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Characteristics and Management of Diffuse Large B-Cell Lymphoma Cases in New Brunswick



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Executive Summary

Research Objectives

This study provides the first population-level examination of Diffuse Large B-Cell Lymphoma (DLBCL) in New Brunswick from 2006 to 2021. Two primary objectives were addressed:

Part 1 **Characterize the DLBCL population:** Describe disease burden through prevalence, incidence, and mortality rates, patient demographics, and comorbidity profiles.

Part 2 **Examine treatment pathways and outcomes:** Describe real-world treatment pathways (first- through third-line therapies), survival outcomes, healthcare resource utilization, and reasons for treatment discontinuation.

Study Overview and Methods

The primary data used in this study were linked, population-level administrative data accessed through DataNB, supplemented with clinical chart data from New Brunswick's two Regional Health Authorities (Horizon and Vitalité Health Networks). Part 1 of the study examined all DLBCL cases identified in New Brunswick from 1992 to 2021 (n=1,861), while Part 2 focused on a treatment cohort (for which IV chemotherapy treatment data were available) diagnosed between 2006 and 2018 (n=455-460) over a 5-year follow-up period.

Analyses included descriptive statistics for epidemiological trends and patient characteristics, Kaplan-Meier survival analysis, and Cox proportional hazards modeling to identify mortality predictors. Treatment regimens were categorized based on IV chemotherapy combinations, with transitions between therapy lines defined by changes in drug combination composition; administration of the same drug combination following a gap of more than seven days was treated as new cycle within the same therapy line.

Key Findings

Epidemiology and population characteristics

DLBCL incidence in New Brunswick increased from 8.7 per 100,000 in 2006-2007 to 13.4 per 100,000 in 2020-2021, consistent with global trends. The prevalent population more than doubled from 365 cases in 2006-2007 to 795 in 2020-2021. The mean age at diagnosis was 66.2 years, with males comprising 54.5% of cases. Among staged cases, 28.9% presented with advanced stage 4 disease, and the majority of incident cases (68.5%) had hypertension at diagnosis. Notably, 65.5% of patients resided in lower-to-middle income neighbourhoods.

Treatment pathways and access to care

Standard R-CHOP therapy[1] was the predominant therapy, with 86.8% receiving it as first-line treatment. Only 34% of patients received second-line therapy, and 16.5% received third-line or beyond, indicating that most achieved remission with the initial treatment. Geographic disparities existed, with Vitalité patients traveling longer distances to treatment (87.4 km) compared to Horizon patients (69.3 km). The observed HSCT[2] rate (6.5%) was lower than expected based on the anticipated rate of refractory or relapsed disease (approximately 30%) – a disparity that likely reflects limited in-province transplant capacity (as out-of-province treatments are not reliably captured in the administrative data sources examined).

Survival outcomes

Five-year overall survival was 62%, comparable to international benchmarks. First-line R-CHOP therapy was associated with markedly better outcomes (72% 3-year survival) compared to other first-line regimens (49%). Cox modeling identified significant mortality predictors, including older age at diagnosis (HR=1.05 per year), stage 4 disease at diagnosis (HR=1.89), and non-R-CHOP regimens (when used first-line or as therapy of longest duration) (HR=2.58-4.91). The elevated hazard ratios for alternative regimens likely reflect more aggressive disease or contraindications to standard treatment, and not necessarily inferior efficacy. Comorbid hypertension at diagnosis was associated with reduced mortality risk (HR=0.56) – an observation likely explained by increased medical monitoring of known hypertensive patients leading to earlier detection of lymphomas and consequently better outcomes.

Healthcare resource utilization

DLBCL patients demonstrated substantial healthcare needs: 82.6% required at least one non-elective hospitalization, with a hospital admission rate of 77.3 per 100 person-years across the treatment cohort. ICU admission was required by 20.7% of patients, with a rate of 6.5 per 100 person-years. Among patients in the emergency department (ED) subsample (n=350), the ED visit rate was 12.0 per 100 person-years. Across both primary and longest duration regimen analyses, patients receiving non-R-CHOP regimens showed higher hospital admission and ICU admission rates compared to R-CHOP recipients, while ED visit rates were broadly comparable across regimen groups.

Treatment discontinuation

Among patients with available discontinuation data, 23.8% discontinued treatment at least once. Adverse effects, safety concerns, or drug intolerance drove 50% of initial discontinuations, while lack of treatment response was the predominant reason for second and subsequent discontinuations. This pattern suggests that tolerability drives initial treatment modifications, while lack of efficacy becomes the primary concern for patients requiring multiple regimen changes –

[1] Rituximab combined with cyclophosphamide, doxorubicin, vincristine, and prednisone.
[2] Hematopoietic stem cell transplantation.

though the small number of patients with second and third discontinuations warrants cautious interpretation.

Limitations and Future Research

Key limitations of this study include substantial missing data for stage at diagnosis (~70% of the prevalent population and ~40% of the treatment cohort) and discontinuation information (53.8%), absence of out-of-province treatment data (particularly HSCT), restricted ED visit analysis due to limited data availability (2017-2021), and lack of clinical variables such as molecular subtypes of disease, treatment intent, and ECOG performance status. Notably, staging information may be selectively missing among older and frailer patients (who may be more likely to bypass invasive staging procedures), potentially skewing the demographic profiles of the staged and unstaged groups. Small sample sizes for some subgroups limited detailed stratified analyses. Random rounding to multiples of 5 for confidentiality introduced imprecision into estimates.

Future data development and research priorities include the establishment of prospective disease registries comprising standardized clinical data, improved interprovincial collaboration to capture out-of-province health services, dedicated health equity research to address socioeconomic and geographic disparities within NB's DLBCL patient population, cost-effectiveness analyses of novel therapies, and integration of patient-reported outcomes to complement clinical and administrative data studies.

Findings from this study establish necessary baseline data to inform future real-world evidence studies, including evaluation of novel therapies, and support evidence-informed policy and practice decisions for DLBCL care in New Brunswick.

1. Introduction

1.1 Background

Diffuse Large B-Cell Lymphoma (DLBCL) is the most common type of non-Hodgkin Lymphoma, accounting for approximately 30% of diagnosed lymphoma cases globally and in Canada [1,2]. DLBCL is characterized by aggressive growth, presenting as rapidly enlarging masses or lymph nodes.

DLBCL risk increases with age, with most diagnoses occurring between ages 60 to 70, though the disease can affect patients of any age, including children and young adults, with males slightly more affected than females [3,4]. DLBCL incidence rates are steadily increasing in both Canada and the U.S., with Canada averaging 34.18 cases per million individuals per year from 1992 to 2010 [5], while cases in the U.S. increased from 5.52 per 100,000 in 2000 to 6.51 per 100,000 in 2021 [6]. This growing incidence translates to considerable healthcare utilization, with treatment intensity varying by disease stage, treatment response, and patient frailty. An Ontario study found that during frontline chemoimmunotherapy, frail DLBCL patients had significantly higher rates of emergency department visits and hospitalizations compared to non-frail patients across all treatment phases; however, regardless of frailty status, 84% of patients required hospital admission, and 27% needed intensive care during the end-of-life phase [7].

Despite its aggressive nature, DLBCL responds well to first-line treatment with R-CHOP chemoimmunotherapy (rituximab combined with cyclophosphamide, doxorubicin, vincristine, and prednisone), administered in six cycles every 21 days, which cures approximately 60% of patients [2,8,9]. Yet, 30% to 40% will be refractory to R-CHOP or will relapse and require additional therapy [10]. Refractory disease occurs when DLBCL does not respond to R-CHOP, while relapsed disease refers to DLBCL that initially responds and enters a period of remission but recurs after, typically within two to three years [4]. Among patients who relapse or who are refractory to initial therapy, further treatment options are available depending on the patients' status. The standard of care for relapsed/refractory (RR) fit patients – typically under the age of 65 to 70 without comorbidities – is salvage chemotherapy followed by high-dose conditioning therapy and autologous hematopoietic stem cell transplantation (ASCT/HSCT) [2,4,9,10]. For transplant-ineligible patients, no standard approach exists as the majority have comorbidities that contraindicate intensive therapy and require palliative management. Treatment selection for ineligible patients requires individualized combination regimens or sequential single agents based on patient tolerance and performance status [10].

Salvage therapy regimens are administered prior to high-dose therapy and HSCT to maximize patients' response to treatment and overall survival. These non-cross-resistant salvage therapies are employed for cytoreduction and to determine chemotherapy sensitivity, as HSCT is generally ineffective in patients with chemotherapy-refractory disease. Salvage regimens often include R-DHAP (rituximab, dexamethasone, cytarabine, cisplatin), R-ICE (ifosfamide, carboplatin, etoposide, with or without rituximab), R-GDP (gemcitabine, dexamethasone, cisplatin, with or without rituximab), and R-GEMOX (rituximab, gemcitabine, and oxaliplatin) [4,8,11,12]. Following salvage therapy, high-dose conditioning regimens such as BEAM (carmustine, etoposide,

cytarabine, melphalan) or R-BEAM (with rituximab) are administered prior to HSCT as the standard conditioning approach [10]. Radiation therapy is an additional treatment modality for localized residual disease or bulky lesions (>10 cm) following chemotherapy in both limited-stage and relapsed/refractory DLBCL [8]. These treatment approaches are intended to improve the prognosis of patients with relapsed and refractory DLBCL.

Overall, while first-line R-CHOP therapy achieves remission in approximately 60% of patients, outcomes for those with relapsed or refractory DLBCL remain poor. The largest global analysis of refractory DLBCL patients [13] demonstrated poor outcomes, with only 26% of patients responding to salvage therapy and a median survival of 6.3 months from refractory disease. Only 20% survived to two years, primarily those who responded to salvage therapy and received HSCT. The majority (73%) either failed salvage therapy or were ineligible for HSCT, highlighting the urgent need for improved treatment options through enhanced salvage regimens that increase HSCT eligibility or novel therapeutic approaches.

This study used administrative data to conduct a retrospective examination of DLBCL cases in the province of New Brunswick (NB) from 2006 to 2021, providing baseline understanding that may inform subsequent real-world evidence studies. While previous research has used administrative data to characterize incidence and mortality of Hodgkin's and non-Hodgkin's lymphoma in NB [14], this represents the first population-level analysis of DLBCL-specific epidemiology, treatment pathways, healthcare utilization, and outcomes in the province.

The results are anticipated to improve understanding of real-world DLBCL management in NB and provide insights to support evidence-informed policy and practice decisions.

1.2 Study Objectives

This study provides the first population-level examination of DLBCL epidemiology, treatment pathways, and outcomes in New Brunswick. By linking deidentified personal administrative health data with clinical chart information, this work offers unprecedented depth of evidence to inform policy and practice decisions within the province and beyond.

The study has two primary objectives in examining DLBCL patients in NB from 2006 to 2021:

Part 1 **Characterize the DLBCL population:** Describe disease burden through prevalence, incidence, and mortality rates, patient demographics, and comorbidity profiles.

Part 2 **Examine treatment pathways and outcomes:** Describe real-world treatment pathways (first- through third-line therapies), survival outcomes, healthcare resource utilization, and reasons for treatment discontinuation.

2. Data Sources and Study Outcomes

2.1 Data Sources

This study was conducted using a variety of administrative data sets accessed via DataNB (formerly the New Brunswick Institute for Research, Data and Training). Located at the University of New Brunswick, DataNB is an administrative data repository for the province of New Brunswick and serves as a data custodian for over 130 linkable data sets. DataNB makes administrative data accessible to researchers through established processes that maintain data security and protect individual privacy while permitting linkage of person-level data across multiple data sets through the use of a scrambled unique identifier. When individual-level administrative data were not available for a variable of interest, such as neighbourhood income indicators, an area-level proxy was created instead. To create the proxy, Statistics Canada data were used to determine the average value for a given variable (e.g., income quintile) in a Dissemination Area (DA; a small geographic area comprising ~200-300 people), and then every individual residing in that DA (determined by their postal code) was assigned that value for the variable.

Other individual-level information required for this work – such as staging and treatment discontinuation – was not available in administrative data. As such, stage at diagnosis and treatment discontinuation data, including reasons for discontinuation, were sourced from patient clinical charts accessed through New Brunswick's two Regional Health Authorities: Horizon Health Network (HHN) and Vitalité Health Network (VHN). Charts were identified for review by screening hospital discharge records for lymphoma ICD-10 codes (C83.3, C83.8, C83.9, C85.2) over the period April 1, 2006, to March 31, 2021. As chart review was based on hospital discharge records, only patients with at least one hospitalization during this period were eligible for chart review. At VHN sites, only electronic charts were reviewed; patients with exclusively paper-based charts were excluded. These data were collected by research services personnel at both authorities and transferred to DataNB for linkage with administrative data sets.

A summary of the administrative data sets used in this study is provided in Supplemental Table 1 and Supplemental Table 2 in the Appendix.

2.2 Study Outcomes

Using these linked data sources, the following outcomes were examined:

Epidemiological trends and characteristics of the DLBCL population

- Annual incidence, prevalence, and mortality rates
- Patient demographics (age, sex, geographic location, income quintile)
- Disease characteristics (stage at diagnosis)
- Comorbidities

Clinical outcomes

- Treatment regimens and therapy lines
- Survival outcomes
- Treatment discontinuation patterns

Healthcare utilization outcomes

- Non-elective hospital admissions
- Intensive care unit admissions
- Emergency department visits

Specific analytic approaches for each outcome vary according to data availability and are described in the Methods section below.

3. Methods

This is a retrospective descriptive study with two parts, each addressing multiple research objectives. The study population for each objective varies based on the available date range of the corresponding administrative data. This section describes the methodological approach for Parts 1 and 2, applied across all study outcomes.

3.1 Definition of DLBCL Study Population

For each part, DLBCL cases were defined using ICD-O-3 diagnostic codes from the New Brunswick Cancer Registry Data, as summarized in **Table 1** below.

Individuals were classified as cases if they resided in New Brunswick at any point during the study period (date ranges for study Parts 1 and 2 defined below) and had a record containing a relevant diagnostic code.[3]

[3] A small number of individuals had multiple DLBCL diagnosis records with different dates. To prevent overestimation of prevalence and incidence rates, only the first recorded diagnosis date was retained for analysis.

Table 1. Definition of DLBCL Study Population

ICD-O-3 Code	Disease
9680/3	Malignant lymphoma, large B-cell, diffuse, NOS
9679/3	Mediastinal large B-cell lymphoma
9688/3	T-cell/histiocyte rich large B-cell lymphoma

Note: Most cases were coded as 9680/3 (DLBCL, NOS). Although 9679/3 (PMBCL) and 9688/3 (THRLBCL) were historically classified as DLBCL subtypes, both have since been recognized by the World Health Organization as distinct entities (PMBCL since 2016 [15]; THRLBCL since 2008 [16]). All three codes are included in the analyses; however, given that 9680/3 accounts for over 99% of cases, the study population is referred to throughout as DLBCL.

3.2 Part 1 Methods – DLBCL Incidence, Prevalence, and Patient Demographics in New Brunswick

3.2.1 Annual disease incidence, prevalence, and mortality

Annual incidence, prevalence, and mortality rates were calculated by fiscal year (April 1 – March 31) from 2006-2007 to 2020-2021. Rates were calculated per 100,000 population using annual New Brunswick population counts sourced from the province's Citizen Data as the denominator.

NB Citizen Data tracked individuals who died or moved away from the province during the study period. Individuals who died within a fiscal year were included in incidence, prevalence, mortality, and prevalent case fatality calculations for that year but were excluded from subsequent years' counts. Individuals who moved away from NB were similarly excluded from prevalence counts in subsequent years.

a. **Incidence** was defined as the number of new DLBCL diagnoses recorded within a given fiscal year, divided by the NB population for that year.

b. **Prevalence** was calculated as a running cumulative count of active cases in each fiscal year. The prevalent population for a given year was defined as all individuals with a DLBCL diagnosis from April 1, 1992, onward who had not yet died or moved out of province prior to that year, plus any new incident cases diagnosed within that year, divided by the NB population for that year. Since NB Cancer Registry Data has recorded incident cases since 1992, prevalence estimates include cases diagnosed from April 1, 1992, onward; individuals diagnosed prior to this date are not captured in the prevalence calculation.

c. **Mortality** was defined as the number of individuals with a DLBCL diagnosis who died within a given fiscal year, divided by the NB population for that year. Cause of death was not used to determine mortality. That is, any death occurring among active DLBCL cases was counted.

d. **Prevalent case fatality** was calculated as the number of deaths among active DLBCL cases in a given fiscal year divided by the total prevalent DLBCL population for that year (i.e., individuals previously diagnosed who were alive and residing in the province). Given the relatively small number of DLBCL cases and deaths, the rate is expressed per 100 prevalent cases rather than per 100,000.

3.2.2 Patient characteristics – age, sex, location of residence, income quintile, stage at diagnosis

The incident DLBCL population diagnosed from 2006-2007 to 2020-2021 was characterized at the time of diagnosis on the following dimensions: mean age, sex distribution, location of residence, income quintile, and disease stage at diagnosis. Age, sex, and location of residence were sourced from NB Citizen Data. Location of residence was derived from postal codes and categorized by NB Health Zone (seven regions across the province).

Individual income quintile was determined using Statistics Canada's census-derived before-tax income quintiles (QABTIPPE) for the dissemination area (DA) of residence. Stage at diagnosis was collected through review of patient charts from Horizon and Vitalité oncology clinics.

These same characteristics were then tracked annually among the prevalent DLBCL population (individuals previously diagnosed who were alive and residing in the province) from 2006-2007 to 2020-2021. For time-varying characteristics – location of residence and income quintile – values were estimated on April 1 of each fiscal year.

3.2.3. Patient characteristics – comorbidities

Canadian Chronic Disease Surveillance System (CCDSS) data were used to describe the frequency of the following comorbidities among DLBCL patients: acute myocardial infarction, heart failure, hypertension, ischemic heart disease, stroke, chronic obstructive pulmonary disease (COPD), and diabetes. At the time of DLBCL diagnosis, comorbidities were defined as any condition recorded in the CCDSS on or before the year of diagnosis.

These comorbidities were also tracked annually among the prevalent DLBCL population, with each fiscal year reflecting any comorbidity recorded up to and including that year, thereby capturing conditions that developed after DLBCL diagnosis.

Comorbidity data are available through 2018-2019, reflecting the CCDSS data range. As such, both incident and prevalent comorbidity estimates are reported from 2006-2007 to 2018-2019. Since CCDSS data provide only the year of diagnosis (without month or day), individuals with a CCDSS diagnosis in a given year were assumed to have that diagnosis as of April 1 of that year.

3.3 Part 2 Methods – DLBCL Treatment Pathways, Outcomes, and Healthcare Utilization

For Part 2, a DLBCL treatment cohort was established. An individual was included in the treatment cohort (and thus in the analyses for Part 2) if their DLBCL diagnosis date (determined using ICD-O-3 codes in NB Cancer Registry Data, as described above) was within the accrual period specified for the site at which they received their chemotherapy treatment. For individuals treated at multiple sites, accrual eligibility was determined based on the site of earliest treatment.

Accrual periods for each site were determined based on site-specific available date ranges of IV Oncology Data (i.e., chemotherapy treatment records) to permit a 5-year follow-up period for chemotherapy treatment data after DLBCL diagnosis for each individual in the treatment cohort. IV Oncology Data date ranges, accrual periods, and maximum follow-up end dates for each site are summarized in **Table 2**.

For all analyses, patients in the treatment cohort were followed for five years from diagnosis (except for select survival analyses, as noted below), censoring patients who died or left NB during the follow-up period.

