

Treatment Patterns, Overall Survival (OS), and Healthcare Resource Utilization (HCRU) among Patients with HER2-Positive (HER2+), High- or Intermediate-Risk, Early-Stage Breast Cancer (eBC) in Canada

Winson Cheung^{1-3*}, Simran Shokar,⁴ Matthew Warkentin,^{1,2} Zhor Senhaji-Mouhri⁴, Anna Parackal-Rochard⁴, Jan-Willem Henning²

¹Oncology Outcomes Initiative, University of Calgary, Calgary, AB, Canada;

²Department of Oncology, University of Calgary, Calgary, AB, Canada;

³Alberta Health Services, Calgary, AB, Canada;

⁴AstraZeneca Canada Inc., Mississauga, ON, Canada

*Corresponding author

Objective

- We conducted an observational cohort study in Alberta, Canada to characterize the current treatment landscape, OS, and HCRU among patients with HER2+ high- or intermediate-risk eBC, who are eligible for NAT.

Conclusions

- Patients with high-risk, HER2+ eBC had shorter 5-year survival rates than intermediate-risk, signalling an unmet need among these patients.
- Most patients who were NAT-eligible had high-risk disease, but only half of these patients received NAT; less than a quarter of the neoadjuvant-eligible intermediate-risk patients received NAT.
- Irrespective of risk, patients treated with NAT had better survival relative to patients who were not treated with NAT.
- This study reinforced the importance of NAT for eligible patients to achieve optimal clinical outcomes.
- As novel NATs become available, the improved survival rates and short-term HCRU needs that may be anticipated with further adoption of NAT use should be thoughtfully considered in future healthcare system planning and resource allocation.

Plain language summary

- Why did we perform this research?**
- To understand what treatments are used in the real world for patients with HER2-positive early breast cancer who are considered high or intermediate risk. These are patients who are more likely to have their cancer come back due to many reasons including their tumor size and the involvement of lymph nodes.
 - To understand long-term survival from diagnosis by risk status and to understand use of healthcare services after treatment.
- How did we perform this research?**
- We analyzed cases from a cancer registry in Alberta, Canada, combining them with pharmacy and administrative records to study treatment use, survival, and healthcare services use.
- What were the findings of this research?**
- About 50% of high-risk and 20% of intermediate-risk patients received neoadjuvant therapy (treatment before surgery), with a higher survival rate at 5 years if they received NAT. Healthcare services use is highest in the first year from starting neoadjuvant treatment.
- What are the implications of this research**
- As new neoadjuvant therapies become available, the benefits of improved survival and healthcare services use should be considered in healthcare planning and decision-making.

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Introduction

- Breast cancer is the most common cancer and second leading cause of cancer death among women in Canada.¹
- More patients are being diagnosed with early-stage breast cancer due to improved screening efforts.²
- HER2 is overexpressed in approximately 15-20% of breast cancers and is associated with increased cancer growth rate and metastases while decreasing overall survival.³⁻⁵
- The prognosis for patients with HER+ eBC has improved with the expansion of HER2-directed therapies to eBC.⁶
- Patients with high or intermediate-risk breast cancer (large tumors or positive nodal status) may benefit from HER2-directed NAT, which can be used to reduce tumor size, assess treatment response, and allow for breast-conserving surgery where it was initially not possible.⁷
- Although trials have shown pathological complete response rates of 60% or more, not all patients will reach a pathological complete response following NAT.^{8,9}
- Treatment pathways, clinical outcomes, and HCRU are largely unknown among NAT-eligible patients with HER2+, high- or intermediate-risk eBC.

Results

Baseline Characteristics

- In total, we identified 1,342 (63.4%) NAT-eligible women diagnosed with HER2+ eBC among all HER2+ eBC cases.
- Mean (SD) age was 54.9 (13.0) years and mean follow-up was 4.5 (2.3) years.
- Among them, 990 (73.8%) were considered high-risk and 352 (26.2%) were considered intermediate-risk.
- 50.4% of eligible high-risk patients received NAT while 19.9% of eligible intermediate risk patients received NAT over the study period.

