)	0–5 y	5–10 y	>10 y
70–79	2.08 (1.51–2.87)	2.06 (1.39–3.05)	3.21 (2.13–4.83)
≥80	6.68 (4.95–9.01)	11.61 (7.97–16.89)	10.83 (6.01–19.50)
Regional stage	1.37 (1.10–1.70)	1.20 (0.91–1.59)	1.04 (0.73–1.48)

CV events per period: 334 (0–5 years), 199 (5–10 years), 132 (>10 years); total: 665. **Abbreviations:** CV, cardiovascular; HR, hazard ratio; ref, reference category; surv, survival time.

Table S5. Fine-gray subdistribution-hazard model for cardiovascular mortality (complementary to the cause-specific model) in the non-metastatic cohort

Covariate	**sHR**	**95% CI**	***p***
Age <60 (ref 60–69)	0.36	0.27–0.49	<0.001
Age 70–79	1.90	1.54–2.34	<0.001
Age ≥80	4.08	3.32–5.02	<0.001
Regional stage (ref localized)	1.08	0.92–1.25	0.346
Unmarried (ref married)	1.11	0.95–1.31	0.193
White (ref Black)	0.81	0.64–1.03	0.088
Other race	0.73	0.47–1.14	0.166
Unknown race	0.72	0.18–2.81	0.635

n = 6702; 665 events. A Fine–Gray model with robust standard errors was employed. Age remained strongly associated with cardiovascular mortality, whereas the associations with disease stage and marital status were attenuated to non-significance. This finding is consistent with the methodological distinction between cause-specific (etiologic) and subdistribution (absolute-risk) hazard models. **Abbreviations:** CI, confidence interval; ref, reference category; sHR, subdistribution hazard ratio.

Table S6. Descriptive treatment sensitivity model (not interpreted etiologically)

Covariate	HR	95% CI	*p*
Age ≥80 (ref 60–69)	7.15	5.70–8.96	<0.001
Surgery (ref no/unknown)	0.49	0.37–0.64	<0.001
Radiotherapy (ref no/unknown)	0.76	0.62–0.93	0.009
Chemotherapy (ref no/unknown)	0.72	0.58–0.89	0.002

Full model *n* = 6702; 665 events. Treatment associations most plausibly reflect confounding by indication. **Abbreviations**: CI, confidence interval; HR, hazard ratio.

Table S7. Conditional (landmark) 10-year incidence.

Landmark	At risk	10y BC (%)	10y CV (%)
At diagnosis	6702	16.0	10.8
1-year survivors	6010	16.5	10.8
3-year survivors	4781	16.4	11.2
5-year survivors	3652	14.6	12.3

Abbreviations: BC, breast cancer; CV, cardiovascular.

Table S8. Subtype-specific cumulative incidence of breast-cancer and cardiovascular mortality in non-metastatic men diagnosed 2010–2022 (*n* = 4005)

Molecular subtype	*n*	BC deaths	CV deaths	BC 5-y (%)	CV 5-y (%)	BC 10-y (%)	CV 10-y (%)
HR+/HER2−	3483	291	225	7.8	5.4	14.1	11.0
HR+/HER2+	435	61	26	12.6	5.4	23.3	10.0
HR−/HER2+	24	3	0	NE	NE	NE	NE
Triple-negative (HR−/HER2−)	63	10	0	16.7	NE	20.2	NE

Cumulative incidence was estimated using the Aalen–Johansen estimator, which accounts for competing risks. Molecular subtype was defined by SEER-derived hormone-receptor and HER2 status, available from 2010 onward. These stratified analyses are exploratory and hypothesis-generating. **Abbreviations:** BC, breast cancer; CV, cardiovascular; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; NE, not estimable (fewer than five events of the relevant cause).