Table 2. Accrual Periods and Maximum End Date of Follow-Up, by Site of Chemotherapy Administration

Site of chemotherapy administration	IV oncology data date range	Accrual period	Duration of Accrual Period (years)	Max Follow-up end date
Bathurst	Jan 2 2012 – Nov 1 2023	Jan 2 2012 – Nov 1 2018	6	Nov 1 2023
Campbellton	Sept 29 2003 – Nov 1 2023	Sept 29 2003 – Nov 1 2018	15	Nov 1 2023
Edmundston	Apr 15 2011 – Nov 1 2023	Apr 15 2011 – Nov 1 2018	7	Nov 1 2023
Moncton (VHN)	Jul 18 2003 – Nov 6 2023	July 18 2003 – Nov 6 2018	15	Nov 6 2023
Moncton (HHN)	Feb 20 2006 – Apr 17 2023	Feb 20 2006 – Apr 17 2018	12	Apr 17 2023
Saint John	Jan 4 2010 – Feb 10 2023	Jan 4 2010 – Feb 10 2018	8	Feb 10 2023
Fredericton	Jan 3 2012 – Oct 11 2023	Jan 3 2012 – Oct 11 2018	6	Oct 11 2023

3.3.1 DLBCL treatment cohort characteristics – age, sex, location of residence, income quintile, stage at diagnosis, comorbidities, travel distance to treatment site, and COVID-19 infection

Patient characteristics of the DLBCL treatment cohort were described using mean age, sex, geographic distribution, and income quintile (as described in Section 3.2.2), with values captured on the index date of each case. Stage at diagnosis and comorbidities were assessed using the same methods described in Sections 3.2.2 and 3.2.3.

Descriptive statistics were calculated for the overall DLBCL treatment cohort. Stratified results by chemotherapy administration site (Fredericton, Moncton HHN, Saint John, Vitalité sites) are presented in Supplemental Figures 1, 2, and 3 (see Appendix).

Travel distance was estimated as the driving distance in kilometres (KMs) across all treatment visits during the 5-year follow-up period. For each treatment visit, distance was calculated from the centroid (or, centre) of the patient's dissemination area of residence – derived from their Forward Sortation Area (FSA; the first three characters of their postal code) – to the postal code of their treatment site visited. As patients may have received treatment at multiple sites and may have changed residence during follow-up, both treatment location and residential FSA were updated at each visit when applicable, and distances were averaged across all visits to produce a single per-person estimate.

Frequency of COVID-19 infection among hospitalized DLBCL patients was determined using ICD-10 code U07.1 from Discharge Abstract Data (DAD) records from March 2019 onward.

3.3.2. Treatments – IV chemotherapy, radiation therapy, and hematopoietic stem cell transplant (HSCT)

Chemotherapy treatment patterns among the DLBCL treatment cohort were assessed using IV Oncology Data. Administered IV chemotherapy drugs were categorized according to treatment regimen and line of therapy (1, 2, 3+). Treatment line transitions were defined by changes in drug combination composition. Within a given regimen, a new treatment cycle was defined as administration of the same drug combination following a gap of more than seven days. For reporting purposes, third and subsequent lines of therapy were collapsed into a single category (3+) to ensure adequate sample sizes and to maintain patient confidentiality. Frequency of chemotherapy regimens, mean duration of regimen (number of days), and line of therapy were described for the DLBCL treatment cohort during the 5-year follow-up period, based on regimens ever administered and regimens of longest duration.

Cancer Treatment Access Repository (CTAR) Radiation Therapy data were used to describe the frequency and duration (days) of radiation therapy among the cohort during the same follow-up period. Hematopoietic stem cell transplants (HSCT) were identified using procedure codes 1LZ19HHU7A (autologous stem cell transfusion) and 1LZ19HHU7J (homologous stem cell transfusion) from Discharge Abstract Data; and frequency and timing (mean days from DLBCL diagnosis date) of in-hospital HSCT were described over the 5-year follow-up period.

Chemotherapy analyses were stratified by treatment site type (academic or community hospital) and Regional Health Authority (Vitalité or Horizon Health Network); and radiation and HSCT analyses were stratified by Regional Health Authority. Stratified results are presented in Supplemental Figures 4, 5, 6, 7, and 8 (see Appendix).

3.3.3. Survival

Using NB Citizen Data to identify date of death, survival analysis employed the Kaplan-Meier method to estimate overall survival of the DLBCL treatment cohort over a 5-year follow-up period from diagnosis date. Due to limited sample size, survival by primary and most common treatment regimen was estimated over a 3-year follow-up period.

Cox proportional hazards models were used to assess the impact of treatment regimen (first-line, and regimen of longest duration) and the following covariates on survival over the 5-year follow-up period:

- **Age at diagnosis** *(continuous; NB Citizen Data);*
- **Sex** *(male/female; NB Citizen Data);*
- **Disease stage at diagnosis** *(stages 1-4; patient chart review, Horizon and Vitalité oncology clinics);*
- **Location of residence** *(seven NB Health Zones; NB Citizen Data);*
- **Income quintile** *(Statistics Canada census-derived before-tax income quintiles for dissemination area of residence; NB Citizen Data);*
- **Comorbidities** *(any condition recorded in CCDSS on or before the year of DLBCL diagnosis, or identified during the 5-year follow-up period; CCDSS);*
- **Chemotherapy administration site** *(Fredericton, Moncton HHN, Saint John, Vitalité sites; IV Oncology data);*
- **Mean driving distance to treatment site** *(KMs; FSA of residence to treatment site postal code);*
- **Receipt of radiation treatment** *(yes/no; CTAR Radiation Therapy data);*
- **Receipt of hematopoietic stem cell transplantation** *(yes/no; DAD).*

3.3.4. Discontinuation of IV chemotherapy

Patient chart review data were used to assess the frequency of discontinuation of IV chemotherapy drugs in the DLBCL treatment cohort during the 5-year follow-up period. Discontinuation was defined as cessation of drug therapy prior to the originally intended completion of a planned treatment cycle. Each discontinuation of a single drug was counted as a separate discontinuation event. Treatment pauses (when the same treatment was eventually resumed) and death of the patient were not counted as discontinuation events.

The reason for each discontinuation was documented, selecting from among the following four mutually exclusive categories based on chart information:

1) Adverse effects, safety concern, or drug not tolerated;
2) Patient not responding to drug (or regimen that includes drug);
3) Patient desires to stop treatment;
4) Other reason, or reason unspecified.

In some cases, categories 3 and 4 were combined for reporting purposes due to low frequency counts. Frequency counts of patients with any, one, two, or three or more discontinuation events were reported, and discontinuation events were stratified by reason for discontinuation and by treatment regimen.

3.3.5. Healthcare resource utilization – non-elective hospital admissions, length of stay, ICU admissions, and emergency department visits

Discharge Abstract Data were used to describe frequency of non-elective hospital admissions, length of stay (mean and median), and frequency of ICU admissions in the DLBCL treatment cohort over the 5-year follow-up period – overall and by treatment regimen (first-line regimen, and regimen of longest duration). Admission and visit rates were calculated per person-years, where the denominator represents the total accumulated follow-up time across all cohort members, with each individual contributing time from diagnosis until death, departure from NB, or the end of the 5-year follow-up period, whichever occurred first. Rates are expressed per 100 person-years.

NB Emergency Department (ED) Data were used to describe ED visit frequency in the treatment cohort. ED data were only available from January 1, 2017, to December 1, 2021, so a 5-year follow-up period was not possible. Instead, ED visit analysis was limited to patients who had at least a 1-year period post-DLBCL diagnosis falling within the period of ED data availability, establishing an ED subsample of 350 patients. For each included patient, ED visit frequency was assessed during the 365-day period nearest to their DLBCL diagnosis date that fell within the period of ED data availability. ED visit rates were similarly calculated per person-years using accumulated follow-up time within each patient's eligible 365-day window. ED visit frequency was described overall and by treatment regimen.

3.4 Management of Small Cell Counts

DataNB minimum release requirements specify that frequency counts of less than 5, or measures of central tendency with corresponding counts less than 10, cannot be released from the secure research environment to minimize risk of disclosure of personally identifying information. To permit disclosure of all results values, results containing one or more frequency counts lower than 5 were randomly rounded to mitigate disclosure risk. Random rounding involves rounding results values up or down to a multiple of 5 following a pre-determined probability algorithm. The process is

applied uniformly across all results values (regardless of whether the unrounded values meet or do not meet minimum release requirements).

The random rounding process is conducted as follows:

- Each result value is divided by 5, and the remainder is determined.
- Values with a remainder of 0 are not rounded.
- Values with a non-zero remainder are randomly rounded up or down to the next highest or lowest multiple of 5, according to the following probability algorithm: The probability of rounding up is given by (remainder/5), and the probability of rounding down is given by [1 – (remainder/5)].

3.5 Statistical Analysis

Statistical analysis for Part 1 was conducted using Stata 17.0 for frequency counts and descriptive statistics (means). Prevalence, incidence, mortality, and prevalent case fatality rates were calculated in Excel. Individuals diagnosed outside of New Brunswick were not captured in these analyses, as case identification relied on NB Cancer Registry records, which include only diagnoses made within the province.

Part 2 analysis used Stata 17.0 for frequency counts, descriptive statistics (means and medians), Cox proportional hazards models, and survival analysis. Survival data were declared using Stata's stset function, with death as the event of interest. Cox proportional hazards models (stcox) were used to estimate predictors of mortality, generating hazard ratios with 95% confidence intervals and p-values.

Two models were fitted: one using the individual's first-line treatment regimen and another using their regimen of longest duration. Kaplan-Meier survival curves were generated to estimate median survival time and to visualize survival probabilities for the overall cohort and stratified by first-line and longest duration regimens. Survival estimates from Stata were exported and visualized using the ggplot2 package in RStudio.

4. Results

Results are presented in two parts. Part 1 (Section 4.1) describes the epidemiology and characteristics of all DLBCL cases identified in New Brunswick with diagnosis dates between April 1, 1992, and March 31, 2021 (n=1,861), including incidence, prevalence, mortality rates, and demographic distributions.

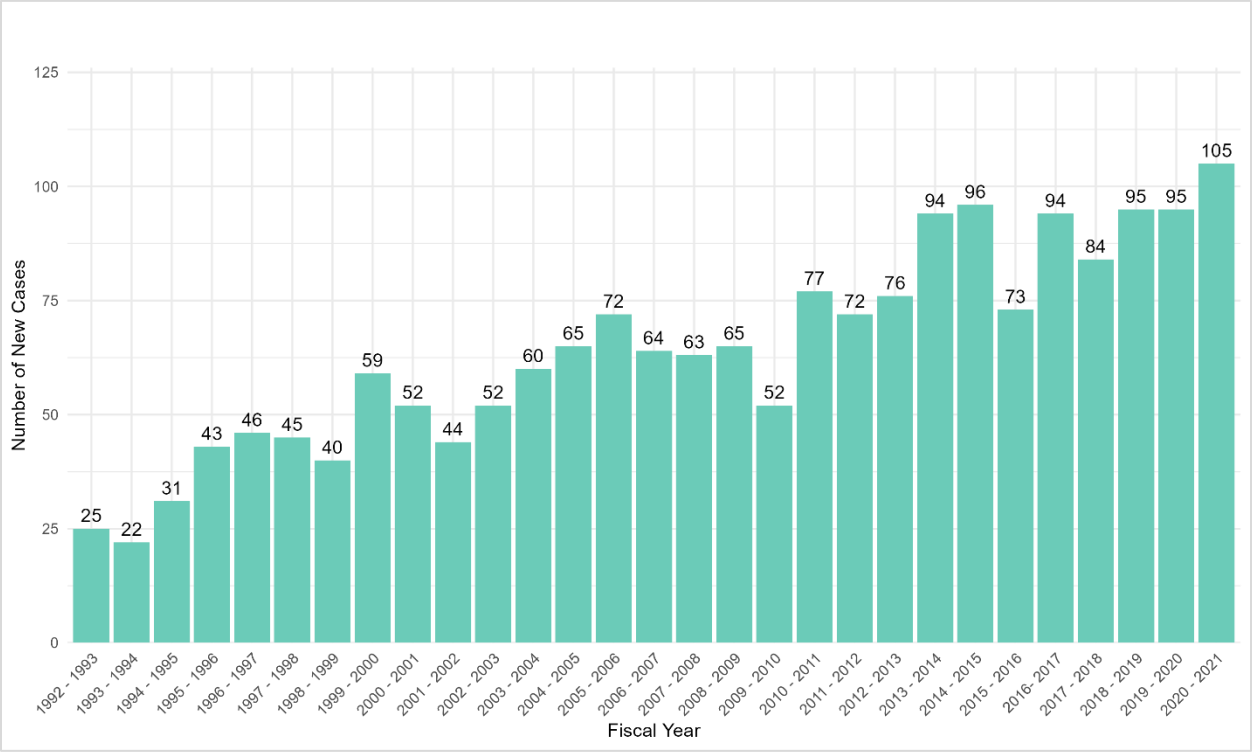
Part 2 (Section 4.2) examines a subset of patients diagnosed between 2006 and 2018 who were linked to IV Oncology Data (n=455-460), describing treatment patterns, survival outcomes, and healthcare resource utilization over a 5-year follow-up period.

4.1 Part 1 Results: DLBCL Population Epidemiology and Characteristics

4.1.1 DLBCL population and demographic characteristics

Figure 1 shows annual incident DLBCL cases from the 1992-1993 to 2020-2021 fiscal years (April 1 to March 31). A total of 1,861 cases were identified, with incidence rising from 25 cases in 1992-1993 to 105 cases in 2020-2021.

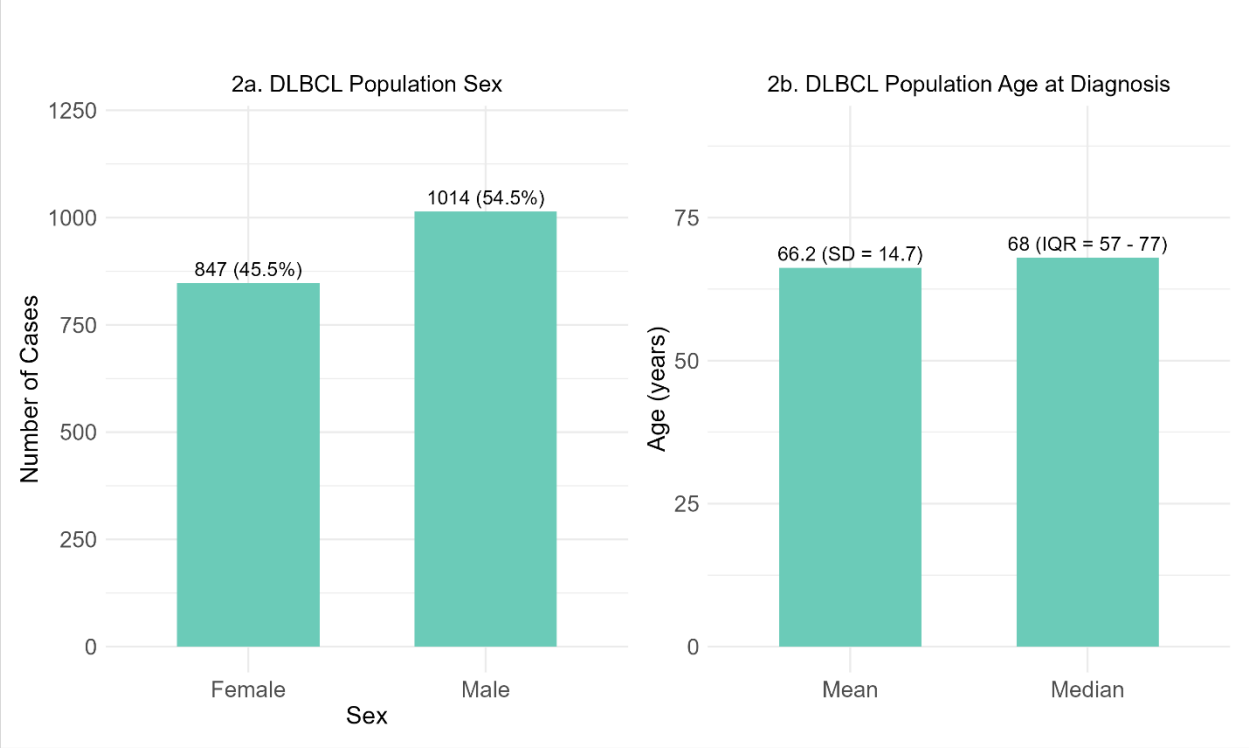
Figure 1. Incident Diffuse Large B-Cell Lymphoma Cases by Fiscal Year, April 1st, 1992, to March 31st, 2021 (n=1,861).



Among the 1,861 cases identified from April 1, 1992, to March 31, 2021, **Figure 2** presents the distribution by sex (Figure 2a) and age at diagnosis (Figure 2b).

Males comprised a larger proportion of cases than females (54.5% vs. 45.5%). The mean age at diagnosis was 66.2 years (SD=14.7), with a median of 68.0 years (IQR=57-77).

Figure 2. Sex and Age Distribution Among Incident DLBCL Cases, April 1st, 1992, to March 31st, 2021 (n=1,861).



4.1.2 DLBCL epidemiology – prevalence, incidence, and mortality

Prevalence, incidence, mortality, and prevalent case fatality rates are presented in **Figure 3** below. Prevalence, incidence, and mortality rates (Figures 3a, 3b, 3c) are expressed per 100,000 New Brunswick residents; prevalent case fatality rates (3d) are expressed per 100 prevalent DLBCL cases.

Prevalence (Figure 3a) was calculated as the total number of individuals living with or having survived DLBCL divided by the total New Brunswick population for each fiscal year. Prevalence estimates include only individuals diagnosed from April 1, 1992, onward. DLBCL prevalence increased over time as the surviving population accumulated.

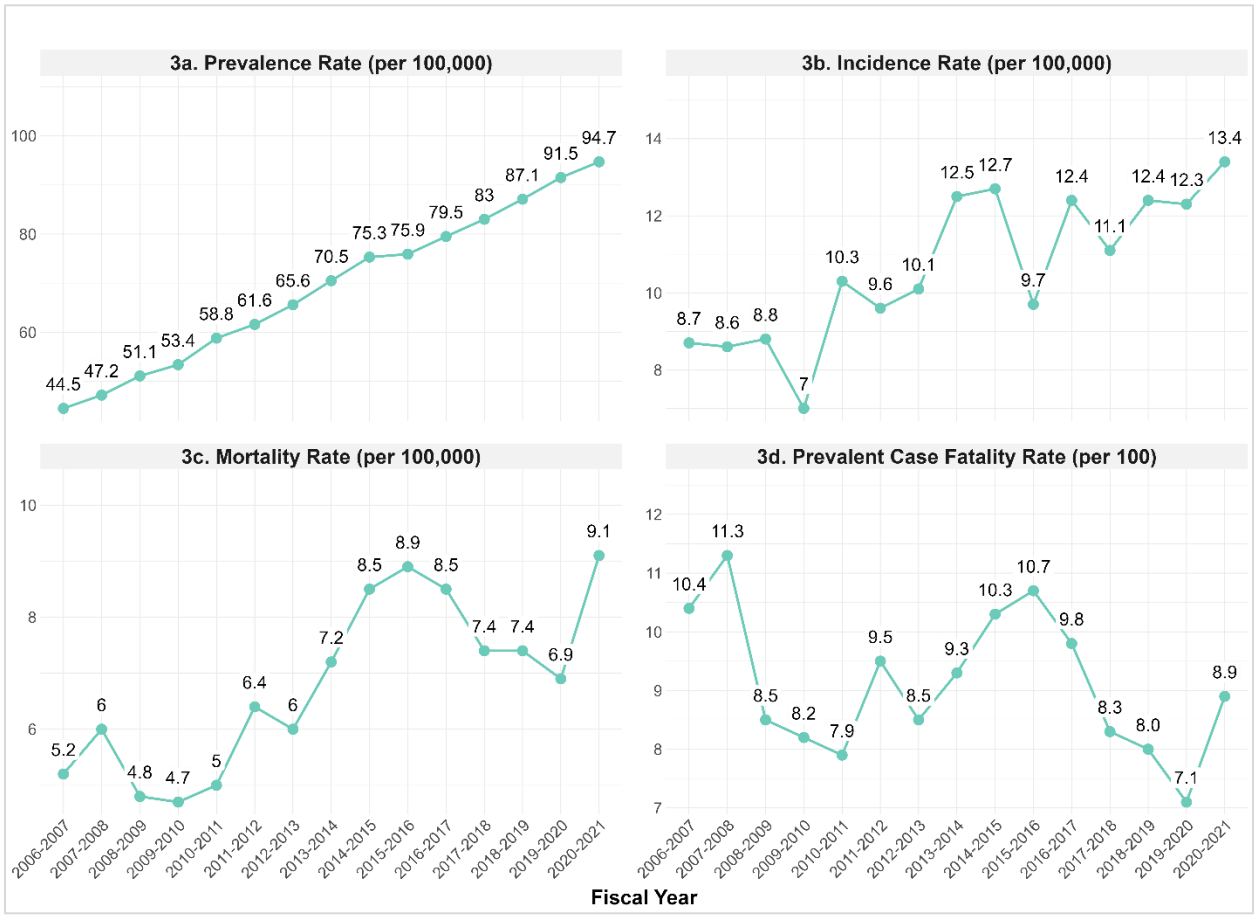
Incidence rates (Figure 3b), consistent with trends shown in Figure 1, generally increased over time, with notable fluctuation around 2015. Incidence per 100,000 dropped from 12.7 in 2014-2015 to 9.7 in 2015-2016 before rebounding to 12.4 in 2016-2017, progressing to 13.4 by 2020-2021.