Table 1. Patient characteristics for HER+ eBC in Alberta, 2013-2020

Variable	Level	Overall
n		1342
Sex	Female	1324 (100%)
Year of diagnosis	2013 - 2014	320 (23.9%)
	2015 - 2016	325 (24.2%)
	2017 - 2018	347 (25.9%)
	2019 - 2020	350 (26.1%)
Stage at diagnosis	1A, 1B	215 (16.1%)
	2A, 2B	762 (56.8%)
TNM risk group	High	990 (73.8%)
	Intermediate	352 (26.2%)
Vital status*	Alive	1192 (88.8%)
	Deceased	150 (11.2%)
Treatment facility	Rural	187 (13.9%)
	Urban	1155 (86.1%)

*Proportion of patients alive/deceased at the end of the study period

Abbreviations

HER2: Human epidermal growth factor receptor 2
 NAT: Neoadjuvant therapy
 OS: Overall survival
 HCRU: Healthcare resource utilization
 eBC: Early-stage breast cancer

Treatment Patterns

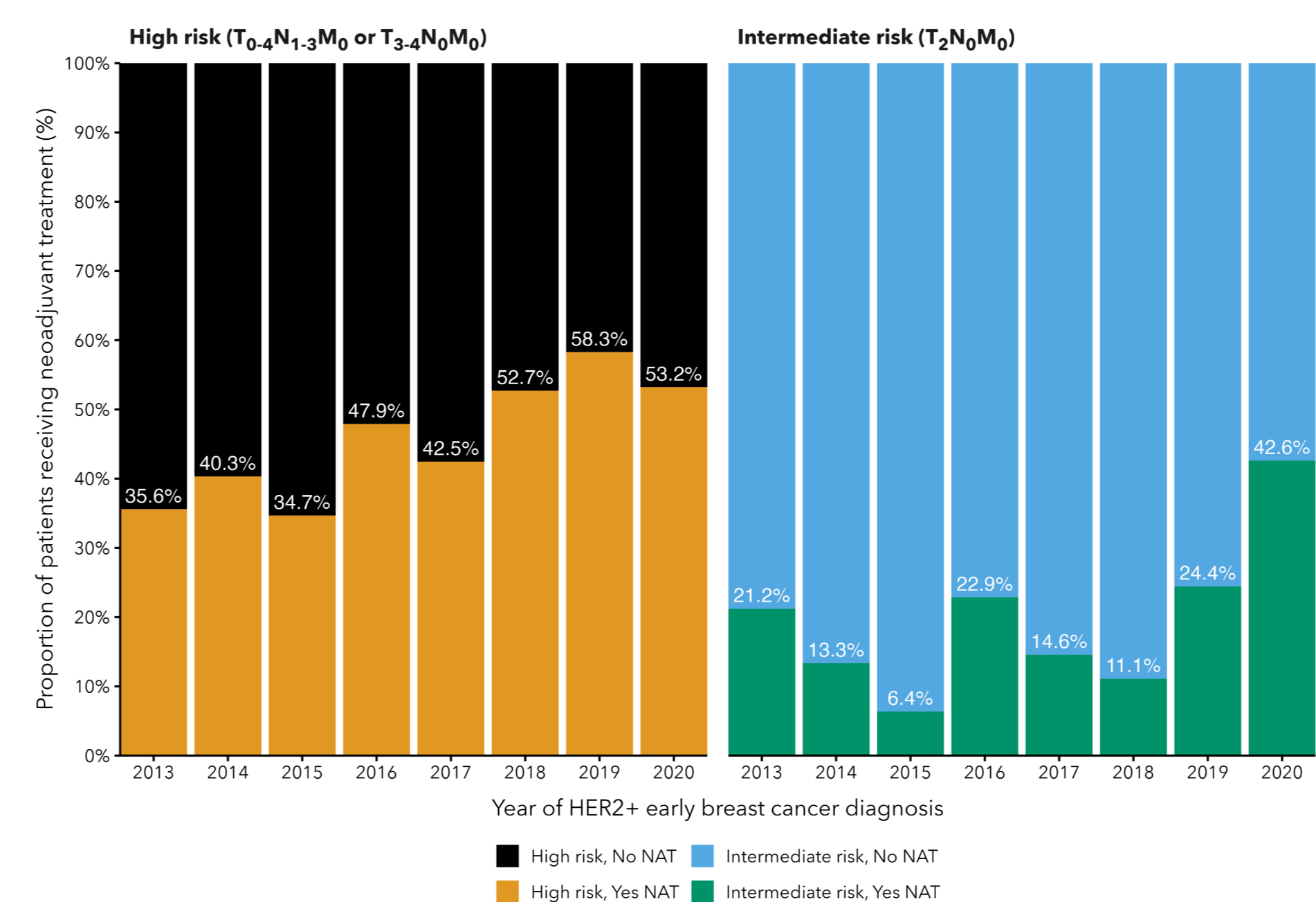
- The most frequently used NAT in the high-risk group was chemotherapy plus HER2-directed therapy (without anthracycline).