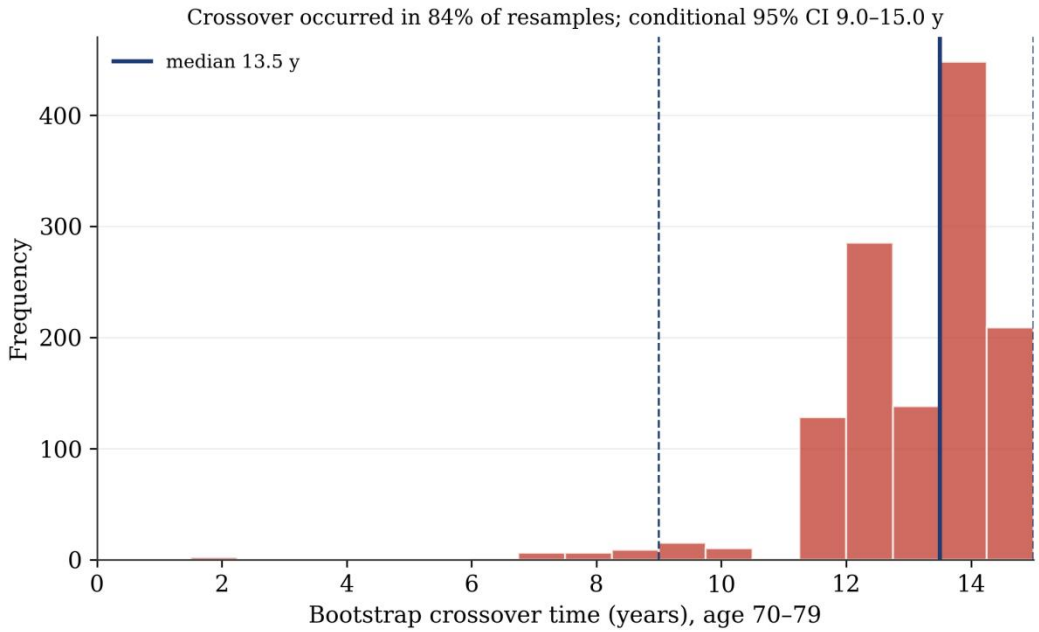


Figure S1. Bootstrap distribution of the sustained cardiovascular–breast cancer mortality crossover time in men aged 70–79 years. The histogram shows the conditional distribution of crossover times among 2000 patient-level bootstrap resamples in which cardiovascular cumulative incidence remained at or above breast cancer cumulative incidence through the 15-year follow-up horizon. A sustained crossover occurred in 84% of resamples. The solid vertical line indicates the conditional median crossover time of 13.5 years, and the dashed vertical lines indicate the 2.5th and 97.5th percentiles of the distribution (9.0–15.0 years). Because the estimated crossover lies beyond the primary 10-year horizon and is based on a declining late follow-up risk set, it should be interpreted as exploratory. **Abbreviation:** CI, confidence interval.