Mortality was evaluated using two different approaches.

The mortality rate (Figure 3c) – all-cause deaths among DLBCL cases per 100,000 NB residents – showed a steady increase from 5.2 in 2006-2007 to 9.1 in 2020-2021, likely reflecting the growing prevalent DLBCL population.

The prevalent case fatality rate (3d) – all-cause deaths per 100 prevalent DLBCL cases -- decreased from 11.3 per 100 in 2007-2008 to 8.9 in 2020-2021, indicating improved survival among those living with or previously diagnosed with DLBCL.

Figure 3. DLBCL Prevalence, Incidence, and Mortality Rates by Fiscal Year, April 1st, 2006, to March 31st, 2021.



4.1.3 DLBCL geographic, socioeconomic, and health characteristics

Figure 4 illustrates the geographic and socioeconomic distribution of DLBCL cases diagnosed from 2006-2007 to 2020-2021 (n=1,205).

Location of residence (Figure 4a) at diagnosis was categorized by New Brunswick's seven health zones: Moncton, Saint John, Fredericton, Bathurst, Edmundston, Campbellton, and Miramichi. The three urban areas (Moncton, Saint John, and Fredericton) accounted for nearly 70% of all cases, with Moncton representing the largest share at 27.7%. Among remaining regions, 14% of cases resided in Bathurst, followed by Miramichi (7.5%), Edmundston (5.2%), and Campbellton (3.6%).

Neighbourhood income quintile distribution (Figure 4b) at diagnosis shows higher DLBCL case concentration in lower-income areas. The three lowest quintiles accounted for 65.5% of cases (Q1: 21.7%, Q2: 22.2%, Q3: 21.6%), while the two highest quintiles comprised 33.7% (Q4: 16.3%, Q5: 17.4%).

Figure 4. DLBCL Geographic and Socioeconomic Distribution at Diagnosis, April 1st, 2006, to March 31st, 2021 (n=1,205).

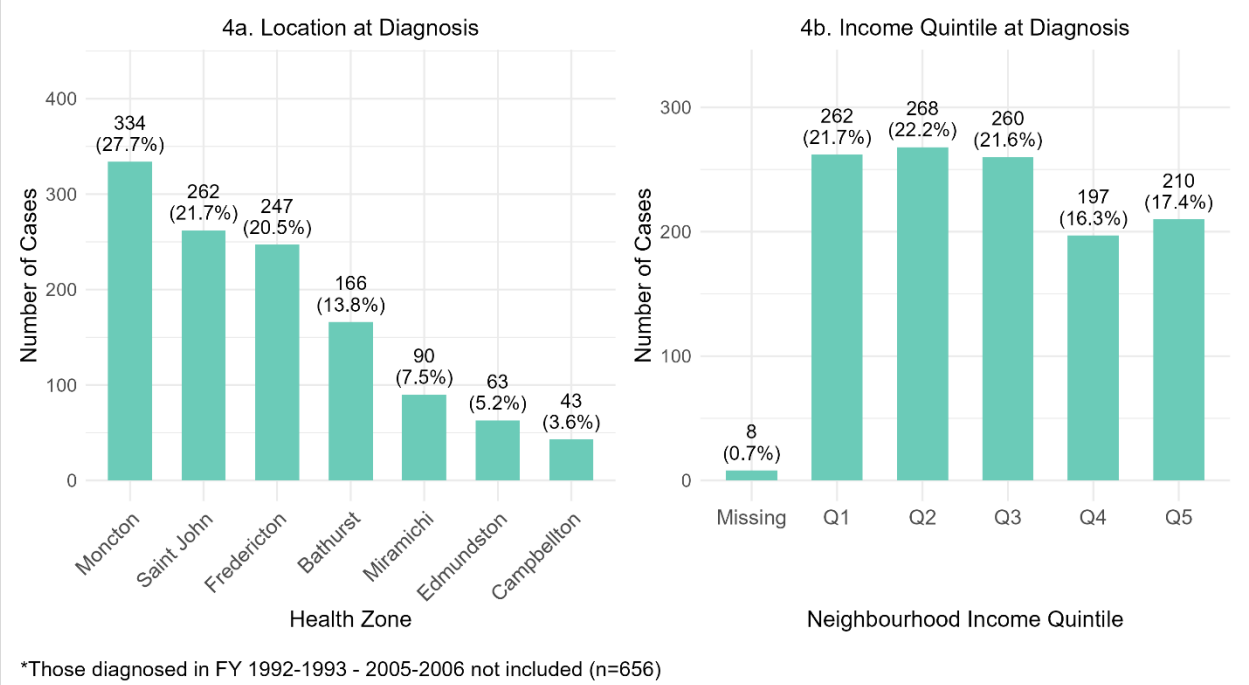
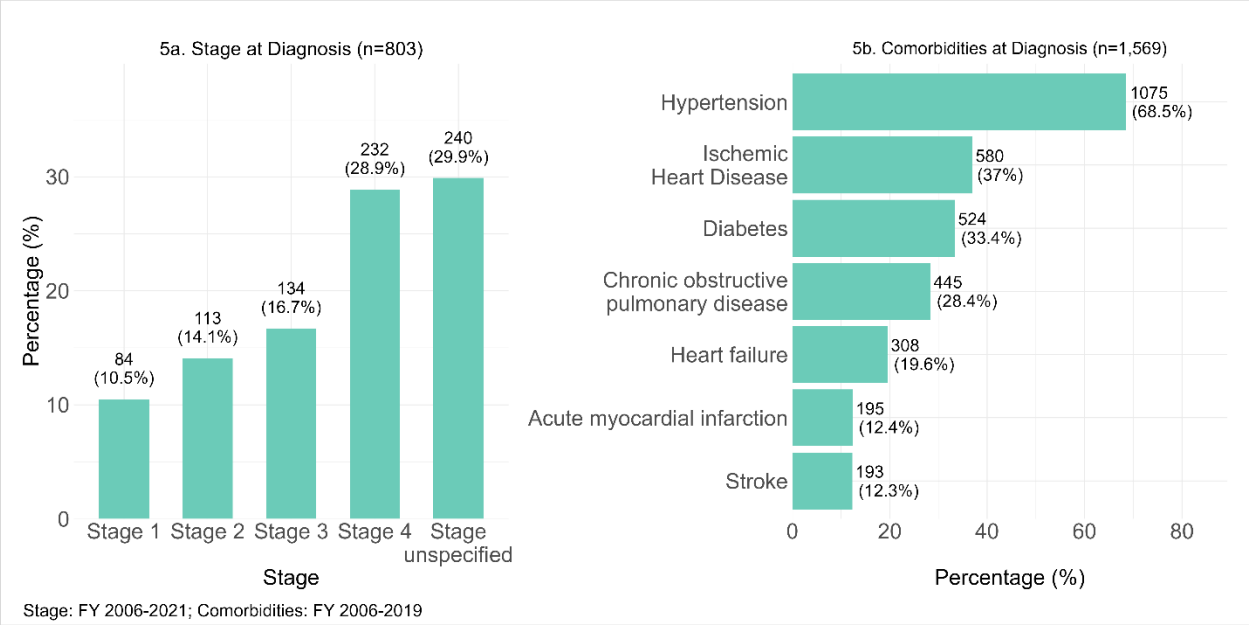


Figure 5 presents stage at diagnosis (5a) and comorbidities at diagnosis (5b) for the incident DLBCL population.

Stage at diagnosis (Figure 5a) was available for a subset of patients with chart data (n=803). Of these, 29.9% (n=240) had no stage recorded (unspecified). Among those with documented staging (n=563), stage 4 was most common (28.9%), followed by stage 3 (16.7%), stage 2 (14.1%), and stage 1 (10.5%).

Comorbidities at diagnosis (Figure 5b) are reported for DLBCL patients between 2006 and 2019 (n=1,569). Hypertension was most prevalent (68.5%), followed by ischemic heart disease (37.0%) and diabetes (33.4%). Chronic obstructive pulmonary disease affected 28.4% of individuals diagnosed with DLBCL. Heart failure (19.6%), acute myocardial infarction (12.4%), and stroke (12.3%) were less common.

Figure 5. DLBCL Population Stage at Diagnosis, April 1st, 2006, to March 31st 2021 (n=803) and Comorbidities 2006 to 2019 (n=1,569).



4.1.4 DLBCL characteristics over fiscal years (April 1st, 2006, to March 31st, 2021)

Figures 6, 7, and 8 display characteristics of the prevalent DLBCL population annually by fiscal year from 2006-2007 to 2020-2021. The prevalent population includes all individuals diagnosed with DLBCL from April 1, 1992, onward who remained alive and residing in New Brunswick during each fiscal year. Certain characteristics are fixed at diagnosis and carried forward (e.g., stage at diagnosis), while others are time-varying and updated annually (e.g., location of residence, comorbidities). All values have been randomly rounded (as described under the Methods above) to protect patient privacy.

Figure 6 presents the total size of the prevalent population (Figure 6a), sex distribution (Figure 6b), and mean age (Figure 6c) by fiscal year. The prevalent population increased substantially over time, more than doubling from 365 cases in 2006-2007 to 795 cases in 2020-2021. Sex distribution remained stable throughout, with males comprising approximately 51-55% of the prevalent population and females comprising 45-49% annually. Mean age increased gradually from 65.2 years (SD=15.5) in 2006-2007 to 68.7 years (SD=13.1) in 2020-2021.

Figure 6. Demographic Characteristics of the Prevalent DLBCL Population Across Fiscal Years, April 1st, 2006, to March 31st, 2021.

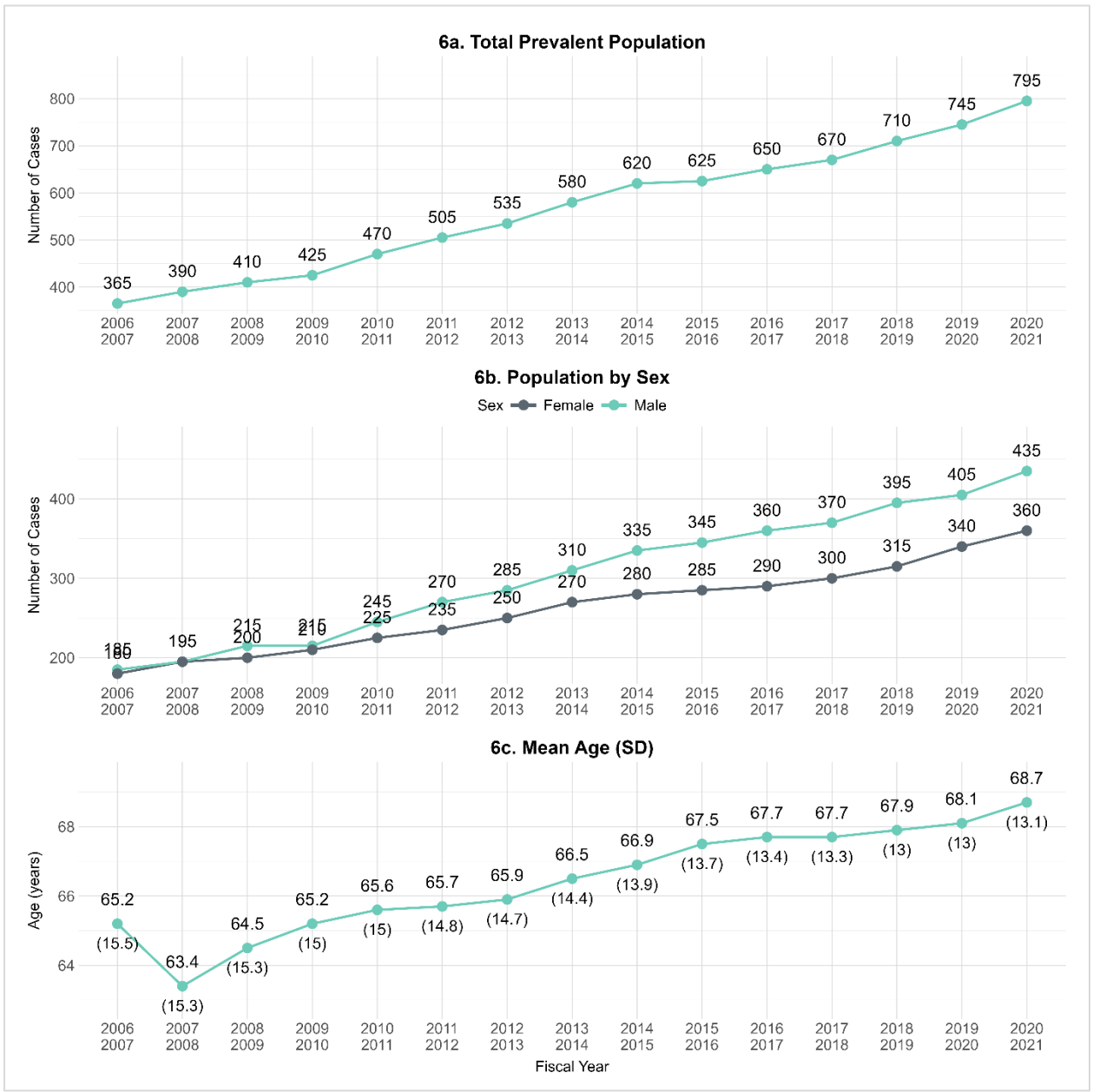


Figure 7 displays the annual geographic (Figure 7a) and socioeconomic distribution (Figure 7b) of the prevalent DLBCL population. The Moncton region consistently contained the largest share of prevalent cases, increasing from 105 in 2006-2007 to 240 in 2020-2021. All other regions also grew over time, with more substantial growth in larger regions (Fredericton, Saint John) and more modest growth in smaller regions (Campbellton, Edmundston, Miramichi).

Neighbourhood income quintile distribution (Figure 7b) showed a broadly consistent pattern across the study period, with Q2 and Q3 accounting for the largest shares of prevalent cases, and Q5 accounting for the smallest. All quintiles increased at a similar rate over time, with no meaningful divergence in trends across socioeconomic groups.

Figure 7. Location of Residence and Income Quintile Distribution of the Prevalent DLBCL Population Across Fiscal Years, April 1st, 2006, to March 31st, 2021.

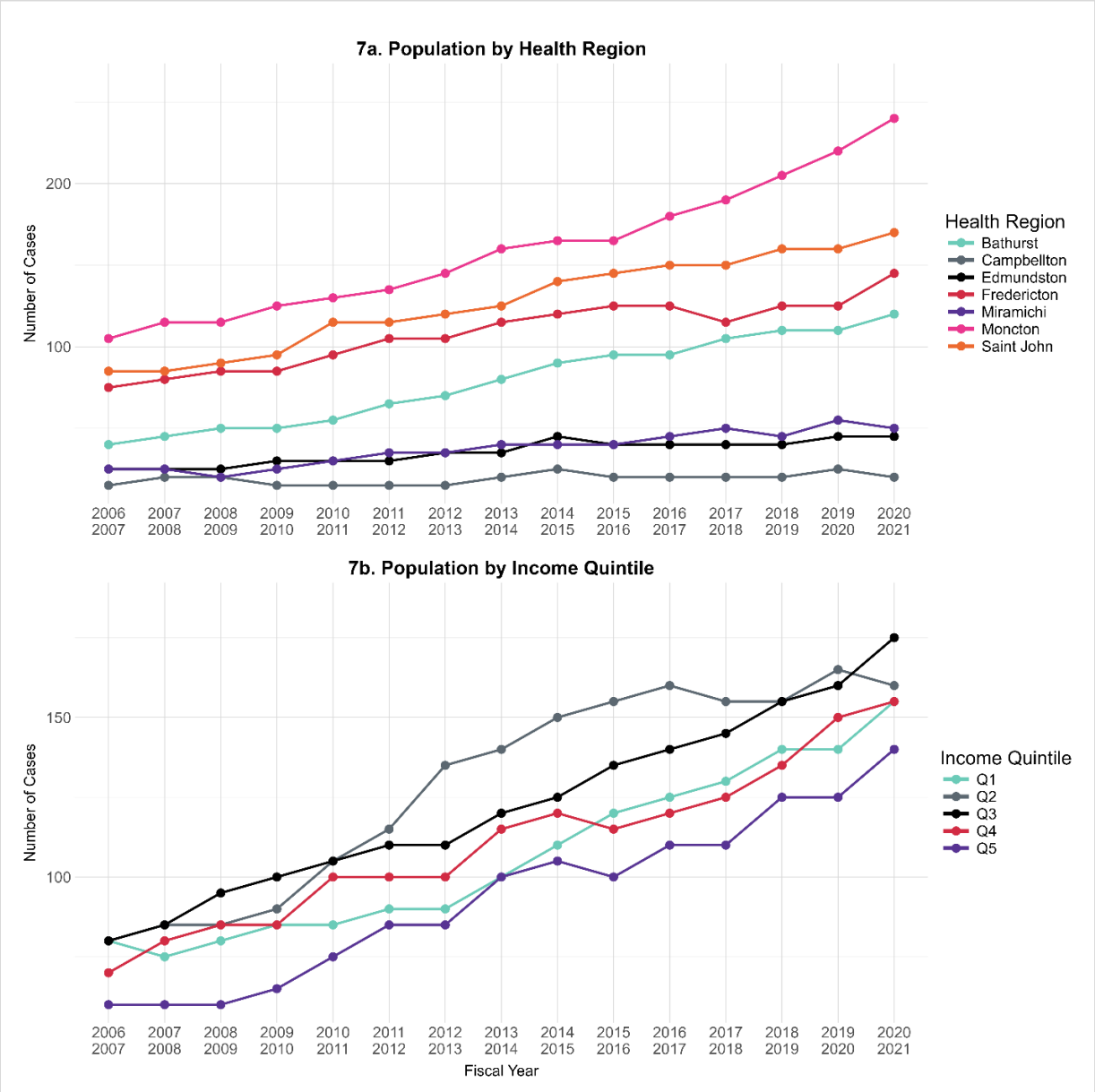


Figure 8 below presents stage at diagnosis (Figure 8a) and comorbidities (Figure 8b) among the prevalent DLBCL population by fiscal year.

