Association of polygenic-based breast cancer risk prediction with patient management

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Background

- Tyzer-Cuzick (TC)[1] is a validated risk model that estimates BC risk.
- Combining TC with a polygenic risk score ("combined risk score" or CRS) improves prediction accuracy.[2]
- Guidelines recommend individuals with a ≥20% lifetime risk of breast cancer (BC) undergo enhanced management,[3] including:
  - Annual screening mammography (SM)
  - Annual breast magnetic resonance imaging (MRI)
  - Genetic counseling (GC)

Objective:

Evaluate the association between CRS and TC results and patient management in a real-world cohort

Methods

- TC and CRS results were linked with claims data from the Optum Labs Data Warehouse using a tokenization.

Figure 2. Dataset development

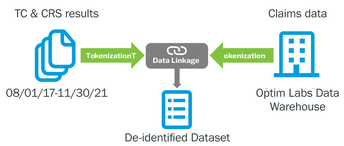


Table 1. Inclusion and exclusion criteria

Patients included if

- Age 18 years AND they had continuous medical and pharmacy enrollment for ≥360 days prior to AND after the CRS result.

Patients excluded if they had

- A history of breast malignancy or BC.
- Any metastatic cancer during baseline.
- Evidence of BC prevention measures prior to receiving CRS results.
- Evidence of any cancer diagnosis in the >360 days after receiving CRS results.

Figure 3. Four subgroups were created based on their lifetime risk prediction

- "+" indicates high risk (≥20%) by CRS and/or TC. "-" indicates average risk (<20%) by CRS and TC.

CRS+ TC+ | CRS+ TC– | CRS– TC+ | CRS– TC–

Results

- The total cohort and subgroups are shown in **Figure 4**.
- Patients with high risk (CRS+ and/or TC+) had an increase uptake of enhanced management when compared to average risk patients (CRS– TC–) (**Figure 5**).
- Patients were 1.9 to 2.4x more likely to have SM at age <40 if high risk, with those who were CRS+ being 2.2 to 2.4x more likely (**Figure 5**).
- Patients were 7.9 to 13.8x more likely to have breast MRI at age <40 if high risk, with those who were CRS+ being 8.4 to 13.8 more likely (**Figure 5**).
- Patients were 2.4 to 3.2x more likely to to receive genetic counseling if high risk, with those who were CRS+ being 2.9 to 3.2x more likely (**Figure 5**).

Figure 4. Risk categorization

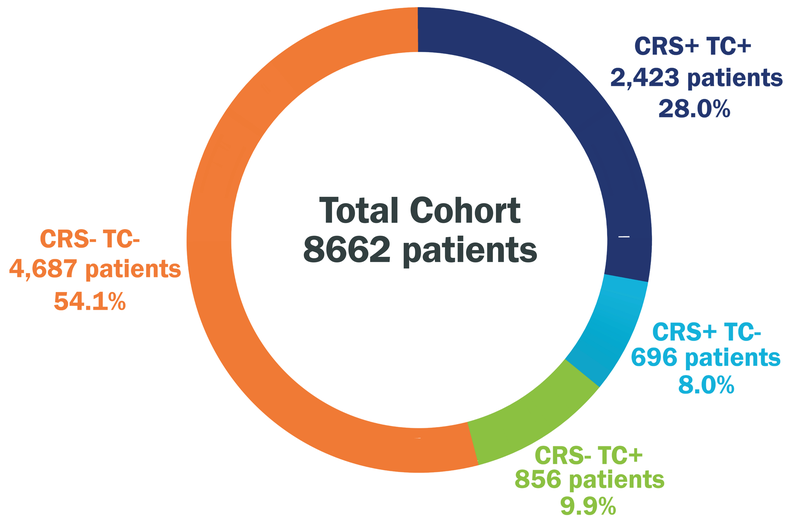
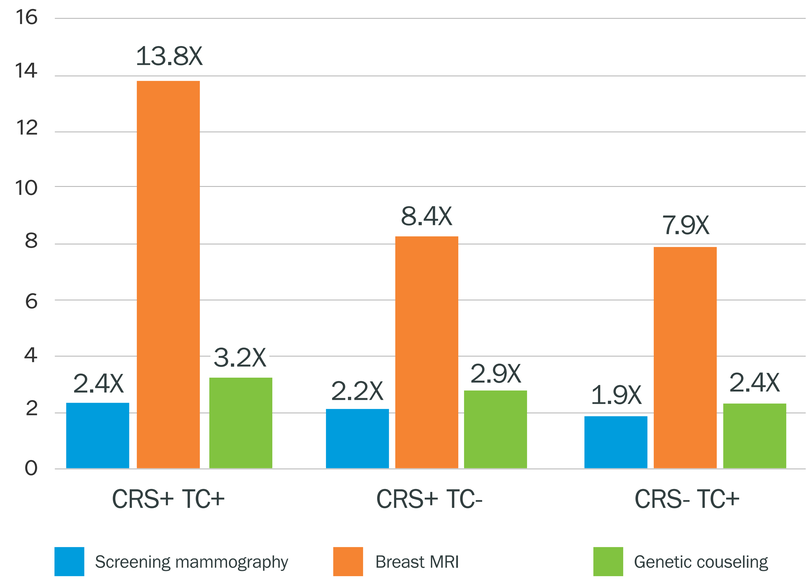


Figure 5. Rates per 1,000 person-days of screening relative to CRS-TC-, variable follow up period



Conclusions

- CRS predicted a different risk level than TC for a substantial proportion of patients.
- Those with CRS+ and/or TC+ undertook screening consistent with guidelines.
- Clinicians appeared to rely on CRS+ results to guide enhanced management.

Refernces: 1. Tyrer J, et al. Statistics in Medicine. 2004;23(7):1111-1130. 2. Mabey B, et al. Genetics in Medicine. 2024;26(7):101128. 3. NCCN Breast Cancer Screening and Diagnosis, V4.2024 4. Johansen Taber, et al. JCO Precision Oncology. 2025; 9:e2400716

Disclosures: Authors who are current employees of Myriad Genetics, Inc., receive salary and stock as compensation.

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