Table 2. Number and proportion of patients by type of NAT in the high-risk group

NAT type	Overall
Chemotherapy + HER2-directed	264 (58%)
Chemotherapy + HER2-directed + Anthracycline	178 (39%)
Chemotherapy +/- Anthracycline	12 (3%)

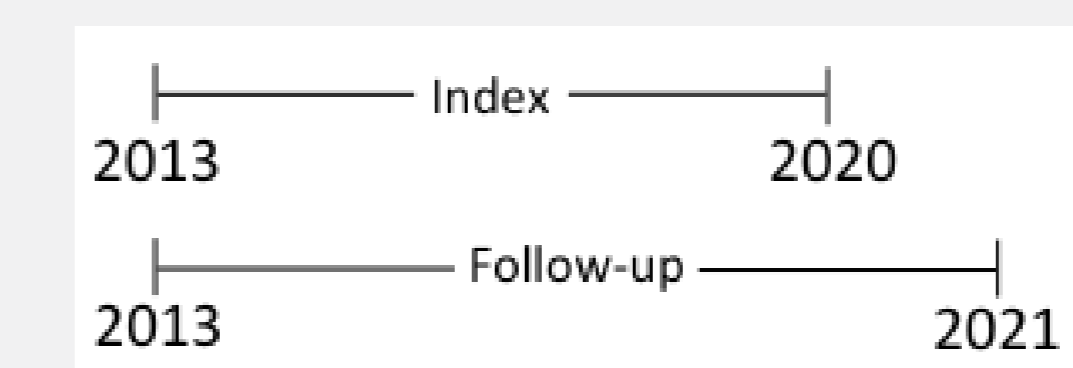
- The proportion of patients treated with NAT increased from 35.6% in 2013 to 53.2% in 2020 in the high-risk group.
- The proportion of patients treated with NAT increased from 21.2% in 2013 to 42.6% in 2020 in the intermediate-risk group.

Figure 1. Prevalence of NAT among NAT-eligible patients with HER2+ eBC



Methods

- NAT-eligible HER2+ eBC cases diagnosed between 2013 and 2020 were identified (as defined by international guidelines) from the population-based cancer registry in Alberta, Canada, and followed up until December 2021.