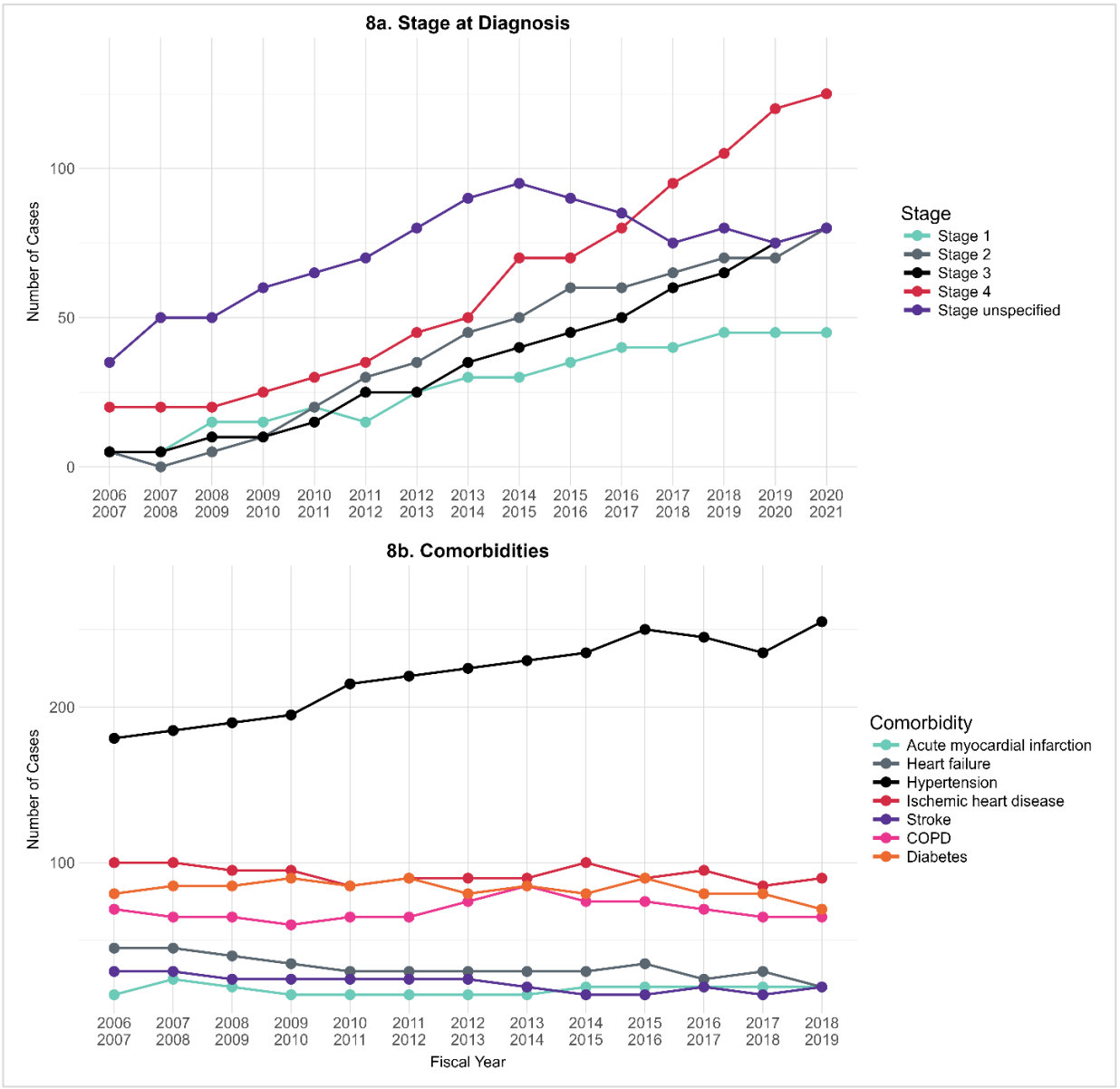
Stage at diagnosis (Figure 8a) was sourced from chart reviews and could not be determined for a substantial proportion of the prevalent population in each year, ranging from 48.4% missing in 2020-2021 to 80.8% in 2006-2007, reflecting the smaller number of charts available in earlier years. Of those with chart data available, a further 19.5% to 50.0% had no stage recorded in the chart (unspecified). Among those with documented staging, stage 4 disease was consistently most common, followed by stage 3, stage 2, and stage 1, with all staged categories showing modest increases in case counts over time.

Comorbidity estimates (Figure 8b) reflect the annual prevalent population and should not be directly compared to the incident cohort figures in Figure 5b as they represent different populations at different points in time.

Among comorbidities tracked from 2006-2007 to 2018-2019, hypertension was most common, affecting 35.9% to 49.3% of the prevalent population annually. These figures are lower than the 68.5% reported at diagnosis for the incident cohort (Figure 5b), likely because of the inclusion of younger, more recently diagnosed cases who may not yet have developed hypertension, as well as attrition of older cases with hypertension due to mortality over time.

Ischemic heart disease affected 18.1% to 27.4% of the prevalent population annually, followed by diabetes (9.9% to 17.8%) and COPD (9.7% to 15.9%). Heart failure (2.8% to 12.3%), stroke (2.4% to 8.2%), and acute myocardial infarction (4.1% to 6.4%) were less common. All comorbidities showed a declining share of the prevalent population over time

Figure 8. Stage at Diagnosis (2006 to 2020) and Comorbidities (2006 to 2018) Among the Prevalent DLBCL Population Across Fiscal Years.



4.2 Part 2 Results: DLBCL Treatment Pathways, Outcomes, and Associated Healthcare Resource Utilization

4.2.1 Treatment cohort characteristics

A subset of the DLBCL population described in Section 4.1 was linked to IV Oncology Data to create the DLBCL treatment cohort for further analysis (as described under the Methods, above). Between 455 and 460 individuals diagnosed from 2006 to 2018 were included in the cohort and examined over a 5-year follow-up period (reported number of individuals in cohort varies by analysis due to random rounding). Patients were censored upon death or departure from NB during the follow-up period, yielding a mean observation time for the cohort of 3.7 years (SD=1.9). Characteristics of the treatment cohort are summarized in **Table 3 below**.

The largest share of patients received their first-line chemotherapy at Saint John (39.6%), followed by Moncton Horizon (37.4%), Vitalité sites collectively (18.7%), and Fredericton (4.4%). Vitalité site-level counts were suppressed below the minimum reporting threshold and are reported in aggregate form only. The mean age at diagnosis was 65.6 years (SD=12.8), with males comprising 59.3% of the cohort and females comprising 40.7%.

At diagnosis, the largest share of the cohort resided in Saint John (30.8%), followed by Moncton (26.4%), Fredericton (15.4%), and Bathurst (14.3%), with the remaining 13.2% distributed across Miramichi (8.8%), Campbellton (3.3%), and Edmundston (1.1%), respectively. Neighbourhood income quintile distribution shows that 45.1% of patients lived in lower-income areas (Q1: 19.8% and Q2: 25.3%), 22.0% in middle-income areas (Q3), and 33.0% in higher-income areas (Q4: 17.6% and Q5: 15.4%).

Stage at diagnosis was documented for 54.9% of the treatment cohort (n=250). A further 5.5% of the treatment cohort (n=25) had charts available but no stage recorded (unspecified), while 39.6% of the treatment cohort had no chart available (n=180). Among those with documented staging (n=250), stage 4 was most common (44.0%), followed by stage 3 (22.0%), stage 2 (20.0%), and stage 1 (14.0%).

Comorbidity patterns reflect those observed in Part 1, with hypertension being most prevalent (52.7%), followed by diabetes (23.1%), ischemic heart disease (22.0.%), and chronic obstructive pulmonary disease (18.7%). Acute myocardial infarction (8.8%), heart failure (6.6%), and stroke (5.5%) were less common.

COVID-19 diagnoses were identified using ICD code U07.1 in the Discharge Abstract Data, which captures hospitalized cases only. Approximately 5 patients (1.1%) had a documented COVID-19 hospitalization following their DLBCL diagnosis, with no COVID-19 deaths recorded among the cohort. This likely represents an underestimate of the true COVID-19 burden, as non-hospitalized cases are not captured in these data.

Characteristics stratified by treatment site are available in Supplemental Figures 4, 5, 6, 7, and 8 (see Appendix).

Table 3. Characteristics of DLBCL Treatment Cohort, Diagnosed 2006-2018 (n=455)

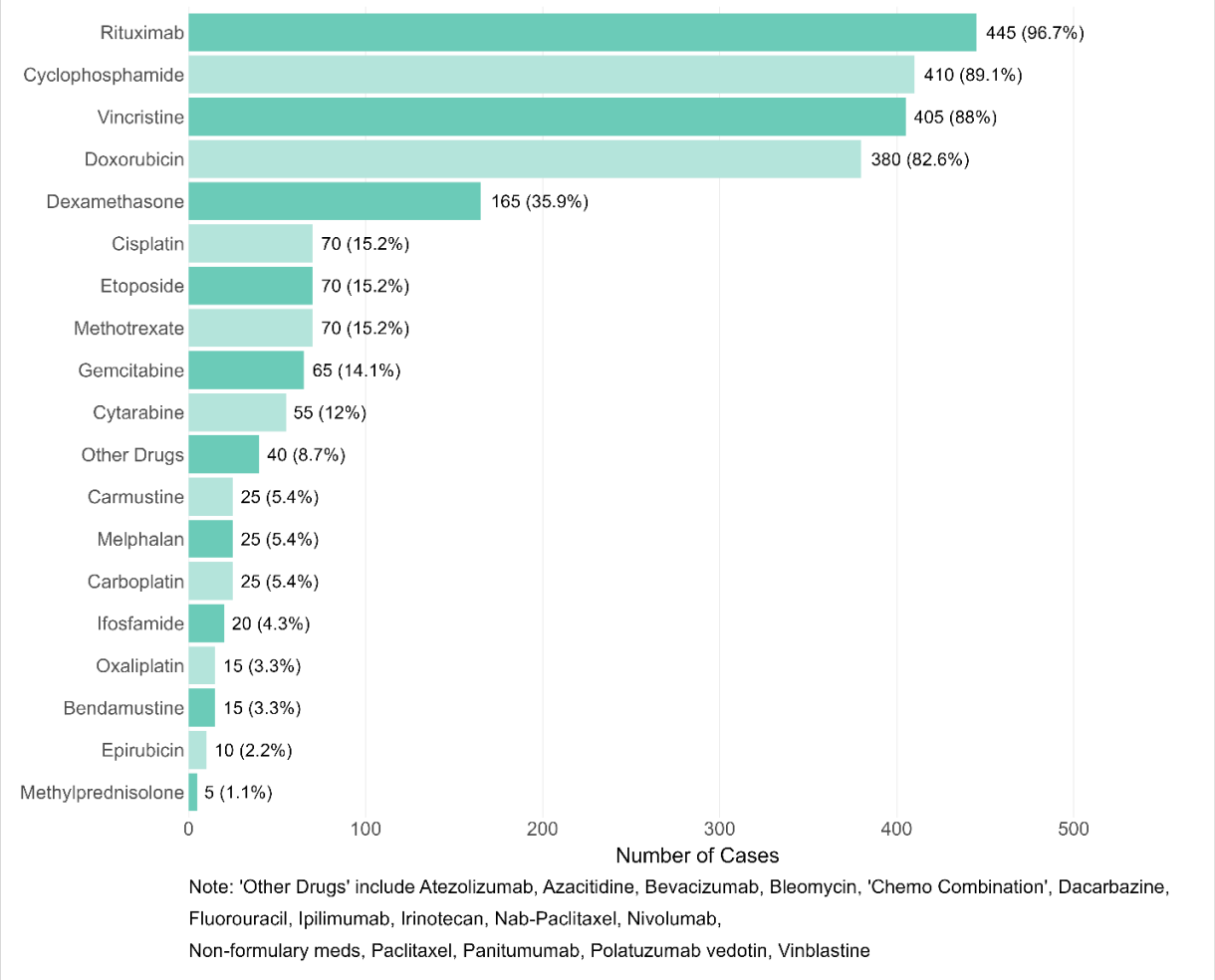
	Estimate (N, (%)), (M, (SD))
Treatment cohort by first-line therapy site	
Vitalité	85 (18.7%)
Fredericton	20 (4.4%)
Moncton, HHN	170 (37.4%)
Saint John	180 (39.6%)
Mean observation time in years(M(SD))	3.7 (1.9)
Treatment cohort socio-demographics and health characteristics	
Age at diagnosis	65.6 (12.8)
Sex	
Male	270 (59.3%)
Female	185 (40.7%)
Location of residence	
Bathurst	65 (14.3%)
Campbellton	15 (3.3%)
Edmundston	5 (1.1%)
Fredericton	70 (15.4%)
Miramichi	40 (8.8%)
Moncton	120 (26.4%)
Saint John	140 (30.8%)
Neighbourhood income quintile	
Q1	90 (19.8%)
Q2	115 (25.3%)
Q3	100 (22.0%)
Q4	80 (17.6%)
Q5	70 (15.4%)
Stage at diagnosis (n=250)	
Stage 1	35 (14.0%)
Stage 2	50 (20.0%)
Stage 3	55 (22.0%)
Stage 4	110 (44.0%)
Comorbidities	
Acute myocardial infarction	40 (8.8%)
Heart failure	30 (6.6%)
Hypertension	240 (52.7%)
Ischemic heart disease	100 (22.0%)
Stroke	25 (5.5%)
Chronic obstructive pulmonary disease	85 (18.7%)
Diabetes	105 (23.1%)
COVID-19 infection among hospitalized DLBCL patients	5 (1.1%)
COVID-19 deaths among DLBCL patients	0 (0.0%)

4.2.2 Treatment cohort chemotherapy agents administered

Chemotherapy regimens were characterized based on individual agents identified in IV Oncology Data. **Figure 9** displays the frequency of chemotherapy agents ever administered to patients during their follow-up period (defined as receiving an agent at least once). Rituximab was the most commonly administered agent, received by 96.7% of patients at least once. The other components of standard R-CHOP regimens were also frequently administered: cyclophosphamide (89.1%), vincristine (88%), and doxorubicin (82.6%). Dexamethasone, often used as supportive care or in alternative regimens, was administered to 35.9% of patients.

Second-line and salvage regimen agents were less common but still notable. Cisplatin, etoposide, and methotrexate were each administered to 15.2% of patients, while gemcitabine (14.1%) and cytarabine (12%) were also used. Other less commonly used agents included carmustine, melphalan, carboplatin, ifosfamide, oxaliplatin, bendamustine, epirubicin, and methylprednisolone, which were each administered to 5.4% or fewer patients. The "Other Drugs" category (8.7%) comprised agents not commonly found in the data set that were administered either for DLBCL treatment or for other cancer diagnoses.

Figure 9. Chemotherapy Agents Ever Administered (n=460).



4.2.3 Chemotherapy regimens

Chemotherapy regimens were identified by analyzing combinations of the 19 agents shown in Figure 9 administered on the same day or within a few days of each other. Patients were assigned to specific regimen categories based on these drug combinations, which reflect standard-of-care treatment protocols for DLBCL in Canada. For example, patients receiving rituximab, cyclophosphamide, vincristine, and doxorubicin (with or without dexamethasone) concurrently were classified as receiving R-CHOP.

Treatment line transitions were defined by changes in drug combination composition; within a given regimen, administration of the sane drug combination following a gap of more than seven days was defined as new treatment cycle rather than a new therapy line. For instance, a patient initially receiving R-CHOP who subsequently received a platinum-based salvage regimen (e.g., R-ICE: rituximab, ifosfamide, etoposide, carboplatin) would be classified as transitioning from first- to second-line therapy. Two complementary analyses were conducted to characterize treatment patterns:

Figure 10 presents regimens ever administered (at least once during follow-up), allowing examination of the full range of therapies patients received across all treatment lines.

Figure 11 shows regimens of longest duration, identifying the primary treatment approach for each patient based on the regimen they received for the greatest length of time. Due to small sample sizes in the longest duration analysis, individual platinum-based salvage regimens were collapsed into a single category for reporting purposes.

Chemotherapy regimens were categorized into four treatment groups: R-CHOP therapies (Figure 10a), platinum-based salvage therapies (Figure 10b), high-dosage therapies (Figure 10c), and alternative therapies (Figure 10d).

a. **R-CHOP (Figure 10a)** is the standard first-line treatment for DLBCL, consisting of rituximab, cyclophosphamide, doxorubicin, and vincristine administered intravenously. Prednisone, the fifth component, is administered orally in outpatient settings and therefore is not captured in IV Oncology Data. **R-CHOP variants** include cases where patients did not receive all essential agents (e.g., vincristine omitted) or received alternative agents (e.g., etoposide substituted for doxorubicin). **Less intensive R-CHOP** regimens were identified when epirubicin was substituted for doxorubicin, typically initiated for patients unable to tolerate standard dosing.

b. **Platinum-based salvage therapies (Figure 10b)** are typically used as second-line treatment following R-CHOP failure or relapse.

- **R-GDP** consists of rituximab with gemcitabine, dexamethasone, and cisplatin.
- **R-ICE** includes rituximab with ifosfamide, carboplatin, and etoposide.
- **R-DHAP** contains rituximab, dexamethasone, cytarabine, and cisplatin.
- **R-GemOx** comprises rituximab, gemcitabine, and oxaliplatin.

- **BR** (bendamustine and rituximab) represents a less intensive salvage option, often used for older patients, those with comorbidities, or palliative care.

c. **High-dosage therapy (Figure 10c)** refers to **BEAM**, an intensive 6-day conditioning regimen administered prior to HSCT. The regimen begins with carmustine on day 1, followed by etoposide and cytarabine on days 2-5, and concludes with melphalan on day 6. While considered a salvage therapy, BEAM is categorized separately due to its intensive nature and specific role in transplant preparation.

d. **Alternative therapies (Figure 10d)** include **single-agent therapies**, consisting of a single chemotherapy agent administered without concurrent regimens (e.g., rituximab monotherapy or dexamethasone alone). **Other regimens** comprise combinations administered to few patients or drug combinations that did not fit standard treatment categories. **Other drug combinations** include regimens containing the various agents listed in the Other Drugs category in Figure 9.

As shown in Figure 10, most of the treatment cohort (82.6%) received standard R-CHOP therapy at least once during follow-up, with smaller proportions receiving R-CHOP variants (5.4%) or less intensive R-CHOP formulations (1.1%). Among platinum-based salvage therapies, R-GDP was most common (12%), followed by R-ICE (4.3%), R-DHAP (3.3%), R-GemOx (3.3%), and BR (2.2%). High-dose BEAM therapy was administered to 5.4% of patients. Alternative therapies were also utilized: single-agent therapies in 13% of patients, other regimens in 7.6%, and other drug combinations in 4.3%.

Figure 10. Chemotherapy Regimens Ever Administered (n=460).

