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Survival Outcomes and Tumor Site Distribution by Molecular Subtype in Breast Cancer Patients Under 40

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Abstract

- Breast cancer screening generally starts at age 40, potentially delaying detection in younger women.
- Women under 40 face unique risks, often with late-stage diagnosis, resulting in poor outcomes.
- Molecular subtype distribution in this population remains underexplored.
- Survival outcomes and tumor-site patterns in younger patients remain insufficiently defined, highlighting an important opportunity to better identify early warning signs, refine risk-stratified treatment strategies, and improve patient counseling

Introduction

- Breast cancer in women under 40 is uncommon but clinically significant, accounting for only 5–7% of diagnoses yet contributing disproportionately to morbidity and mortality.
- Younger patients frequently present with aggressive tumor biology, higher-grade disease, and a greater likelihood of delayed detection due to age-based screening practices that typically begin at 40.
- Prior studies show that molecular subtype, reflecting hormone receptor and HER2 status, strongly influences prognosis; however, the survival patterns and tumor-site distributions of these subtypes in very young women remain insufficiently characterized.
- **Comprehensive population-level analyses of subtype-specific survival outcomes in women under 40, and how these patterns compare with those aged 40–50, are limited**.
- **Our study leverages SEER population data to evaluate molecular subtype distribution, tumor site patterns, and survival differences in young women**, with the goal of informing earlier detection strategies and refining personalized treatment approaches.

Methods and Materials

- **Data Source**: SEER-18 (2018), identifying 5,007 women <40 with invasive breast cancer after excluding incomplete records.
- **Subtypes**: Luminal A (HR+/HER2−), Luminal B (HR+/HER2+), HER2-Enriched (HR−/HER2+), Triple-Negative (HR−/HER2−).
- **Age Groups: 15–29, 30–39.**
- **Analyses**: Chi-square tests for subtype and tumor-site distribution; Kaplan–Meier 5-year CSS with log-rank tests; multivariable Cox models.
- **Tumor Site**: Classified using ICD-O-3 topography codes C50.0–C50.9.
- **Post hoc Analysis**: Molecular Subtype Survival curves examined across <40, 40–44, and 45–49 years.

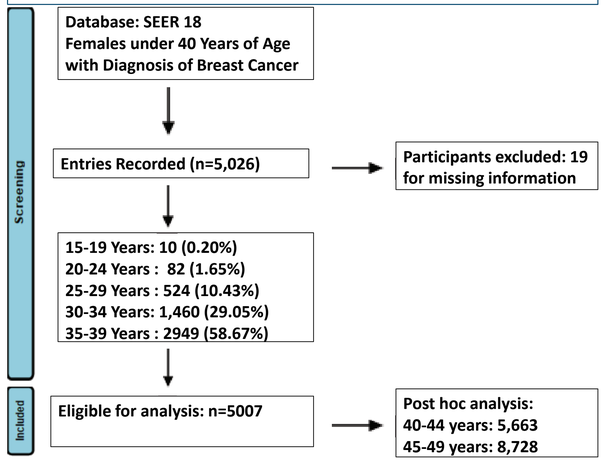


Figure 1. Study Cohort Selection

Results

- **Subtype Distribution (<40):** Luminal A was most common (52.6%), followed by Triple-Negative (18.5%), Luminal B (17.0%), HER2-Enriched (6.1%), and unclassified (5.9%).
- **Molecular Subtype Survival Outcomes**:
  - **Under 40: Luminal B shows better survival than Luminal A**, an unexpected pattern. (log-rank p < 0.0001)
  - **Ages 40–50:** Survival normalizes, with **Luminal A** regaining its expected advantage, and Triple negative continues to show worst outcomes in both groups. (log-rank p < 0.0001)
- **Tumor Site Survival Outcomes(Figure 4): Upper-outer quadrant tumors** showed the **best survival**, while **overlapping and nonspecific sites had significantly worse outcomes**, driven by aggressive subtypes. (log-rank p < 0.0001)

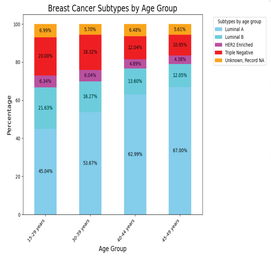


Figure 2. Breast Cancer subtypes by age Group.

Figure 3: Kaplan-Meier curves by subtype of women, different age group (A-C) diagnosed with breast cancer in 2018.

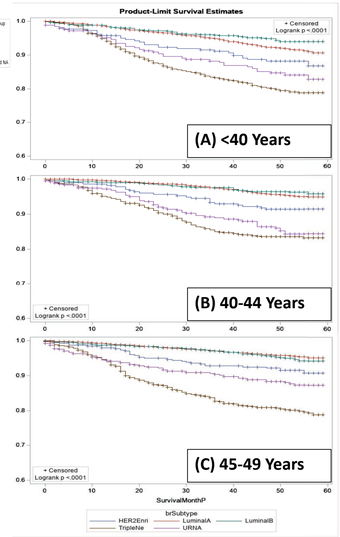
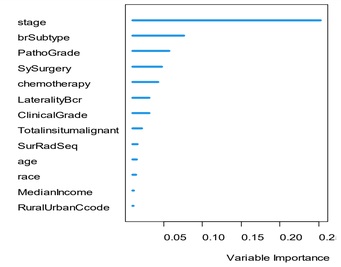


Figure 4: Survival Random Forest prediction of variable importance on breast cancer survival under 40



Discussion

- **Under 40: Luminal B shows better survival than Luminal A — a reversal of expected patterns** — likely because younger patients derive greater relative benefit from HER2-targeted therapies compared with endocrine therapy, which is **less reliable in this age group due to incomplete ovarian suppression and higher endocrine resistance.**
- **Ages 40–50: Survival patterns normalize, with Luminal A regaining its superior outcomes**, reflecting more consistent endocrine responsiveness, better ovarian function suppression, and more stable ER-driven biology as women transition toward late pre-menopause.
- **Upper-outer quadrant tumors demonstrated the most favorable survival outcomes, whereas overlapping and nonspecific primary sites showed significantly poorer survival**—largely reflecting their higher burden of aggressive subtypes such as Triple-Negative and HER2-Enriched disease.

Conclusions

- **Luminal B outperforms Luminal A in women <40, reflecting stronger benefit from modern targeted therapies.**
- **Triple-Negative remains the deadliest subtype,** underscoring the need for earlier detection and novel treatments.
- Young-age breast cancer requires **subtype-driven, personalized care that accounts for biology, genetics, and fertility goals.**

Contact

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