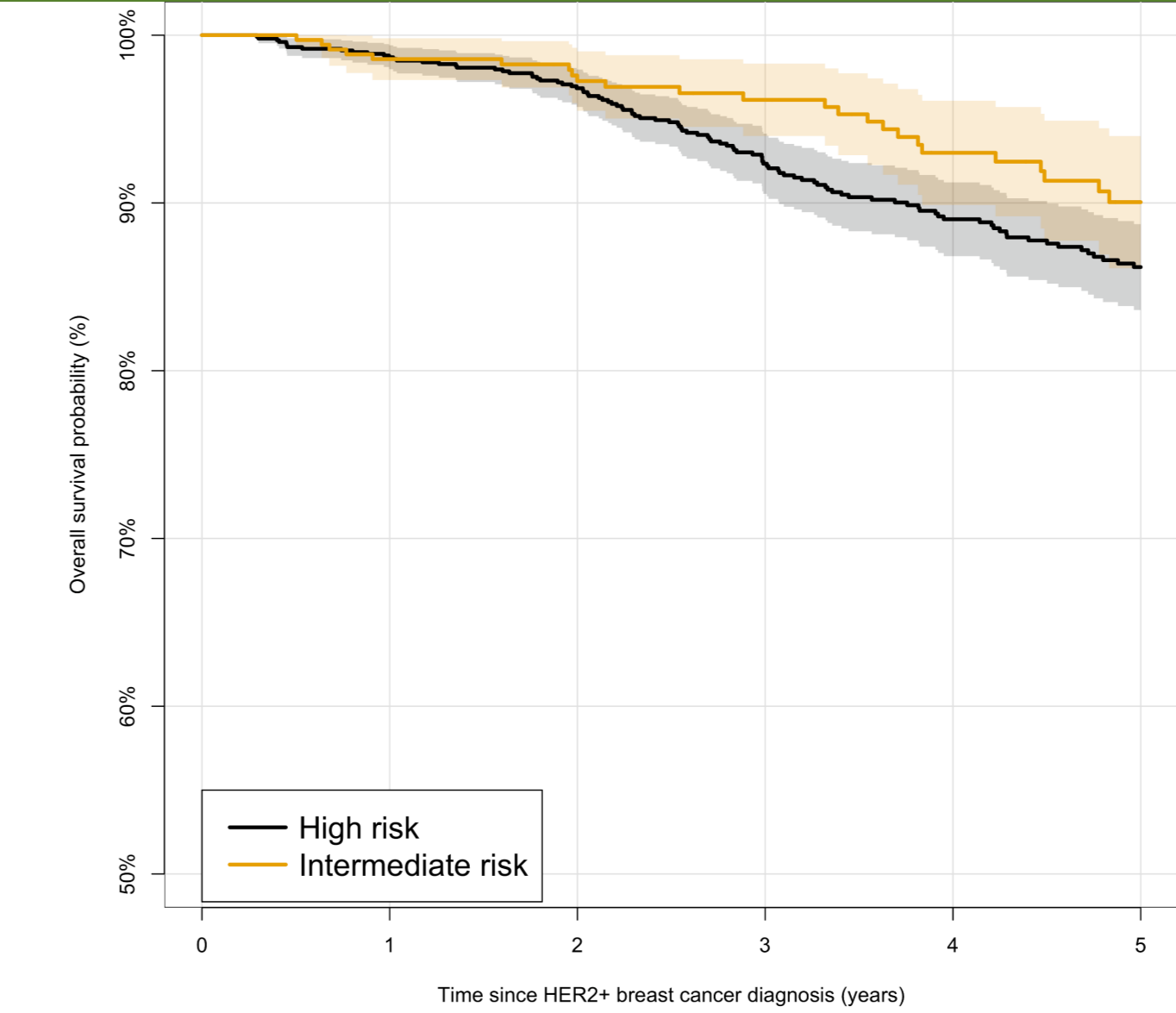


- NAT-eligible patients included high-risk individuals defined as those with T₀₋₄N₁₋₃M₀ or T₃₋₄N₀M₀ tumors and intermediate-risk as those with T₂N₀M₀ tumors.

Overall Survival

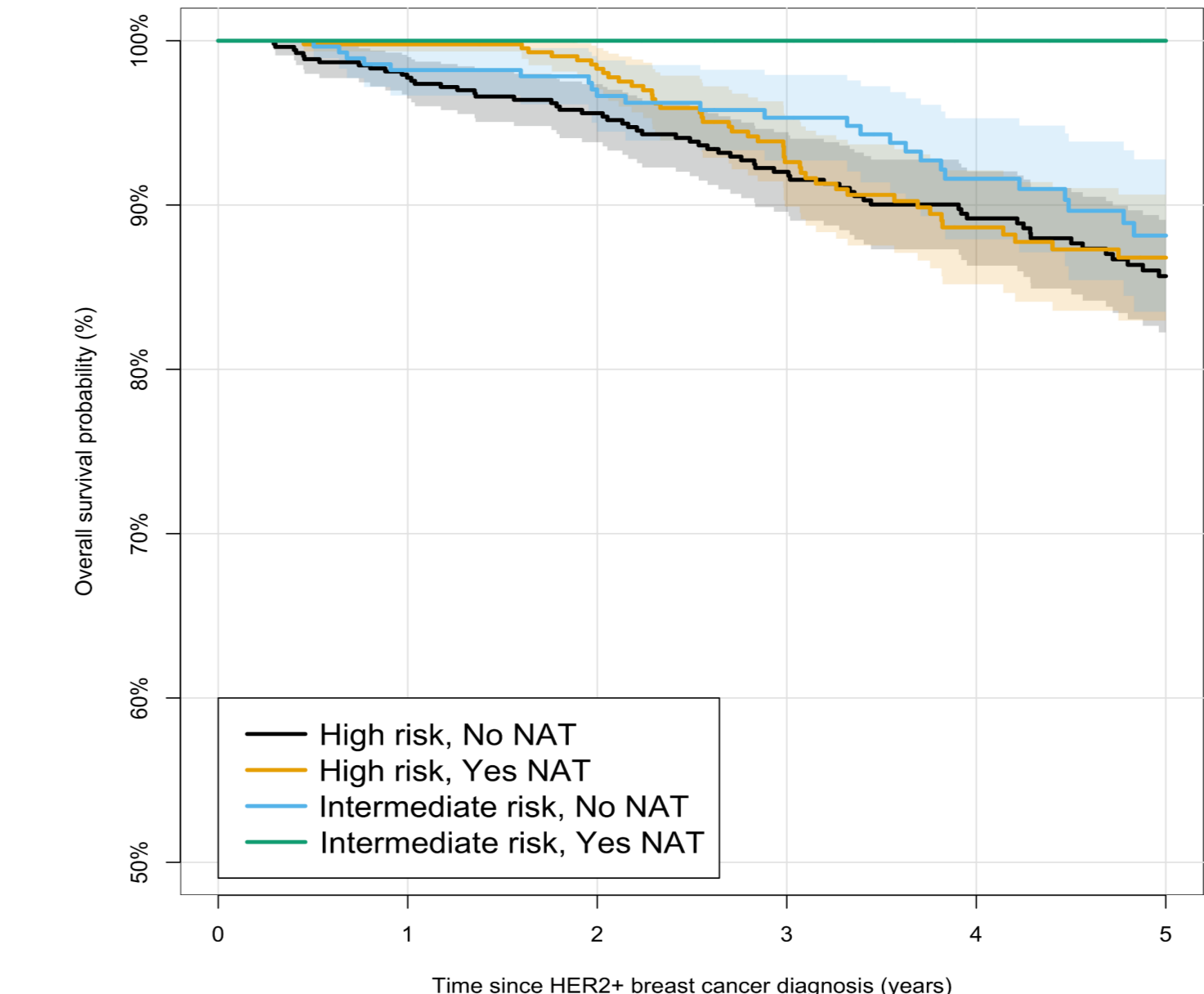
- 5-year OS rates (95% CI) for patients with high-risk eBC were 86.2% (83.6-88.7) and 90.0% (86.2-94.1) for patients with intermediate-risk eBC.