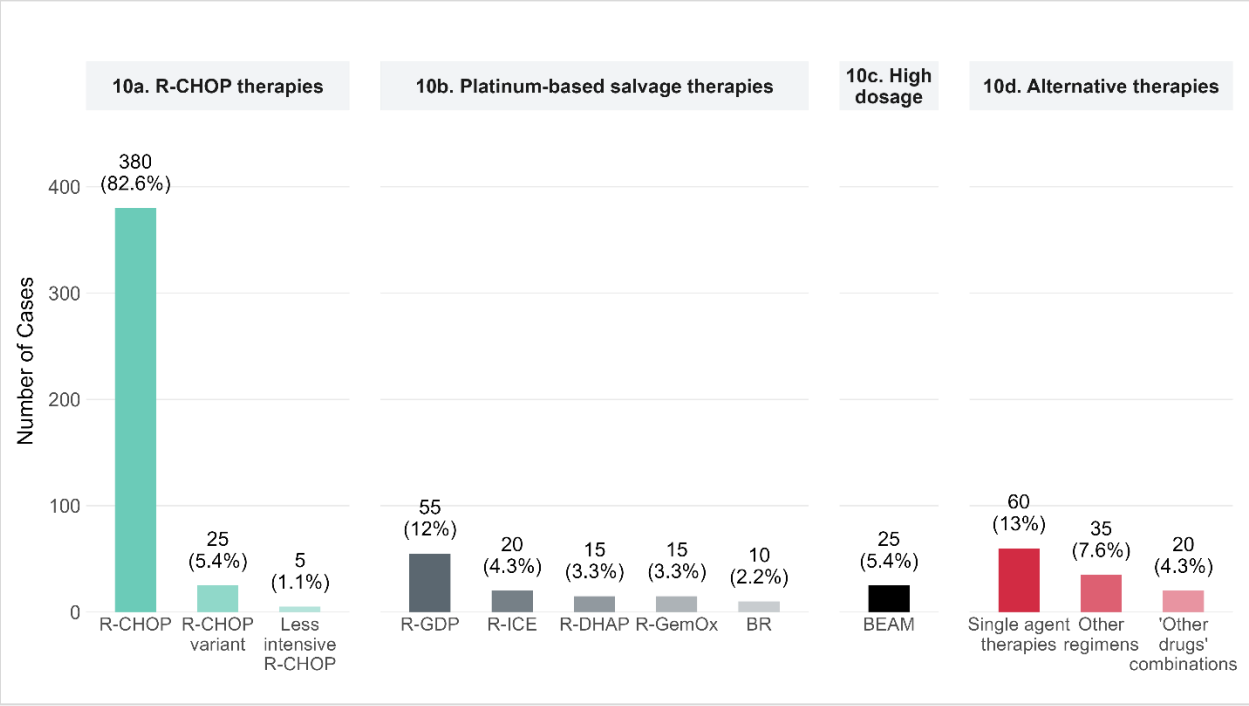
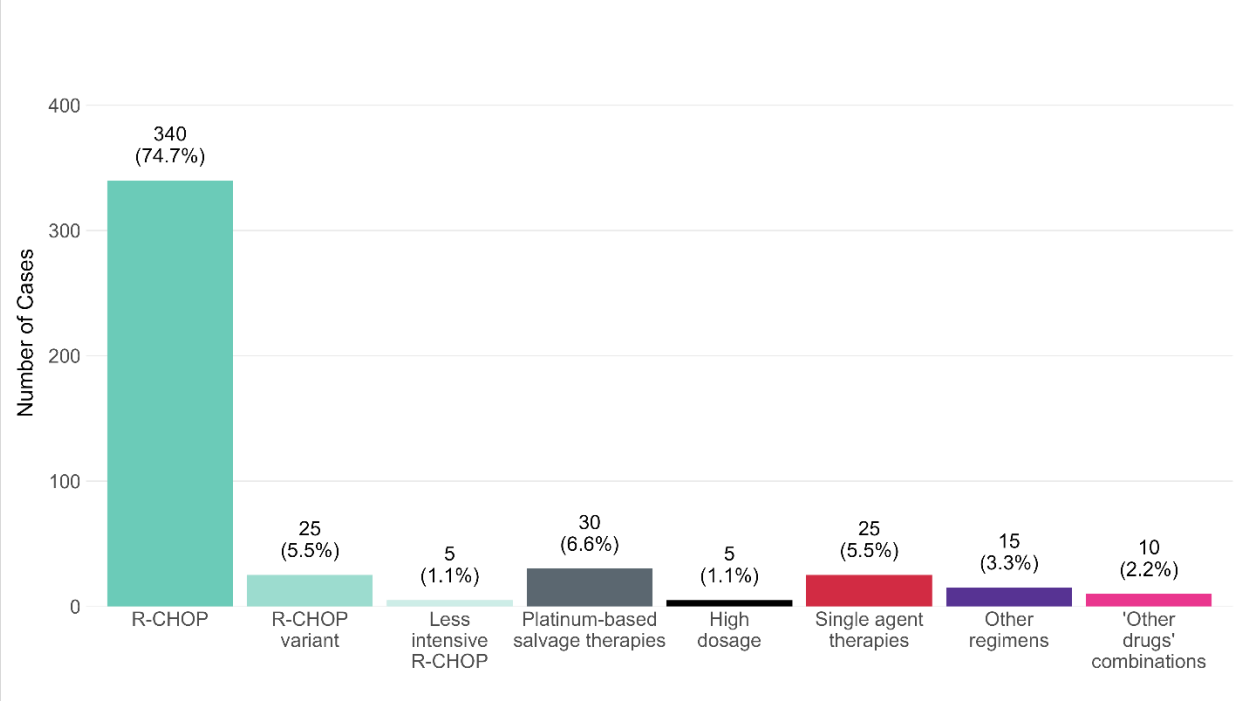


Figure 11 presents regimens of longest duration. Standard R-CHOP was the primary treatment approach for 74.7% of patients, with R-CHOP variants accounting for 5.5% and less intensive formulations accounting for 1.1%. Platinum-based salvage therapy as the longest duration regimen was observed in 6.6% of patients, typically representing cases of refractory disease or relapse requiring second-line treatment. High-dose BEAM was the longest duration regimen for 1.1% of patients. Among alternative therapies, single-agent therapies comprised 5.5%, other regimens 3.3%, and other drug combinations 2.2%.

Figure 11. Chemotherapy Regimens of Longest Duration (n=455).



4.2.4 Therapy lines

Therapy lines were defined based on the timing of treatment regimens described in Section 4.2.3, with transitions between lines defined by changes in drug combination composition. Within a given regimen, a new treatment cycle was defined as administration of the same drug combination following a gap of more than seven days. For reporting purposes, later lines of therapy were combined into a single category (e.g., Line 2+; Line 3+) to avoid reporting low frequency counts and to protect patient privacy.

Figure 12 presents the distribution of patients by line of therapy ever received and mean treatment duration.

Figure 12a presents all regimens combined: all 455 patients received first-line therapy (mean duration 91.5 days, SD=102.1), 155 (34.1%) received second-line therapy (mean duration 132.3 days, SD=194.8), and 60 (13.2%) received third-line or beyond (mean duration 58.4 days, SD=96.3). Figures 12b-12d present distribution of patients by line of therapy within specific

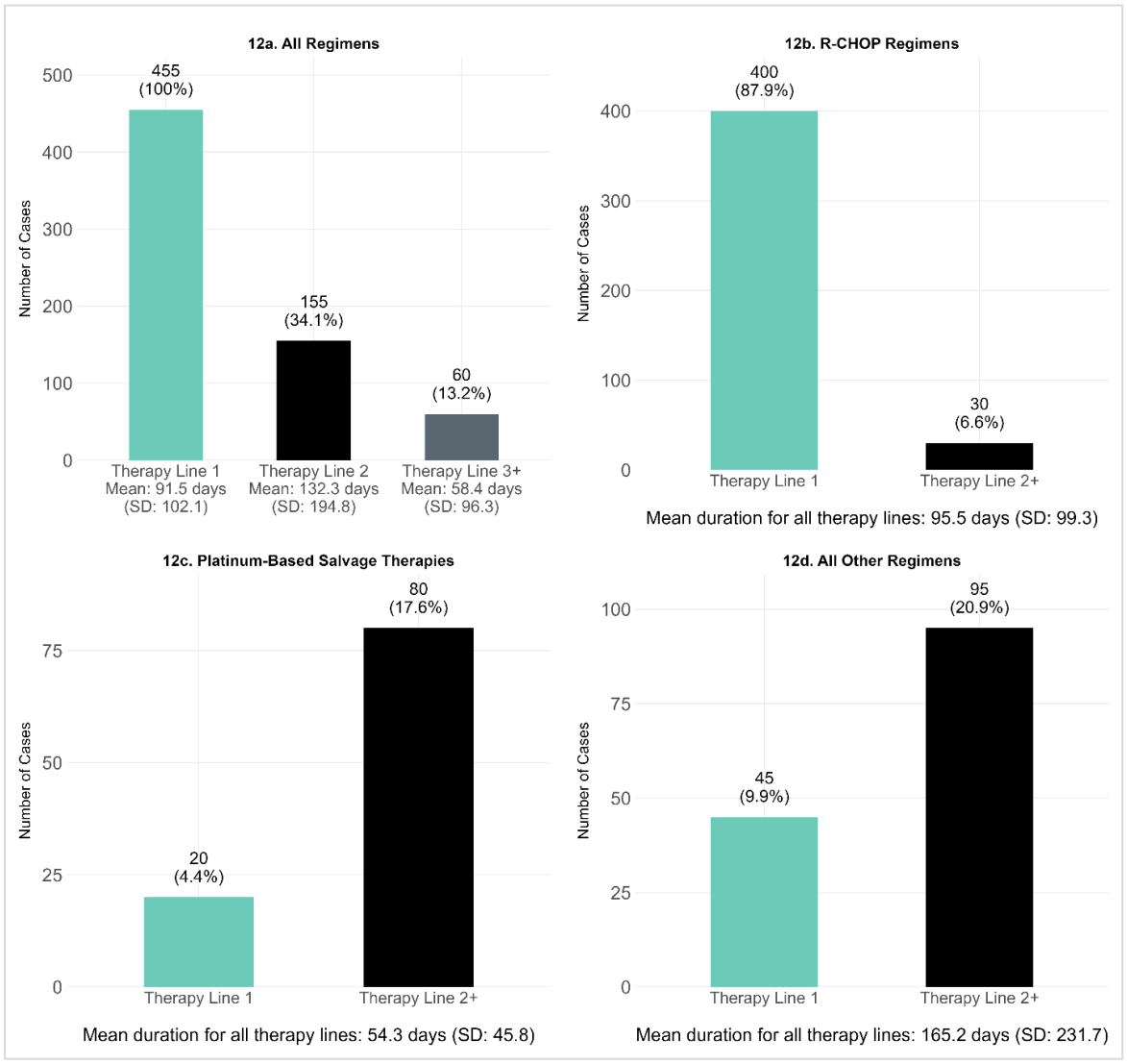
regimen categories. Due to limited sample size, mean treatment durations for regimen categories could not be reported for individual lines of therapy and are instead presented as averages across all therapy lines combined.

Among patients who received R-CHOP regimens (Figure 12b) – including R-CHOP, R-CHOP variants, and less intensive formulations – R-CHOP was first-line for 400 patients (87.9%) and second-line or later for 30 patients (6.6%), with an overall mean duration of 95.5 days (SD=99.3).

Platinum-based salvage therapies (Figure 12c) were first-line for 20 patients (4.4%) and second-line or later for 80 patients (17.6%), with an overall mean duration of 54.3 days (SD=45.8).

All other regimens (Figure 12d) were administered to 45 patients (9.9%) in first-line and 95 patients (20.9%) in second-line or later therapy, with an overall mean duration of 165.2 days (SD=231.7).

Figure 12. Lines of Therapy and Treatment Duration, Overall and by Regimen Type (n=455).



4.2.5 Radiation therapy, and hematopoietic stem cell transplant (HSCT)

Radiation therapy and hematopoietic stem cell transplants (HSCT) were also observed among the treatment cohort, as shown in **Table 4** below.

Of the 460 patients, 115 (25%) received radiation therapy within the follow-up period, with a mean duration of 22.5 days (SD=10.6). Hospital discharge records showed that 30 patients (6.5%) received HSCT within five years of DLBCL diagnosis, with a mean time from diagnosis to transplant of 532.3 days (SD=339.0).

It is important to note, however, that only in-hospital HSCT occurring in New Brunswick hospitals were observable in our data. Outpatient procedures and out-of-province procedures are not captured by the data sources used in this study.

Table 4. Therapy and HSCT Within 5-Year Interval (n=460)

	N (%)	Mean duration (days)	Mean days from diagnosis
Received radiation therapy	115 (25%)	22.5 days (SD:10.6)	
Received HSCT	30 (6.5%)		532.3 (SD: 339.0)

4.2.6 Survival outcomes

Kaplan-Meier (KM) curves were generated to estimate survival time among the DLBCL treatment cohort. Overall survival was analyzed over a 5-year follow-up period from diagnosis date (2006-2018 fiscal years) for all patients.

Regimen-specific survival analyses were conducted separately for patients' primary regimen (first-line therapy) and regimen of longest duration. Due to small event counts beyond three years when stratified by treatment type, regimen-specific analyses were limited to a 3-year follow-up period.

Additionally, treatment categories were collapsed into two groups – R-CHOP regimens, and all other regimens – to ensure adequate sample sizes and maintain patient confidentiality. Events (deaths) occurring after three years in specific regimen subgroups numbered fewer than five, necessitating these analytical restrictions.

Figure 13 presents 5-year overall survival for the DLBCL treatment cohort. Survival probability declined steeply in the first year following diagnosis, from 100% to approximately 85%, followed by a more gradual decline through years two and three, reaching approximately 70% at the 3-year mark. Beyond three years, the decline slowed. The estimated 5-year overall survival was 62%.

Figure 13. 5-Year Overall Survival for DLBCL Treatment Cohort (n = 455).

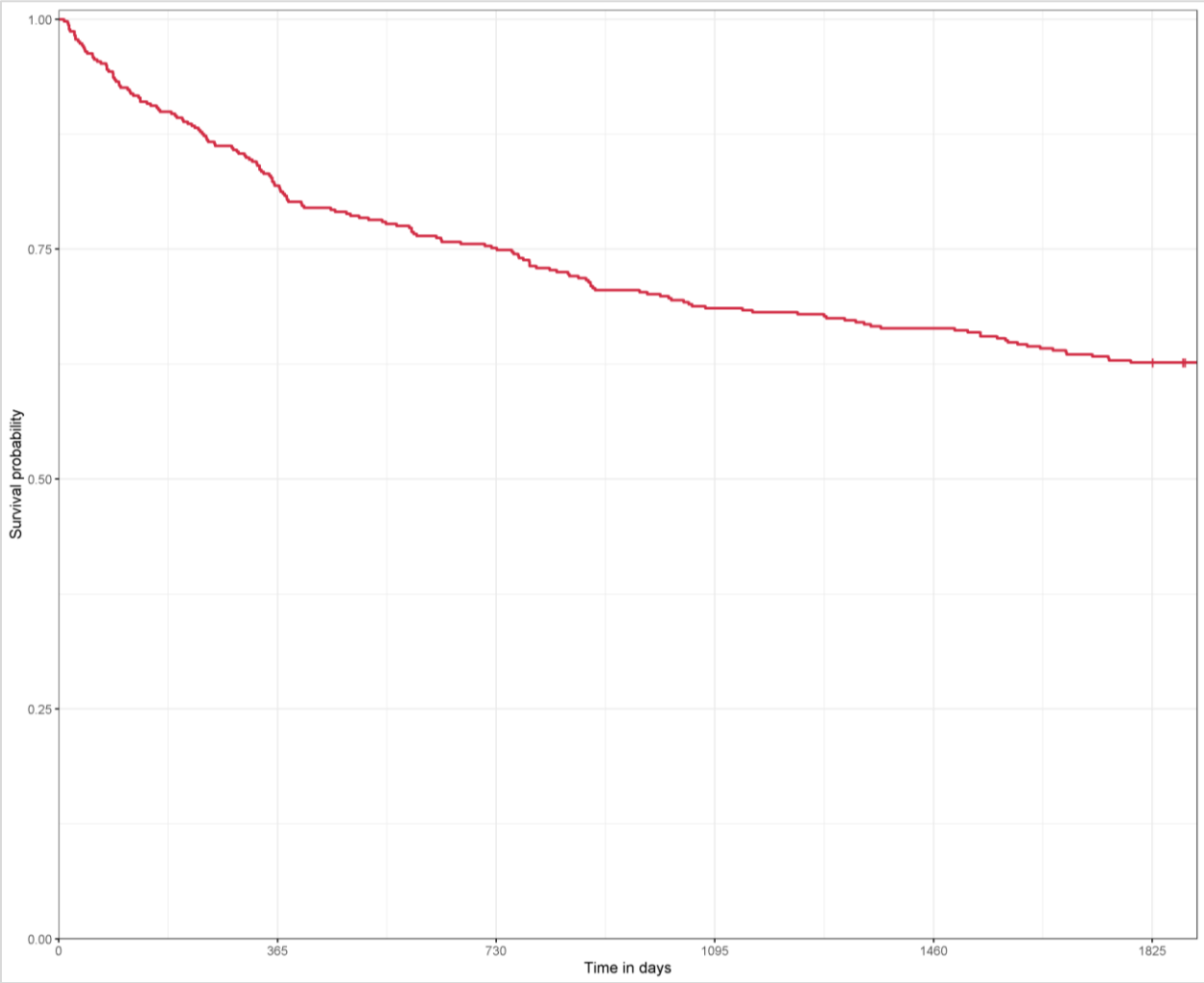


Figure 14 and **Figure 15** display 3-year survival stratified by treatment regimen – by primary regimen (first-line therapy) and by regimen of longest duration, respectively.

Among patients stratified by first-line regimen (Figure 14), the R-CHOP group showed approximately 72% survival at three years compared to approximately 49% for other regimens.

When stratified by regimen of longest duration (Figure 15), differences were less pronounced, with approximately 71% survival at three years for the R-CHOP group compared to approximately 58% for other regimens.

Figure 14. 3-Year Overall Survival for DLBCL Treatment Cohort by Primary Regimen (R-CHOP and Other Regimens).

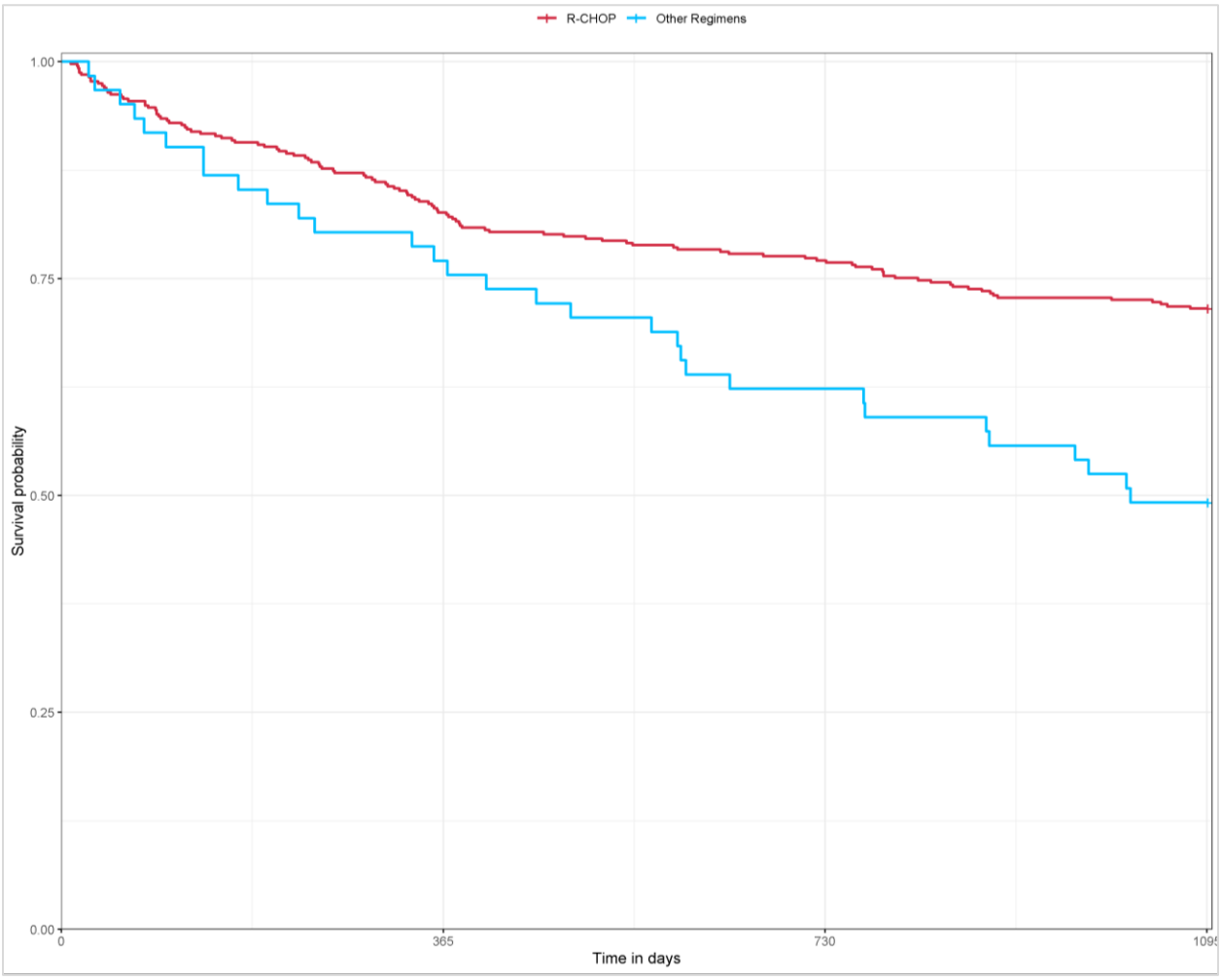
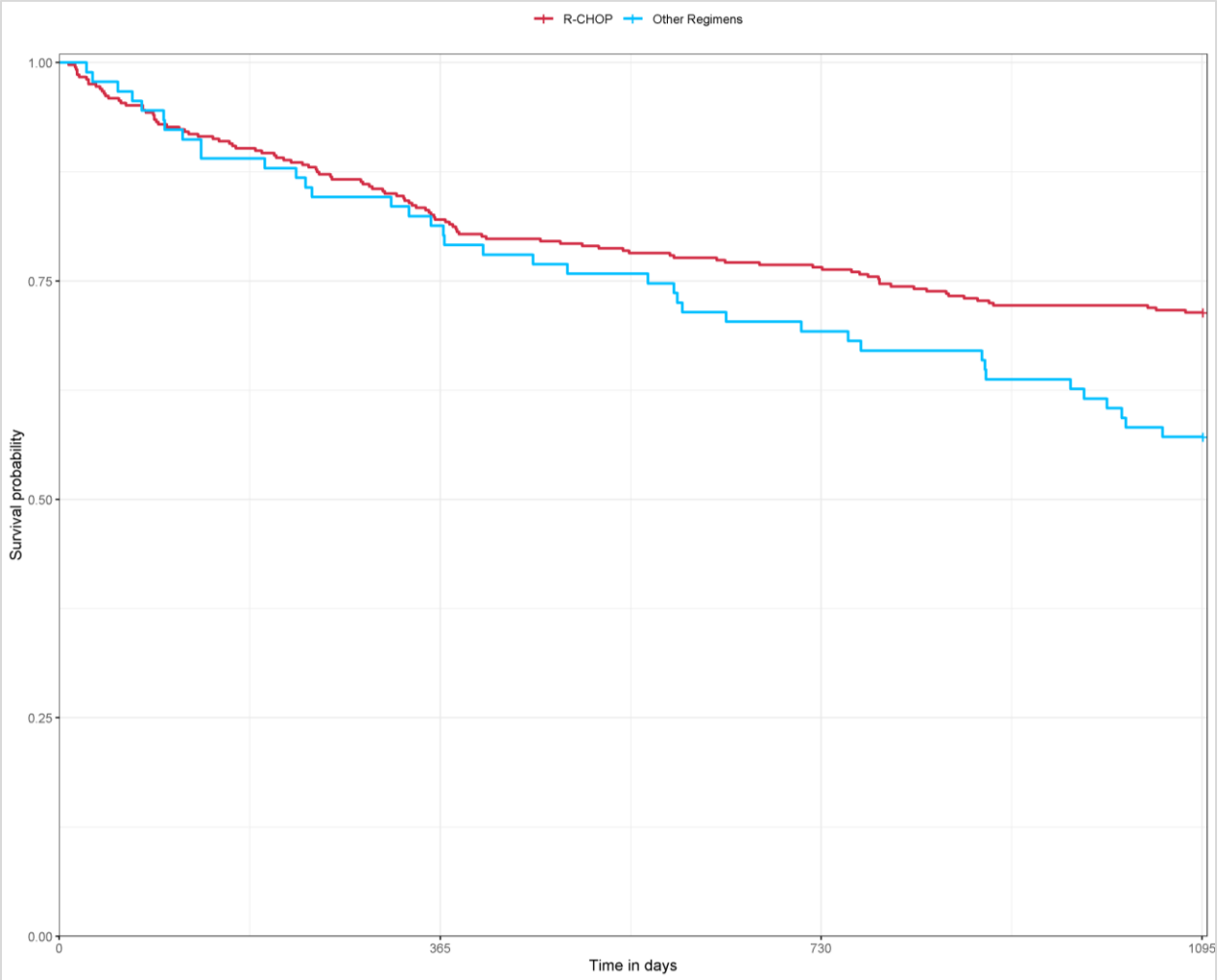