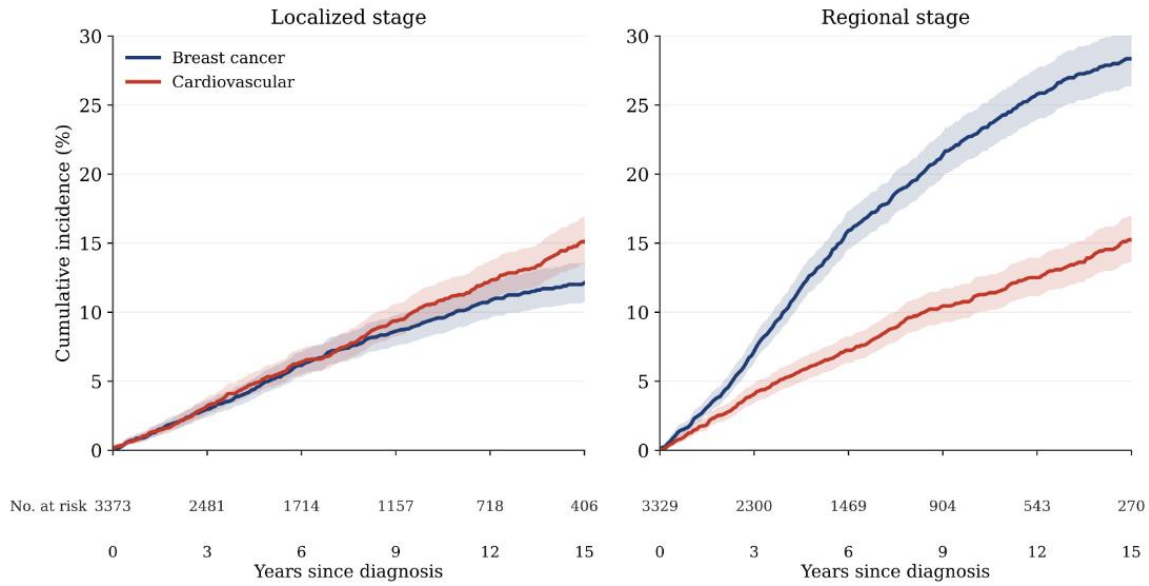


Figure S2. Stage-stratified cumulative incidence of breast cancer and cardiovascular mortality in men with non-metastatic breast cancer. Aalen–Johansen estimates compare the cumulative incidence of breast cancer–specific and cardiovascular death over 15 years of follow-up in patients with localized and regional disease. Solid lines represent cumulative incidence estimates, shaded areas indicate 95% CIs, and the numbers below each panel indicate patients remaining at risk at the corresponding time points. In localized disease, cardiovascular cumulative incidence gradually approached and subsequently exceeded breast cancer cumulative incidence, whereas breast cancer mortality remained consistently higher in regional disease. **Abbreviation:** CI, confidence interval.

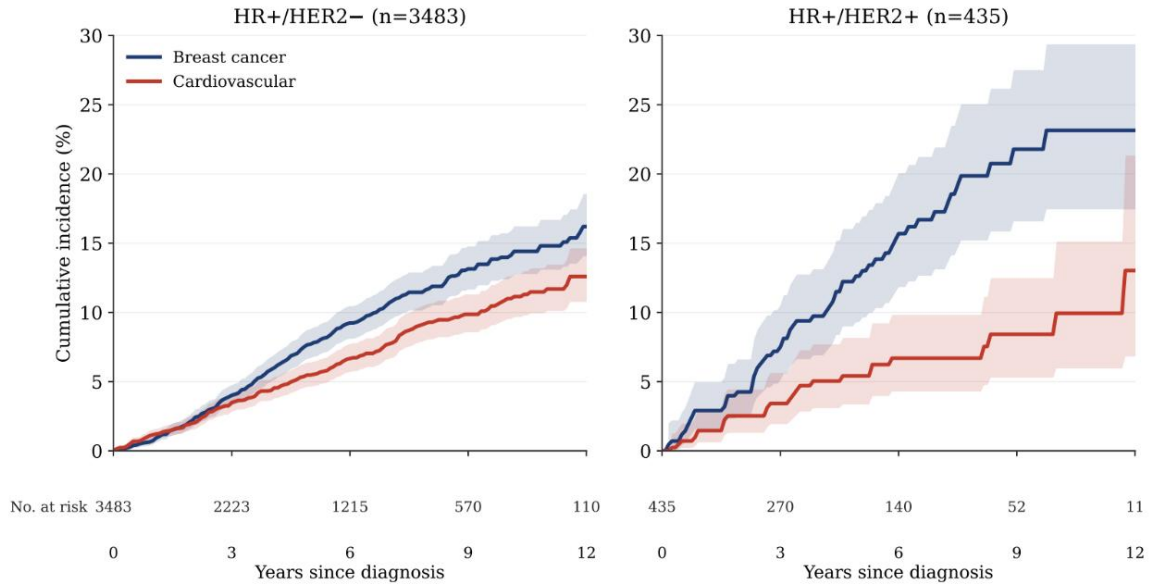


Figure S3. Molecular subtype–stratified cumulative incidence of breast cancer and cardiovascular mortality in men with non-metastatic breast cancer. Aalen–Johansen estimates compare the cumulative incidence of breast cancer–specific and cardiovascular death over 12 years of follow-up among men with hormone receptor–positive/human epidermal growth factor receptor 2–negative tumors (n = 3483) and hormone receptor–positive/human epidermal growth factor receptor 2–positive tumors (n = 435) diagnosed during 2010–2022. Solid lines represent cumulative incidence estimates, shaded areas indicate 95% CIs, and the numbers below each panel indicate patients remaining at risk at the corresponding time points. Breast cancer cumulative incidence remained higher than cardiovascular cumulative incidence in both subtypes; estimates for the hormone receptor–positive/human epidermal growth factor receptor 2–positive subgroup were less precise because of the smaller cohort and sparse late follow-up. **Abbreviations:** CI, confidence interval; HER2, human epidermal growth factor receptor 2; HR, hormone receptor.