Figure 2. K-M curves for OS among patients with HER2+ eBC stratified by risk group



- 5-year OS rates were higher among patients treated with NAT relative to those that did not receive NAT regardless of risk group (86.6% and 100% in the treated high- and intermediate-risk patients vs 85.7% and 88.1% in the untreated high- and intermediate-risk patients, respectively).

Figure 3. K-M curves for OS among patients with HER2+ eBC stratified by risk group and receipt of NAT



- Cases were merged with pharmacy records and administrative data to determine systemic therapy use and frequency of acute care encounters.
- A descriptive analysis was applied to characterize outcomes.
- The patient population included all patients (18 years or older) treated for cancer with an HER2+ tumour, classified as IHC3+ or IHC2+/ISH-.
- Demographic and clinical characteristics of the cohort were reported using the appropriate descriptive statistics.
- Kaplan-Meier (K-M) estimates were used to examine time to event outcomes, including OS.
- HCRU was assessed in high-risk patients who received NAT.

Healthcare Resource Utilization

- For high-risk patients who received NAT, clinic appointments (mean 15.4 per patient) and emergency department visits (mean 1.8 per patient) were most intense during the first year of follow up.
- For these patients, the frequency of total visits decreased in subsequent years (17.26 visits per patient in year 1 vs 2.38 visits per patient in year 9).
- Overall, there were more non-emergency visits compared to emergency visits for these patients.

Table 4. HCRU for high-risk HER2+ eBC patients in Alberta

	Total alive	HSP rate	EMRG rate	Non-EMRG rate	Total visits rate
Year 1	454	0.88	1.84	15.42	17.26
Year 2	453	0.26	0.73	4.77	5.50
Year 3	383	0.26	0.70	3.44	4.14
Year 4	291	0.24	0.61	3.01	3.62
Year 5	206	0.13	0.68	2.39	3.07
Year 6	164	0.09	0.48	2.43	2.91
Year 7	111	0.13	0.65	2.22	2.86
Year 8	76	0.18	0.61	2.20	2.80
Year 9	32	0.13	0.50	1.88	2.38

*HSP: Hospitalizations, EMRG: Emergency visits; Rate reported as visits per patient per year

Limitations

- The administrative databases used in this study only include patients with cancer treated in Alberta, Canada.
- The study may be susceptible to misclassification bias due to coding errors from using administrative health records.
- Residual confounding may be present as variables such as comorbidities are not captured in administrative databases.



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