Figure 15. 3-Year Overall Survival for DLBCL Treatment Cohort by Regimen of Longest Duration (R-CHOP and Other Regimens).



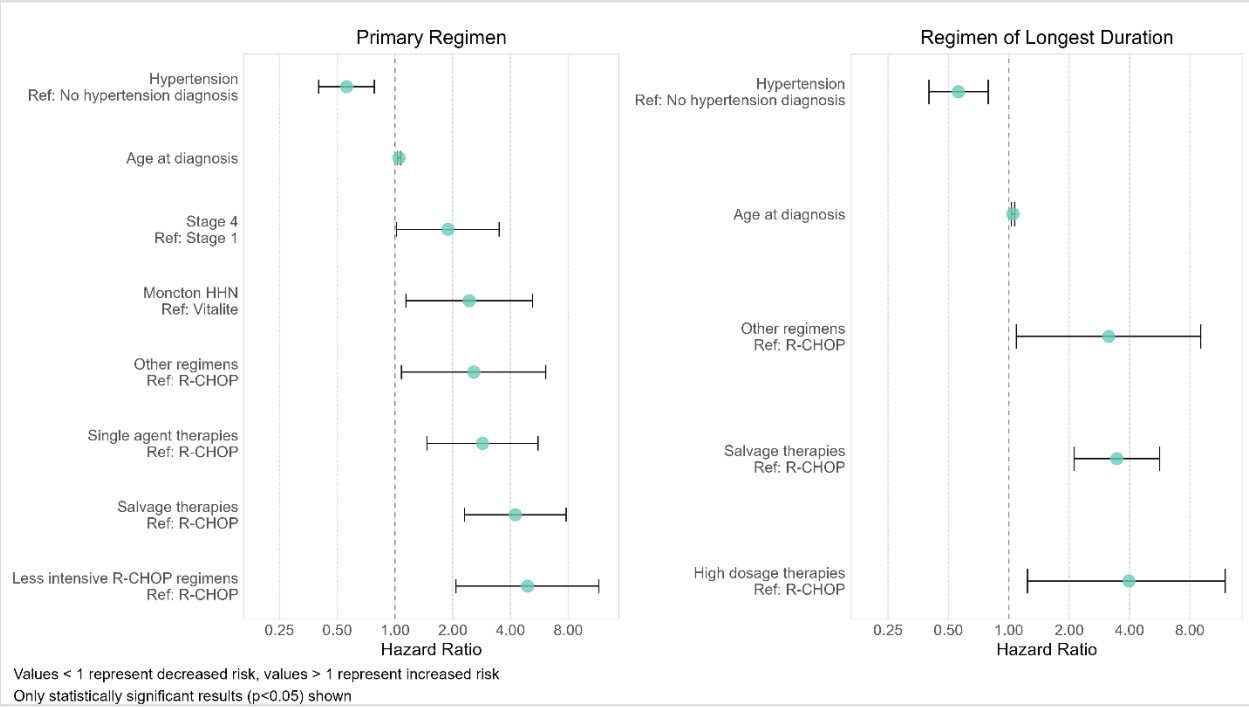
Using Cox proportional hazards models, **Figure 16** below identifies predictors of mortality among the DLBCL treatment cohort during the 5-year follow-up period from diagnosis. The point estimate plots display hazard ratios (HR) with 95% confidence intervals for statistically significant covariates only ($p<0.05$). Values greater than 1 (to the right of the vertical reference line at HR=1) indicate increased risk of death, while values less than 1 (to the left) indicate decreased risk and better survival outcomes.

Results are presented separately for primary regimen (first-line therapy) and regimen of longest duration. Several consistent predictors emerged across both analyses. Increasing age at diagnosis was associated with higher mortality risk (HR=1.05, $p<0.001$), meaning each additional year of age increased the hazard of death by 5%. Patients diagnosed with stage 4 DLBCL had significantly higher mortality risk compared to stage 1 (HR=1.89, $p=0.043$) in the primary regimen analysis. Conversely, comorbid hypertension was paradoxically associated with decreased mortality risk (HR=0.56, $p=0.001$).

Treatment regimen was a strong predictor of survival outcomes. In the primary regimen analysis, patients receiving less intensive R-CHOP (HR=4.91, p<0.001), salvage therapies (HR=4.24, p<0.001), single-agent therapies (HR=2.86, p=0.002), or other regimens (HR=2.58, p=0.032) as first-line treatment had significantly higher mortality risk compared to standard R-CHOP recipients. Patients treated at Moncton HHN also showed increased mortality risk compared to those treated through Vitalité (HR=2.44, p=0.022).

In the regimen of longest duration analysis, salvage therapies (HR=3.46, p<0.001), high-dose therapies (HR=3.97, p=0.021), and other regimens (HR=3.15, p=0.033) remained associated with increased mortality risk compared to R-CHOP. These findings underscore R-CHOP's effectiveness as the gold-standard first-line therapy for DLBCL, with alternative or salvage regimens generally indicating more aggressive disease or treatment failure requiring more intensive approaches. See Supplemental Table 3 and Supplemental Table 4 for the entire model results.

Figure 16. Cox Proportional Hazards Model Predicting Death in 5-Year Follow-up, Primary and Longest Duration Regimens (n=460).



4.2.7 Treatment pathways

Treatment pathways across therapy lines are presented in **Figure 17** below using a Sankey diagram to illustrate treatment transitions during the 5-year follow-up period. Due to random rounding of cell sizes to multiples of 5 for confidentiality protection, total sample sizes vary slightly across categories (ranging from 455 to 460), and estimates may not sum precisely across therapy lines.

R-CHOP first-line pathways (n=395, 86.8%)

The majority of patients received R-CHOP or R-CHOP variants as first-line therapy (n=395). Of these, 270 (68.4%) received no further treatment, with 190 (70.4%) surviving 5+ years post-diagnosis.

Among the 125 patients who received second-line therapy after R-CHOP, 55 transitioned to platinum-based salvage therapy, and 70 received non-platinum-based regimens. Of those receiving platinum-based salvage therapy, 20 received no further treatment (10 survived 5+ years), while 35 progressed to third-line therapy consisting of BEAM+HSCT (n=5), HSCT or BEAM alone (n=10), or BR/other platinum regimens (n=15), with 15 surviving 5+ years.

For patients receiving non-platinum-based second-line therapy (n=70), 50 required no further treatment (30 survived 5+ years), while 25 received third-line therapy: BEAM+HSCT (n=5), HSCT or BEAM alone (n=5), or BR/other platinum regimens (n=15), with only 10 surviving 5+ years.

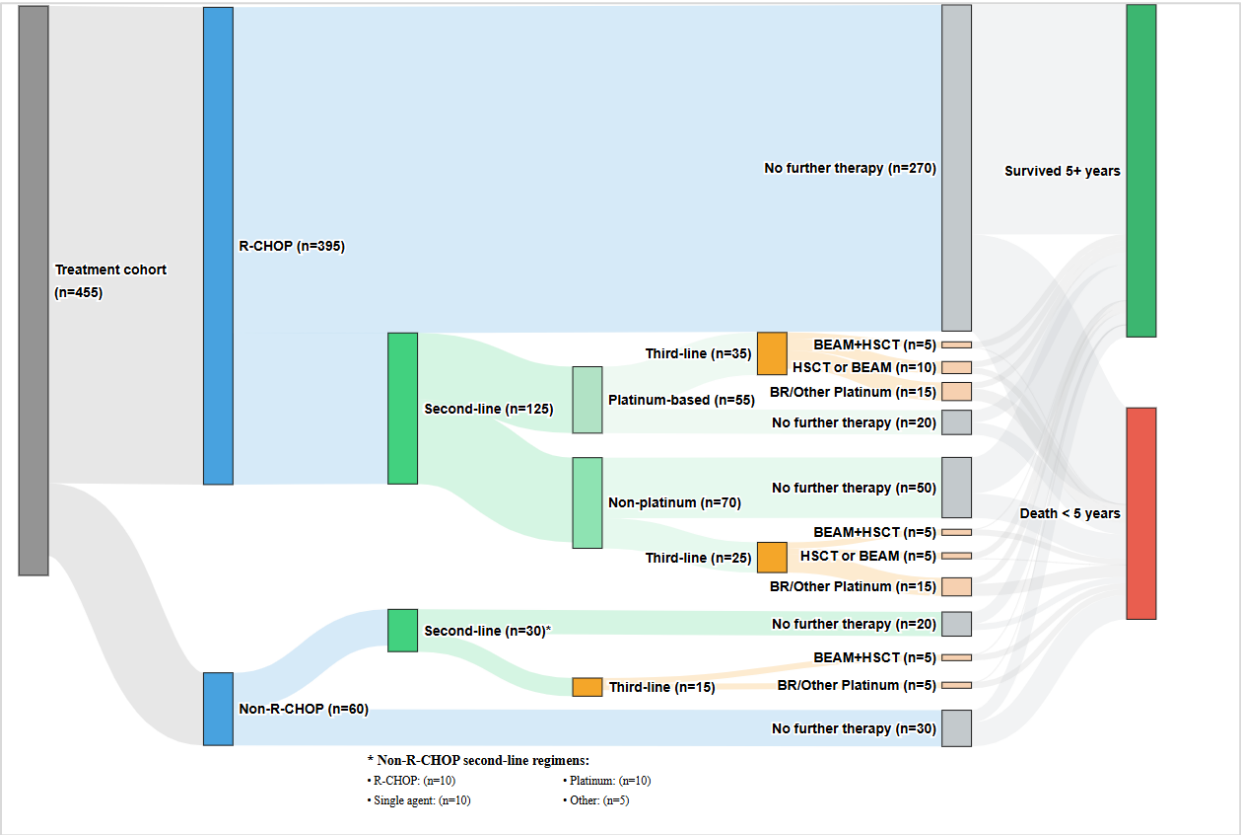
Non-R-CHOP first-line pathways (n=60, 13.2%)

Sixty patients received alternative first-line regimens, including platinum-based salvage therapies (n=20), single-agent therapies (n=15), and other regimens (n=25). Half (n=30) received no further treatment, with only 10 (33.3%) surviving 5+ years – markedly lower than the R-CHOP group.

The remaining 30 patients received second-line therapy: R-CHOP (n=10), platinum-based salvage (n=10), single-agent therapies (n=10), or other regimens (n=5). Of these, 20 received no further treatment, with approximately 10 surviving 5+ years. Fifteen patients progressed to third-line therapy (BEAM+HSCT or BR/other platinum regimens), with none surviving 5+ years, highlighting the poor prognosis associated with non-R-CHOP first-line pathways requiring multiple treatment lines.

Overall, patients receiving R-CHOP as first-line therapy demonstrated substantially better outcomes, with 70.4% of those who received no further treatment surviving 5+ years compared to 33.3% among non-R-CHOP recipients. Treatment with multiple lines of therapy was associated with progressively worse survival, particularly among patients who did not receive R-CHOP initially.

Figure 17. DLBCL Treatment Pathways and 5-Year Outcomes.



4.2.8 Healthcare resource utilization

Healthcare resource utilization was analyzed for the DLBCL treatment cohort, tracking non-elective hospital admissions, intensive care unit (ICU) admissions, and emergency department (ED) visits during the 5-year follow-up period. Admission and visit rates were calculated per 100 person-years, where the denominator represents total accumulated follow-up time across all cohort members from diagnosis until death, departure from the province, or the end of the 5-year follow-up period, whichever occurred first. Mean and median length of stay were calculated among patients with at least one admission or visit.

Results are summarized in **Table 5** below.

Non-elective hospital admissions and ICU utilization

Of the 460 treatment cohort patients, 380 (82.6%) were hospitalized at least once during their 5-year follow-up, with a total of 1,310 non-elective admissions across the cohort. The frequency of hospital admissions varied: 115 patients were admitted once, 75 twice, 50 three times, 45 four times, and the remaining patients five or more times. The mean length of hospital stay was 13.2 days (SD=20.1), with a median of 7.3 days (IQR: 4-13), indicating that most stays were relatively brief with some patients experiencing prolonged hospitalizations. The hospital admission rate was 77.3 per 100 person-years.

Ninety-five patients (20.7%) required at least one ICU admission, with a total of 95 ICU admissions across the cohort – 80 patients admitted once, and 10 admitted twice or more. The mean ICU stay was 4.1 days (SD=4.9), with a median of 2 days (IQR: 1-5). The ICU admission rate was 6.5 per 100 person-years.

Emergency department (ED) visits

ED visits were examined among the subset of the treatment cohort whose follow-up period overlapped with the available date range for NB ED data (January 1, 2017, to December 1, 2021). Patients were included if at least one year of their follow-up fell within this window, establishing an ED subsample (n=350). A total of 160 ED visits were recorded among the ED subsample, with visit frequency ranging from one to four or more visits: 15 patients had a single visit, 5 had two visits, 10 had three visits, and 15 had four or more visits. The ED visit rate was 12.0 per 100 person-years.

Table 5. Healthcare Resource Utilization Among the DLBCL Treatment Cohort During 5-Year Follow-Up (n=460)

Healthcare resource utilization	Count	Rate per 100 PY	Mean (SD) length of stay in days	Median (IQR) length of stay in days
Non-elective hospital admissions				
Total admissions	1,310	77.3	13.2 (20.1)	7.3 (IQR: 4 - 13)
1 admission	115			
2 admissions	75			
3 admissions	50			
4 admissions	45			
5+ admissions	95			
Intensive care unit admissions				
Total admissions	95	6.5	4.1 (4.9)	2 (IQR: 1 - 5)
1 admission	80			
2+ admissions	10			
Emergency department visits (ED subsample; n=350)				
Total ED visits	160	12.0	-	-
1 visit	15			
2 visits	5			
3 visits	10			
4+ visits	15			

Healthcare utilization outcomes stratified by treatment regimen are presented in **Table 6** below, comparing R-CHOP regimens versus all other regimens for both primary (first-line) regimens and

regimens of longest duration. Mean values reflect the average number of admissions or visits per person among those with at least one event. Admission and visit rates, expressed per 100 person-years, are the primary metric of comparison as they account for differences in follow-up time across regimen groups; these are calculated by dividing total events within each regimen group by the total accumulated follow-up time for that group.

Non-elective hospital admissions by treatment regimen

Table 6 shows that among patients receiving R-CHOP as their primary regimen, 325 had at least one non-elective hospital admission, with an average of 3.2 admissions (SD=2.2) among those hospitalized, as well as a hospital admission rate of 68.7 per 100 person-years. The other regimens group showed a notably higher rate of 116.5 admissions per 100 person-years, with 55 patients having at least one admission and an average of 3.9 admissions (SD=2.6). By longest duration regimen, rates were 68.3 and 99.4 per 100 person-years for R-CHOP and other regimens, respectively, with mean admissions of 3.2 and 3.8. Across both analyses, patients receiving non-R-CHOP regimens showed consistently higher hospital admission rates.

Intensive care unit admissions by treatment regimen

As shown in Table 6, among patients receiving R-CHOP as their primary regimen, 75 required at least one ICU admission, with a mean of 1.1 admissions (SD=0.3) and an ICU admission rate of 5.5 per 100 person-years. The other regimens group showed a markedly higher rate of 14.2 per 100 person-years, with 20 (33.3%) patients requiring ICU admission and a mean of 1.4 admissions (SD=0.9). By regimen of longest duration, ICU rates were 6.0 and 8.5 per 100 person-years for R-CHOP and other regimens, respectively, with means of 1.1 (SD=0.3) and 1.4 (SD=0.9), with the difference between groups less pronounced than in the primary regimen analysis.

Emergency department visits by treatment regimen

ED visit rates by treatment regimen are also presented in Table 6. For primary regimens, rates were 11.8 and 13.8 per 100 person-years for R-CHOP and other regimens, with a smaller difference observed by longest duration regimen (12.3 vs 10.9 per 100 person-years). Unlike hospital and ICU admissions, ED visit rates were broadly similar across regimen groups in both analyses. The small number of non-R-CHOP patients in the ED subsample warrants caution in interpretation.

Overall, rates of non-elective hospital admissions and ICU admissions were consistently higher among patients receiving non-R-CHOP regimens compared to those receiving R-CHOP, across both primary and longest duration regimen analyses. However, ED visit rates were comparable across regimen groups. The difference was most pronounced for hospital admissions and ICU admissions in the primary regimen analysis (116.5 vs. 68.7, and 14.2 vs. 5.5 per 100 person-years, respectively).

Table 6. Healthcare Resource Utilization by Treatment Regimen Among the DLBCL Treatment Cohort During 5-Year Follow-Up (n=460).

