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# Mortality in HER2-positive male breast cancer between 2010 and 2022: A population-based study.

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## Background

- 13% of all breast cancers (BC) in men are HER2-positive.
- Men with HER2-positive BC have worse prognosis compared to women with HER2-positive disease.
- Despite advances in HER2-positive BC treatment over recent years, it remains unclear whether mortality rates have decreased in men as they have in women.

## Objective

- **To compare breast cancer-specific mortality (BCSM) between men and women with HER2-positive BC and evaluate changes in BCSM in each sex over time.**

## Materials and Methods

- We evaluated men and women diagnosed with HER2-positive invasive BC between 2010 and 2022, reported in the Surveillance, Epidemiology, and End Results registry.
- Patients were categorized into 2 groups by year of diagnosis: 2010-2015, and 2016-2022.
- BCSM was estimated by cumulative incidence function and differences between groups were compared by Gray's test.
- Adjusted Fine and Gray model was used to compare BCSM between men and women.
- Stratified adjusted Fine and Gray models were fitted for each sex to assess whether there was an association between year of diagnosis and BCSM.
- In all BCSM analyses, deaths from causes other than BC were treated as competing event.

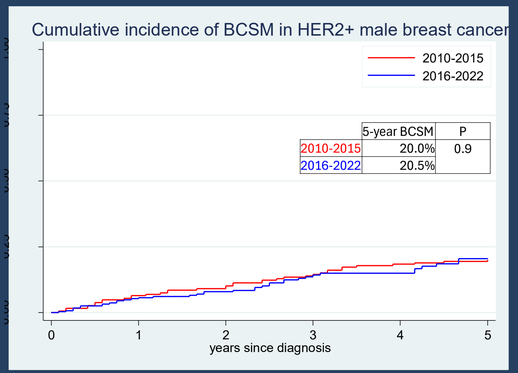
## Results

- We included 483 men (2010-2015: N=189, 2016-2022: N=294) and 85,693 women (2010-2015: N=36,578, 2016-2022: N=49,115) diagnosed with HER2-positive BC.
- Median follow-up for 2010-2015 was 9.4 years in men and 9.5 years in women; for 2016-2022 was 3.4 years in men and 3.3 years in women.
- In adjusted Fine and Gray models evaluating year of diagnosis as a continuous variable, each successive year of diagnosis had no significant association with BCSM in men (aSHR, 0.99; 95% CI, 0.91-1.08; p=0.9), but a significant association with BCSM in women (aSHR, 0.97; 95% CI, 0.96-0.98; p<0.001).
- Women had significant improvement in BCSM across both stage I-III and IV, and across HR+ and HR- disease, whereas men had no significant improvements.
- OS analyses showed similar results as those from BCSM for both sexes.

## Limitations

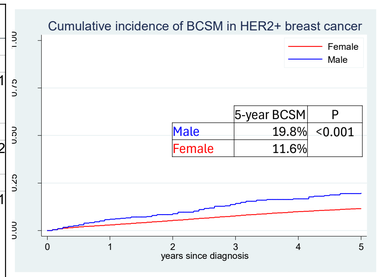
- Detailed systemic therapy regimen information and treatment adherence are unavailable.
- Later years of diagnosis have shorter follow-up.