	Primary Regimens		Regimen of Longest Duration	
	R-CHOP Regimens (n=400)	All Other Regimens (n=60)	R-CHOP Regimens (n=370)	All Other Regimens (n=90)
Hospital admissions				
>= 1 admission	325 (81.3%)	55 (91.7%)	305 (82.4%)	80 (88.9%)
Mean (SD)	3.2 (2.2)	3.9 (2.6)	3.2 (2.2)	3.8 (2.6)
Rate per 100 PY	68.7	116.5	68.3	99.4
ICU admissions				
>= 1 admission	75 (18.8%)	20 (33.3%)	75 (20.3%)	20 (22.2%)
Mean (SD)	1.1 (0.3)	1.4 (0.9)	1.1 (0.3)	1.4 (0.9)
Rate per 100 PY	5.5	14.2	6.0	8.5
ED visits				
ED subsample	300	50	275	80
>= 1 admission	40 (13.3%)	5 (10.0%)	35 (12.7%)	5 (6.3%)
Mean (SD)	3.4 (2.8)	4.4 (4.5)	3.4 (2.8)	3.9 (3.9)
Rate per 100 PY	11.8	13.8	12.3	10.9

Note:>= 1 admission reflects the number of patients with at least one admission/visit. Mean results reflect the average number of admissions/visits among those with at least one event. Rate is expressed per person-year. ED analyses are restricted to patients with follow-up overlapping the ED data window (Jan 1, 2017, to Dec 1, 2021).

4.2.9 Drug discontinuation

Number of discontinuation events

Figure 18a below presents drug discontinuation patterns among the DLBCL treatment cohort. Of the 455 patients, 210 (46.2%) had discontinuation information available from chart reviews, while discontinuation information was not available for 245 (53.8%) patients.

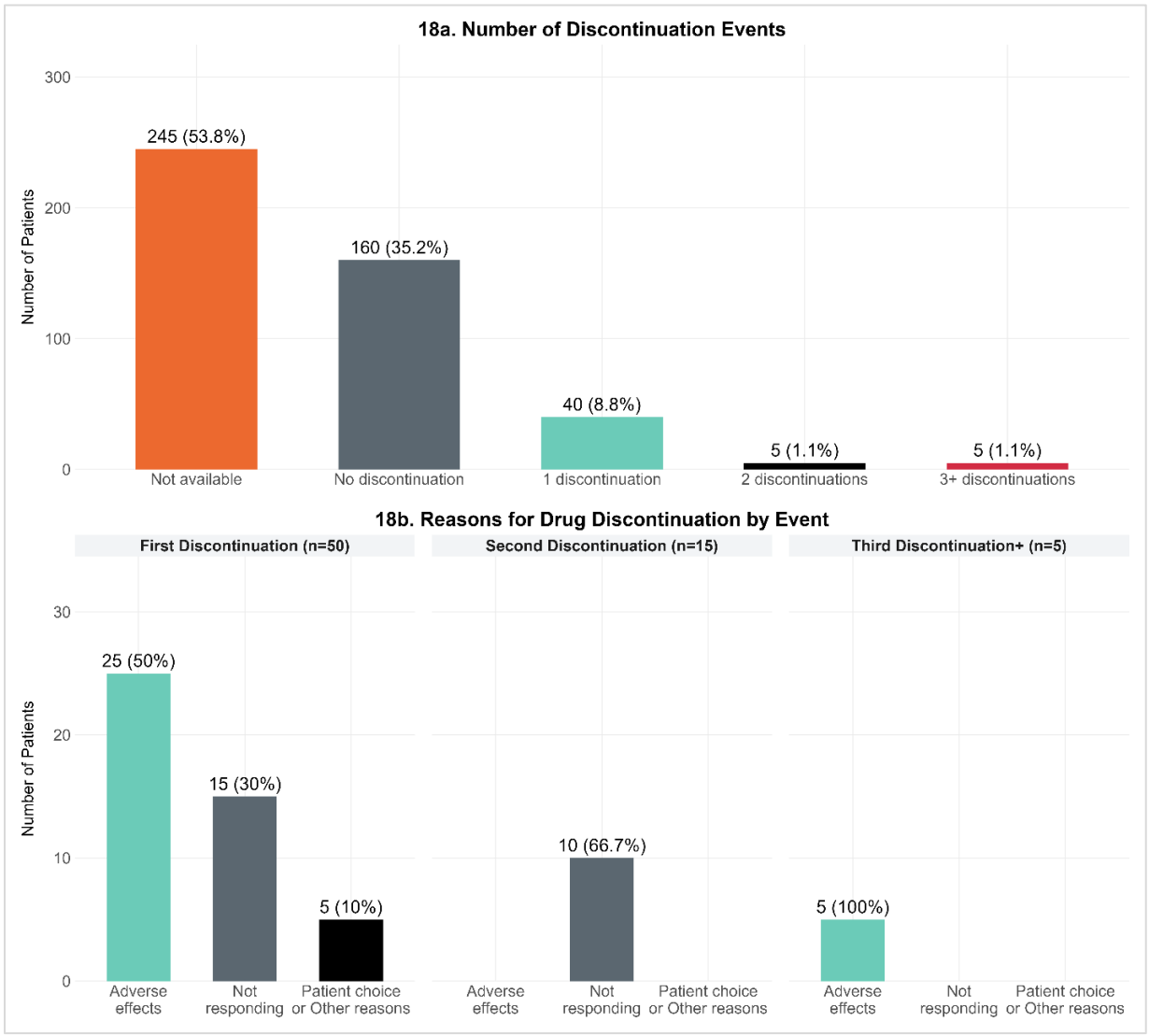
Among those with documented information, 160 patients (76.2%) did not discontinue any chemotherapy drugs (as per the definition of discontinuation described in the Methods, above), and 50 (23.8%) experienced at least one discontinuation. Among patients with at least one discontinuation, 40 patients (80%) had a single discontinuation, 5 patients (10%) had two discontinuations, and 5 patients (10%) had three or more discontinuations.

Reasons for discontinuation

Figure 18b details the reasons for discontinuation by event. Of the 50 patients with at least one discontinuation, the most commonly documented reason for the first discontinuation was adverse effects, safety concern, or drug intolerance (hereafter 'adverse effects') (n=25), followed by lack of response to treatment (hereafter 'not responding')(n=15), and patient desire to stop treatment, other reasons, or reason unspecified (hereafter 'patient choice or other reasons')(n=5).

For second discontinuation events (n=15; slight discrepancy from expected n=10 reflects random rounding), not responding was the most common reason (n=10). In cases of third or subsequent discontinuation (n=5), adverse effects was the documented reason in all cases (n=5).

Figure 18. Chemotherapy Drug Discontinuation, Number of Discontinuations, and Reasons for Discontinuation (n=455).

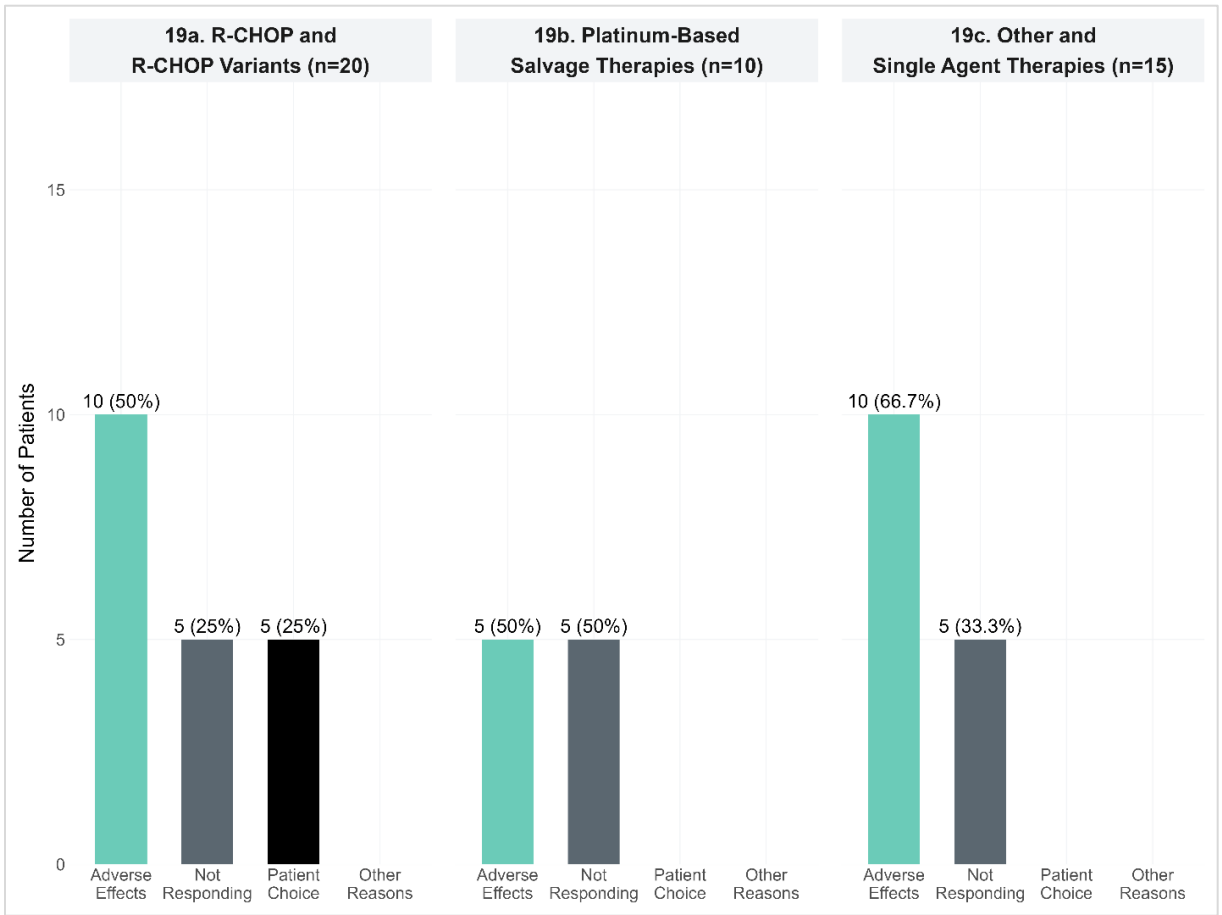


Reason for first discontinuation by treatment regimen

Figure 19 presents first treatment discontinuation by reason, stratified by the regimen discontinued. Of the 50 patients who experienced a first discontinuation, the discontinued regimen was R-CHOP or an R-CHOP variant in 20 cases (40%), another or single-agent regimen in 15 cases (30%), and a platinum-based salvage therapy in 10 cases (20%). Note that figures are subject to random rounding and may not sum to exactly 50.

For R-CHOP and R-CHOP variant discontinuations, adverse effects was the most common reason (n=10), followed by not responding to treatment (n=5) and patient choice (n=5). Salvage therapy discontinuations were split evenly between adverse effects (n=5) and not responding to treatment (n=5). For other regimens or single-agent therapies, adverse effects, safety concerns, or drug intolerance accounted for the majority of discontinuations (n=10), with lack of response to treatment accounting for the remainder (n=5). Similar analyses were attempted for second and third discontinuation events; however, small sample sizes (n=15 and n=5) combined with random rounding requirements limited interpretability. As such, stratified results are presented for first discontinuation only.

Figure 19. First Treatment Discontinuation by Regimen and Reason (n=50).



5. Discussion

This study provides the first population-level analysis of Diffuse Large B-Cell Lymphoma (DLBCL) in the province of New Brunswick, examining epidemiology, treatment pathways, and outcomes from 2006 to 2021 using linked administrative health data. Findings establish baseline epidemiological and clinical characteristics of the New Brunswick DLBCL population, document real-world treatment patterns and healthcare resource utilization, and offer a foundation for future efforts to monitor and improve DLBCL care in the province.

5.1 Discussion of Findings

5.1.1 Epidemiology and population characteristics

DLBCL incidence in New Brunswick increased from 8.7 per 100,000 in 2006-2007 to 13.4 per 100,000 in 2020-2021, aligning with rising global trends [1,5,6] and confirming that New Brunswick mirrors the international pattern of increasing DLBCL diagnoses. The prevalent DLBCL population more than doubled over the study period, growing from 365 cases in 2006-2007 to 795 in 2020-2021 – though prevalence estimates included patients who achieved remission. This growth reflects both increasing incidence and improving survival, creating growing demands on healthcare resources in a province already facing challenges with timely access to healthcare services.

The mean age at diagnosis was 66.2 years, with males comprising 54.5% of cases. Among staged cases, 29% presented with advanced stage 4 disease, and the majority of the entire DLBCL population (68.5%) had hypertension at the time of diagnosis, reflecting the considerable comorbidity burden in this population.

The concentration of cases in lower-to-middle income neighbourhoods (65.5%) warrants attention, as socioeconomic factors may influence access to care, treatment completion, and outcomes. Though not the focus of this analysis, these socioeconomic associations are an area of concern as existing work shows individuals diagnosed with DLBCL living in neighbourhoods of lower socioeconomic status face greater risk of mortality compared to their higher status counterparts [18].

5.1.2 Treatment pathways and access to care

Standard R-CHOP was the predominant first-line therapy. Among the treatment cohort, 82.6% received standard R-CHOP at least once during their 5-year follow-up; when R-CHOP variants are included, 86.8% received an R-CHOP-based regimen as first-line therapy. This demonstrates strong adherence to international and Canadian standard of care and treatment guidelines [2,8,9]. Only 34% of patients received second-line therapy, and 16.5% received third-line therapy or beyond, suggesting that most patients achieved remission with initial treatment.

It should be noted that the observation window for treatment pathways (summarized in Table 2) largely reflects an era of DLBCL management prior to the advent of novel therapies including chimeric antigen receptor T cell (CAR-T) therapy, bispecific antibodies, and polatuzumab. For this reason, the results of this study represent a useful historical comparator for incoming evaluations of recently developed agents and treatment modalities.

Stratified analyses by treatment site are presented in Supplemental Figures 1-8 (see Appendix). Notably, geographic disparities in access to care were evident in travel distance to treatment, with Vitalité Health Network patients traveling longer distances on average (87.4 km) compared to Horizon Health Network patients (69.3 km), likely reflecting the more rural distribution of the Vitalité patient population.

The HSCT rate in the treatment cohort was 6.5%, with an average of 532 days from diagnosis to transplant. Among patients who received salvage therapy – and who would therefore be candidates for HSCT – the transplant rate is notably lower than published estimates from other jurisdictions, where HSCT rates among second-line patients range from approximately 17.9% to 28% [19,20]. This gap suggests either limited transplant capacity within the province, high rates of transplant ineligibility due to age, comorbidities, or disease progression, or both. The absence of data on out-of-province transplants represents an analytical limitation, as some patients may have received HSCT outside New Brunswick and are therefore not captured in this study.

5.1.3 Survival outcomes

Five-year overall survival was 62% for the treatment cohort, aligning with published estimates for R-CHOP-treated DLBCL [2,8,9] and demonstrating outcomes comparable to international benchmarks [13,21]. This suggests that outcomes in New Brunswick are comparable to those reported elsewhere.

Patients receiving R-CHOP as first-line therapy had notably better survival than those receiving other treatments. While first-line R-CHOP therapy demonstrated superior 3-year survival (72%) compared to alternative regimens (49%), these outcomes must be interpreted through the lens of 'confounding by indication.' The elevated HRs for alternative treatments do not necessarily indicate inferior drug efficacy. Instead, patients prescribed non-standard regimens typically present with more aggressive disease, advanced age, or cardiac contraindications that preclude standard anthracycline use. Consequently, the lower survival observed in this cohort may be primarily a reflection of their inherently poorer baseline health status and higher baseline mortality risk.

Cox proportional hazards modeling identified several significant mortality predictors: older age at diagnosis (HR=1.05 per year), stage 4 disease (HR=1.89), and non-R-CHOP therapies as the primary or most commonly administered treatment regimen (HR=2.58-4.91). The elevated hazard ratios for non-R-CHOP regimens likely reflect their use in patients with more advanced/aggressive disease or those with relapsed/refractory DLBCL rather than indicating inferior treatment efficacy [22]. Increased mortality risk associated with alternative first-line regimens may also reflect poor underlying health status, as patients receiving non-R-CHOP therapies may have had contraindications to standard treatment due to age, poor

performance status, or comorbidities. This interpretation is supported by the treatment pathway analysis showing that patients who did not receive R-CHOP as a first-line therapy had markedly worse survival, even when subsequently treated with additional therapy lines.

Documented hypertension at DLBCL diagnosis was associated with reduced mortality risk (HR=0.56). This observation likely reflects surveillance bias, wherein patients with diagnosed hypertension interact more regularly with healthcare providers, resulting in earlier detection and management of incident lymphoma and consequently improved survival.

5.1.4 Healthcare resource utilization

Our findings provide insight into the healthcare resource needs of DLBCL patients throughout their treatment course. The majority of the treatment cohort (82.6%) required at least one non-elective hospitalization, with a hospital admission rate of 77.3 per 100 person-years across the cohort. Such hospitalization burden is consistent with findings from other real-world DLBCL studies reporting high rates of non-elective admissions and comparable lengths of stay among treated patients [7,23,24].

ICU admission was required by 20.7% of patients, with a rate of 6.5 admissions per 100 person-years. Findings align with previous Canadian research demonstrating high healthcare utilization during DLBCL treatment [7] and emphasize the importance of supportive care resources for this population.

Across both primary and longest duration regimen analyses, patients receiving non-R-CHOP regimens showed higher rates of hospital admissions and ICU admissions compared to those receiving R-CHOP. This is a pattern that likely reflects more complex disease among patients requiring alternative therapeutic approaches and/or increased treatment-related toxicity [12]. ED visit rates were broadly comparable across regimen groups in both analyses (primary: 13.8 vs. 11.8 per 100 person-years; longest duration: 10.9 vs. 12.3 per 100 person-years), though the small number of non-R-CHOP patients in the ED subsample warrants caution in interpretation

5.1.5 Treatment discontinuation

Nearly one quarter of patients with available data discontinued treatment at least once, with adverse effects driving the majority of initial discontinuations. Lack of efficacy as the predominant reason for subsequent discontinuations – should this be confirmed with larger samples – suggests a clinically relevant pattern whereby tolerability barriers are addressed through regimen modification, leaving disease refractory to treatment as the primary remaining challenge.

The higher frequency of adverse effect-related discontinuations among patients receiving alternative and single-agent regimens likely reflects both the tolerability profiles of these agents and the characteristics of the patients who receive them, which are often older individuals or those with significant comorbidities for whom standard R-CHOP is contraindicated.

5.2 Strengths and Limitations

5.2.1 Strengths

This study has several strengths that enhance the validity and utility of its findings.

By employing population-level administrative health data, the study includes all patients with an active provincial healthcare number in New Brunswick who were diagnosed with DLBCL over 15 years. This is a strength because the analysis avoids the risk of selection bias, which may occur in single treatment site or clinical trial populations, providing a true representation of real-world practice patterns and outcomes. Additionally, the integration of multiple administrative databases with clinical chart reviews enabled examination of a broad range of outcomes, including epidemiological trends, treatment pathways, survival, healthcare resource utilization, and reasons for treatment discontinuation. Use of administrative data provided a valuable longitudinal perspective, permitting examination of epidemiological trends over a 15-year period and a 5-year follow-up period for the treatment cohort. This approach provided a robust understanding of long-term trends and outcomes, and loss to follow-up was minimized, except for instances where a patient received treatment or moved outside of New Brunswick.

5.2.2 Limitations

Despite the noted strengths, several limitations warrant consideration when interpreting the study's findings.

Data completeness posed significant challenges for elements sourced from patient chart review. Charts were available for review for approximately 43% of the prevalent DLBCL population and 60.4% of the treatment cohort. Among reviewed charts, stage at diagnosis was unspecified in 29.9% of prevalent case charts and 9.1% of treatment cohort charts. Notably, it is expected that staging information is more likely to be missing for older and/or frailer patients who bypassed invasive staging procedures (e.g., bone marrow biopsies or positron emission tomography (PET) scans) in cases where staging was not likely to impact treatment decisions (i.e., when treatment was likely to be palliative regardless of stage). For this reason, demographic profiles of the staged and unstaged groups may be skewed accordingly, and analyses stratified by stage (e.g., the Cox proportional hazards model) should be interpreted with this in mind. Treatment discontinuation information was unavailable for 53.8% of treatment cohort charts. This missingness may not be random: charts were unavailable for some patients due to differences in documentation practices across sites, or because older paper-based records were not always retrievable. At Vitalité sites, only electronic charts were reviewed, further limiting availability. In general, patients with complete chart data may therefore differ systematically from those without, potentially introducing bias into stage and discontinuation estimates.