# **Survival** of **men** with **HER2+** breast cancer **has not improved** since **2010**.




## Table 1. Patient Characteristics

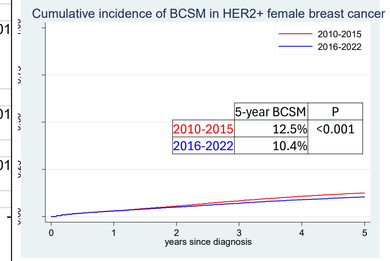
| | Female N | Female % | Male N | Male % | p value |
|---|---|---|---|---|---|
| **All patients** | 85693 | 99.4% | 483 | 0.6% | |
| **Age at diagnosis, y** | | | | | |
| <50 | 25868 | 30.2% | 81 | 16.8% | <0.001 |
| 50-64 | 35194 | 41.1% | 193 | 40.0% | |
| >64 | 24631 | 28.7% | 209 | 43.3% | |
| **Period of diagnosis** | | | | | |
| 2010-2015 | 36578 | 42.7% | 189 | 39.1% | 0.12 |
| 2016-2022 | 49115 | 57.3% | 294 | 60.9% | |
| **Race and Ethnicity** | | | | | |
| Non-Hispanic White | 49693 | 58.0% | 329 | 68.1% | <0.001 |
| Non-Hispanic Black | 10256 | 12.0% | 76 | 15.7% | |
| NHAIAN | 633 | 0.7% | 2 | 0.4% | |
| NHAPI | 10794 | 12.6% | 34 | 7.0% | |
| Hispanic (All Races) | 13846 | 16.2% | 37 | 7.7% | |
| Unknown | 471 | 0.5% | 5 | 1.0% | |
| **Grade** | | | | | |
| I | 3543 | 4.1% | 14 | 2.9% | 0.03 |
| II | 29979 | 35.0% | 195 | 40.4% | |
| III/IV | 45414 | 53.0% | 237 | 49.1% | |
| Unknown | 6757 | 7.9% | 37 | 7.7% | |
| **Stage** | | | | | |
| I | 35982 | 42.0% | 164 | 34.0% | <0.001 |
| II | 26484 | 30.9% | 128 | 26.5% | |
| III | 10642 | 12.4% | 87 | 18.0% | |
| IV | 7845 | 9.2% | 71 | 14.7% | |
| Unknown | 4740 | 5.5% | 33 | 6.8% | |
| **Hormone receptor** | | | | | |
| HR+/HER2+ | 59760 | 69.7% | 456 | 94.4% | <0.001 |
| HR-/HER2+ | 25647 | 29.9% | 27 | 5.6% | |
| HR unknown/HER2+ | 286 | 0.3% | 0 | 0.0% | |
| **Surgery** | | | | | |
| No surgery | 11142 | 13.0% | 92 | 19.0% | <0.001 |
| Partial mastectomy | 36649 | 42.8% | 51 | 10.6% | |
| Mastectomy | 37597 | 43.9% | 338 | 70.0% | |
| Unknown | 305 | 0.4% | 2 | 0.4% | |
| **Radiation** | | | | | |
| No or Unknown | 42779 | 49.9% | 328 | 67.9% | <0.001 |
| Yes | 42914 | 50.1% | 155 | 32.1% | |
| **Chemotherapy** | | | | | |
| No or Unknown | 20033 | 23.4% | 148 | 30.6% | <0.001 |
| Yes | 65660 | 76.6% | 335 | 69.4% | |
| **Status** | | | | | |
| Alive | 71269 | 83.2% | 321 | 66.5% | |
| Dead - breast cancer | 9740 | 11.4% | 94 | 19.5% | |
| Dead - other cause | 4404 | 5.1% | 64 | 13.3% | |
| Dead - unknown cause | 280 | 0.3% | 4 | 0.8% | |




## Table 2. Multivariable Fine and Gray Regression for BCSM

| Variable | Subdistribution hazard ratio | 95.0% CI for hazard ratio Lower | Upper | *P* |
|---|---|---|---|---|
| **Sex (Male vs Female)** | 1.3 | 1.02 | 1.68 | 0.038 |

Adjusted for: Age at diagnosis, Year of diagnosis, Race, Grade, Histology, Stage, Surgery, Radiation, Chemotherapy, HR status, Marital status, Income, Rurality and Region




## Conclusions

- **Men with HER2-positive BC exhibit significantly worse BCSM compared to women.**
- **Since 2010, BCSM has not improved in men with HER2-positive disease, contrasting with the observed reductions in BCSM among women.**
- **Our findings underscore the substantial unmet medical needs for this population.**

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