Additionally, confidentiality requirements necessitated random rounding to multiples of 5 for treatment cohort results, introducing imprecision into estimates. The absence of oral chemotherapy data in our analysis – including prednisone, a key R-CHOP component – means

described treatment regimens may be incomplete, though prednisone administration was inferred for patients receiving the other R-CHOP components.

Treatments received outside New Brunswick, such as HSCT or other therapies only available in other provinces, were not captured, likely leading to an underestimation of the true HSCT rate and potentially affecting interpretation of survival estimates due to the possible impact of undocumented out-of-province treatments. ED visit analysis was restricted to patients with at least one year of follow-up between January 1, 2017, and December 1, 2021, establishing an ED subsample of 350 patients (76.1% of the treatment cohort), and therefore captured only a subset of the treatment cohort. Additionally, ED data capture only visits to New Brunswick emergency departments; patients who sought emergency care outside the province during the observation window would not be reflected in these estimates. Small cell sizes for some subgroups (e.g., community hospitals, third-line therapies, less common chemotherapy regimens) prevented more detailed stratified analyses, particularly affecting examination of treatment pathways for specific platinum-based salvage therapies and documentation of average treatment duration for second- or third-line regimens.

This analysis did not examine certain clinically important factors, including molecular subtypes (cell of origin), International Prognostic Index (IPI) scores, ECOG performance status, and other detailed disease characteristics that influence treatment selection and prognosis.

Importantly, our analysis did not distinguish between curative and palliative treatment intent, which may impact interpretation of results. For instance, some patients receiving alternative regimens may have been treated palliatively, which could explain poor survival outcomes independent of regimen efficacy. The observed survival differences between treatment groups may partly reflect these unmeasured confounders rather than treatment effectiveness alone. Furthermore, despite adjusting for multiple covariates in survival models, residual confounding likely remains due to inter-individual differences in patient health and lifestyle factors, disease biology, and socioeconomic factors beyond income quintile (e.g., education, social support).

Temporal and contextual factors also warrant consideration as treatment approaches have evolved over the 12-year accrual period (2006-2018). Newer therapies and supportive care measures are becoming increasingly available. As such, patients diagnosed earlier may have had different treatment options and outcomes compared to those diagnosed more recently, but this potential difference was not accounted for in our analyses.

Finally, since we examined New Brunswick patients only, our findings may not be generalizable to other Canadian provinces or international settings with different healthcare systems, population demographics, or practice patterns.

5.3 Future Initiatives and Research Directions

This study points to several priorities for ongoing data development and future research, particularly in light of novel DLBCL therapies that are or will soon become available. Establishing

prospective disease registries incorporating standardized clinical data – such as staging, mutation status, treatment intent, and response – would address key data limitations and support future research, including real-world effectiveness studies and pragmatic clinical trials. Improved collaboration with other provinces to capture out-of-province treatments would also be beneficial in this regard.

Future research priorities around DLBLC in New Brunswick include dedicated health equity research to better understand the socioeconomic and geographic disparities uncovered in our findings. Detailed cost-effectiveness analyses of novel therapies, supported by New Brunswick's rich administrative data resources, would also be of interest. Finally, incorporation of patient-reported outcomes would provide valuable additional perspectives on outcomes such as treatment discontinuation.

6. Conclusion

This study provides the first comprehensive, population-level analysis of Diffuse Large B-Cell Lymphoma in New Brunswick, establishing foundational baseline data on epidemiology, treatment pathways, survival, and healthcare resource utilization from 2006 to 2021. The findings demonstrate rising disease burden, strong adherence to guideline-recommended R-CHOP therapy with outcomes comparable to international benchmarks, and considerable healthcare resource needs among the prevalent population. However, significant challenges remain, including poor outcomes for relapsed/refractory patients, potential geographic disparities in access to advanced therapies, and high rates of treatment-related complications necessitating hospitalization and intensive care. These results highlight a clear need for improved therapeutic options for patients who fail or are ineligible for standard treatment.

This work illustrates the potential of New Brunswick's provincial administrative and clinical data resources to support ongoing population-level research. Person-level linkage of administrative records with patient charts enables efficient, comprehensive real-world evidence generation, and further linkage with clinical trial data could allow for deeper characterization of trial participants and long-term follow-up. Future research should leverage these provincial resources to inform policy decisions and ultimately improve outcomes for patients in New Brunswick and beyond.

7. References

1. Sehn, L. H., & Salles, G. (2021). Diffuse large B-cell lymphoma. *New England Journal of Medicine*, *384*(9), 842-858. https://doi.org/10.1056/NEJMra2027612

2. Skrabek, P., Assouline, S., Christofides, A., MacDonald, D., Prica, A., Sangha, R., Matthews, B. A., & Sehn, L. H. (2019). Emerging therapies for the treatment of relapsed or refractory diffuse large B cell lymphoma. *Current Oncology*, *26*(4), 253-265. https://doi.org/10.3747/co.26.5421

3. Gong, I. Y., Cheung, M. C., Chan, K. K. W., Arya, S., Faught, N., Calzavara, A., Liu, N., Odejide, O. O., Abel, G., Kurdyak, P., Raphael, M. J., Kuczmarski, T., Prica, A., & Mozessohn, L. (2023). Mortality among patients with diffuse large B-cell lymphoma and mental disorders: A population-based study. *Journal of the National Cancer Institute*, *115*(10), 1194-1203. https://doi.org/10.1093/jnci/djad149

4. Lymphoma Canada. (2021). *Diffuse large B-cell lymphoma fact sheet*. https://www.lymphoma.ca/wp-content/uploads/2021/08/LymphomaCanada_FactSheet_DLBCL_Digital.pdf

5. Epidemiology of diffuse large B-cell lymphoma in Canada. (2018). *Journal of the American Academy of Dermatology*, *79*(3), AB131. https://doi.org/10.1016/j.jaad.2018.05.546

6. Chihara, D., Ito, H., Matsuda, T., Shibata, A., Katsumi, A., Nakamura, S., Tomotaka, S., Morton, L. M., Weisenburger, D. D., & Matsuo, K. (2022). An epidemiological model to estimate the prevalence of diffuse large B-cell lymphoma in the United States. *Clinical Lymphoma, Myeloma and Leukemia*, *22*(12), e1092-e1099. https://doi.org/10.1016/j.clml.2022.08.008

7. Vijenthira, A., Calzavara, A., Nagamuthu, C., Kaliwal, Y., Liu, N., Blunt, D., Alibhai, S., Prica, A., Cheung, M. C., & Mozessohn, L. (2024). Health care utilization and costs for frail vs nonfrail patients with diffuse large B-cell lymphoma. *Blood Advances*, *8*(17), 4625-4632. https://doi.org/10.1182/bloodadvances.2024013158

8. Masucci, L., Tian, F., Tully, S., Feng, Z., McFarlane, T., Chan, K. K. W., & Wong, W. W. L. (2024). CAR T-cell therapy for diffuse large B-cell lymphoma in Canada: A cost-utility analysis. *Medical Decision Making*, *44*(3), 296-306. https://doi.org/10.1177/0272989X241234070

9. Canadian Cancer Society. (2023). *Diffuse large B-cell lymphoma*.

10. Sarkozy, C., & Sehn, L. H. (2018). Management of relapsed/refractory DLBCL. *Best Practice & Research Clinical Haematology*, *31*(3), 209-216. https://doi.org/10.1016/j.beha.2018.07.014

11. Seshadri, T., Kuruvilla, J., Crump, M., & Keating, A. (2008). Salvage therapy for relapsed/refractory diffuse large B cell lymphoma. *Biology of Blood and Marrow Transplantation*, *14*(3), 259-267. https://doi.org/10.1016/j.bbmt.2007.11.013

12. Garg, M., Puckett, J., Kamal-Bahl, S., Raut, M., Ryland, K. E., Doshi, J. A., & Huntington, S. F. (2024). Real-world survival, healthcare resource utilization, and costs among U.S. elderly patients with diffuse large B-cell lymphoma (DLBCL) treated with R-GemOx in the relapsed/refractory setting. *Clinical Lymphoma, Myeloma and Leukemia*, *24*(5), e181-e190. https://doi.org/10.1016/j.clml.2024.01.010

13. Crump, M., Neelapu, S. S., Farooq, U., Van Den Neste, E., Kuruvilla, J., Westin, J., Link, B. K., Hay, A., Cerhan, J. R., Zhu, L., Boussetta, S., Feng, L., Maurer, M. J., Navale, L., Wiezorek, J., Go, W. Y., & Gisselbrecht, C. (2017). Outcomes in refractory diffuse large B-cell lymphoma: Results from the international SCHOLAR-1 study. *Blood*, *130*(16), 1800-1808. https://doi.org/10.1182/blood-2017-03-769620

14. Zhang, B., et al. (2022). Cancer in New Brunswick 2014-2018. Fredericton, NB: New Brunswick Cancer Network, Department of Health. Accessed February 2024: https://www2.gnb.ca/content/dam/gnb/Departments/h-s/pdf/en/Cancer/CancerInNewBrunswick2014-2018.pdf

15. Swerdlow, S. H., Campo, E., Pileri, S. A., Harris, N. L., Stein, H., Siebert, R., et al. (2016). The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood, 127*(20), 2375-2390. https://doi.org/10.1182/blood-2016-01-643569

16. Tousseyn, T., & De Wolf-Peeters, C. (2011). T cell/histiocyte-rich large B-cell lymphoma: An update on its biology and classification. *Virchows Archiv, 459*(6), 557-563. https://doi.org/10.1007/s00428-011-1165-z

17. National Cancer Institute, Surveillance, Epidemiology, and End Results Program. (n.d.). *Cancer Stat Facts: NHL — Diffuse Large B-Cell Lymphoma (DLBCL)*. Retrieved November 18, 2025, from https://seer.cancer.gov/statfacts/html/dlbcl.html

18. Tao, L., Foran, J. M., Clarke, C. A., Gomez, S. L., & Keegan, T. H. (2014). Socioeconomic disparities in mortality after diffuse large B-cell lymphoma in the modern treatment era. *Blood*, *123*(23), 3553-3562. https://doi.org/10.1182/blood-2013-07-517110

19. Purdum, A., Tieu, R., Reddy, S. R., & Broder, M. S. (2019). Direct costs associated with relapsed diffuse large B-cell lymphoma therapies. *Oncologist*, 24(9), 1229-1236. https://doi.org/10.1634/theoncologist.2018-0490

20. Sineshaw, H. M., Zettler, C. M., Prescott, J., Garg, M., Chakraborty, S., Sarpong, E. M. , Bai, C., Belli, A. J., Fernandes, L. L., & Wang, C. K. (2024). Real-world patient characteristics, treatment patterns, and treatment outcomes of patients with diffuse large B-cell lymphoma by line of therapy. *Cancer Medicine, 13*(7), e7173. https://doi.org/10.1002/cam4.7173

21. Epperla, N., Vaughn, J. L., Othus, M., Hallack, A., & Costa, L. J. (2020). Recent survival trends in diffuse large B-cell lymphoma — Have we made any progress beyond rituximab? *Cancer Medicine, 9*, 5519-5525. https://doi.org/10.1002/cam4.3237

22. Lugtenburg, P. J., & Mutsaers, P. G. N. J. (2023). How I treat older patients with DLBCL in the frontline setting. *Blood*, *141*(21), 2566-2575. https://doi.org/10.1182/blood.2020008239

23. Choday, S., Tran, E., & Gonzalez, M. (2025). Diffuse large B-cell lymphoma: Examining evolving patterns in mortality, incidence, and demographics. *Clinical and Translational Oncology, 27*(8), 3432-3438. https://doi.org/10.1007/s12094-025-03859-4

24. Yang, X., Laliberté, F., Germain, G., Raut, M., Duh, M. S., Sen, S. S., Lejeune, D., Desai, K., & Armand, P. (2021). Real-world characteristics, treatment patterns, health care resource use, and costs of patients with diffuse large B-cell lymphoma in the U.S. *Oncologist, 26*(5), e817-e826. https://doi.org/10.1002/onco.13721

Appendix

Supplemental Table 1. Administrative Data Sets Used and Description.

Data set name	Description (see Supplemental Table 2 for available date ranges)
NB Cancer Data	Includes data on all NB residents, alive or dead, who have been diagnosed with cancer. Collects data on type and incidence (number) of primary cancers; includes date of diagnosis and staging information.
Citizen Data (CD)	Basic demographic and location information on all NB residents who have been issued a provincial Medicare card. Variables include: Age, sex, date of birth, date of death, preferred language, year of arrival to province, citizenship/immigration status, health region of residence, urban/rural indicators, Medicare eligibility status (used for confirmation of residence in NB).
Canadian Chronic Disease Surveillance System (CCDSS)	Compiles individual-level chronic disease diagnoses among NB residents based on hospital discharge and physician billing records; includes year of diagnosis. Diagnosis information is available for the following conditions: Acute myocardial infarction, asthma, COPD, dementia, diabetes, epilepsy, heart failure, hypertension, ischemic heart disease, mental illness, mood and anxiety disorders, multiple sclerosis, Parkinson's disease, schizophrenia, stroke.
IV Oncology Data	Records of IV chemotherapy agents administered at the following sites in NB: Bathurst, Campbellton, Edmundston, Moncton (Vitalité Health Network), Moncton (Horizon Health Network), Saint John, Fredericton, Miramichi. Includes diagnosis, diagnosis date, start and end date of administered IV chemotherapy agents, by drug. Some data sets (Bathurst, Campbellton, Edmundston, Moncton (Vitalité Health Network) also include records of administered radiation therapy treatments (start and end date, dosage, body part treated).
CTAR Radiation Therapy Data	Cancer Treatment Access Repository (CTAR) is used to collect information on radiation treatments for cancer patients in NB.
Discharge Abstract Data (DAD)	Hospital records of patients discharged from NB hospitals. Captures administrative, clinical, and demographic information, including discharge disposition, deaths, sign-outs, and transfers. Includes reason for hospitalization, diagnoses rendered in hospital, procedures performed in hospital, hospital service usage (eg. ICU), length of stay, resource usage.

Data set name	Description (see Supplemental Table 2 for available date ranges)
Emergency Department Data	Emergency department data from NB hospitals. Includes patient intake data, triage data, facility information, reason for visit, wait times.
Patient Chart Data for Diffuse Large B-Cell Lymphoma	Patient chart reviews from Vitalité and Horizon treatment sites. Contains information on stage at diagnosis, treatment discontinuation, number of treatments discontinued, and reason.

Supplemental Table 2. Data Sources and Available Date Ranges by Research Objective

Research Objective	Data Source	Available Date Range of Data Source
DLBCL prevalence, overall and by disease subtype	NB Cancer Data, Citizen Data	**Cancer:** Jan 1 1992 – Dec 31 2021 **Citizen:** Jan 1 1971 – Feb 1 2023
Patient characteristics – age, sex, location of residence	Citizen Data	Jan 1 1971 – Feb 1 2023
Patient characteristics – income quintile	Citizen Data, Census data (Statistics Canada)	Jan 1 1971 – Feb 1 2023
Patient characteristics – stage at diagnosis	NB Cancer Data	Jan 1 1992 – Dec 31 2021
Patient characteristics - comorbidities	Canadian Chronic Disease Surveillance System	Apr 1 1995 – Mar 31 2019
Treatment pathways – IV chemotherapy, radiation therapy (frequency and mean duration of treatments by regimen type and line of therapy (1/2/3L+), treatment	IV Oncology Data CTAR Radiation Therapy Data	**IV Oncology Data:** Bathurst: Jan 2 2012 – Nov 1 2023 Campbellton: Sept 29 2003 – Nov 1 2023 Edmundston: Apr 15 2011 – Nov 1 2023 Moncton (VHN): Jul 18 2003 – Nov 6 2023 Moncton (HHN): Feb 20 2006 – Apr 17 2023 Saint John: Jan 4 2020 – Feb 10 2023 Fredericton: Jan 3 2012 – Nov 10 2023

Research Objective	Data Source	Available Date Range of Data Source
distribution by site of administration)		Miramichi: Apr 24 2020 – Feb 26 2024 **CTAR Radiation Therapy Data:** Feb 1 2012 – Dec 31 2019
Treatment pathways - HSCT (frequency overall and by site, interval from index date)	Discharge Abstract Data	Apr 1 1999 – Mar 31 2021
Survival	IV Oncology Data, Citizen Data	See above
HCRU – non-elective hospital admissions, length of stay, ICU admissions	Discharge Abstract Data	Apr 1 1999 – Mar 31 2021
HCRU – emergency department visits	Emergency Department Data	**HHN**: Jan 1 2017 – Dec 31 2021 **VHN**: Jan 1 2017 – Sept 30 2022
Discontinuation of therapy (frequency; reason)	Patient Charts	April 1 1992 – March 31 2021

Supplemental Table 3. Cox Proportional Hazards Model Predicting Death in 5-Year Follow-Up, Primary Regimens (n=460)

	Hazard Ratio (SE)	P-Value	95% Confidence Interval
Covariates			
Age at diagnosis	1.05 (0.01)	0.000	1.03 - 1.07
Stage at diagnosis (ref: Stage 1)			
Stage 2	0.81 (0.31)	0.574	0.38 - 1.71
Stage 3	1.19 (0.41)	0.618	0.60 - 2.36
Stage 4	1.89 (0.59)	0.043	1.02 - 3.49
Stage unspecified	1.14 (0.53)	0.780	0.46 - 2.83
Missing Stage	1.14 (0.32)	0.658	0.65 - 1.99
Female (ref: Male)	1.04 (0.19)	0.808	0.73 - 1.49

	Hazard Ratio (SE)	P-Value	95% Confidence Interval
Location of Residence (ref: Moncton)			
Bathurst	1.84 (0.77)	0.143	0.81 - 4.17
Campbellton	0.64 (0.56)	0.604	0.11 - 3.53
Edmundston	1.64 (1.61)	0.613	0.24 - 11.27
Fredericton	1.92 (1.03)	0.221	0.67 - 5.49
Miramichi	1.63 (0.58)	0.170	0.81 - 4.17
Saint John	2.26 (1.06)	0.084	0.90 - 5.68
Income Quintile (ref: Q1)			
Q2	0.92 (0.23)	0.746	0.56 - 1.52
Q3	1.08 (0.28)	0.760	0.65 - 1.79
Q4	0.98 (0.27)	0.941	0.57 - 1.67
Q5	1.09 (0.31)	0.751	0.63 - 1.90
Comorbidities			
Acute myocardial infarction	1.58 (0.57)	0.203	0.78 - 3.20
Heart failure	1.23 (0.38)	0.513	0.67 - 2.25
Hypertension	0.56 (0.10)	0.001	0.40 - 0.78
Ischemic Heart Disease	0.68 (0.17)	0.126	0.42 - 1.11
Stroke	0.74 (0.25)	0.369	0.38 - 1.44
Chronic obstructive pulmonary disease	0.83 (0.19)	0.416	0.54 - 1.29
Diabetes	1.21 (0.24)	0.327	0.82 - 1.79
Primary regimen (ref: R-CHOP)			
R-CHOP variants	1.60 (0.57)	0.186	0.80 - 3.22
Less intensive R-CHOP regimens	4.91 (2.15)	0.000	2.08 - 11.56
Salvage therapies	4.24 (1.32)	0.000	2.30 - 7.80
High dosage therapies	3.36 (2.80)	0.145	0.66 - 17.15
Other Regimens	2.58 (1.14)	0.032	1.08 - 6.11
Single agent therapies	2.86 (0.97)	0.002	1.47 - 5.57
Atypical drug combinations for lymphoma	1.90 (2.74)	0.655	0.11 - 31.96
Treatment sites (ref: Vitalité)			
Fredericton	2.23 (1.62)	0.270	0.54 - 9.28

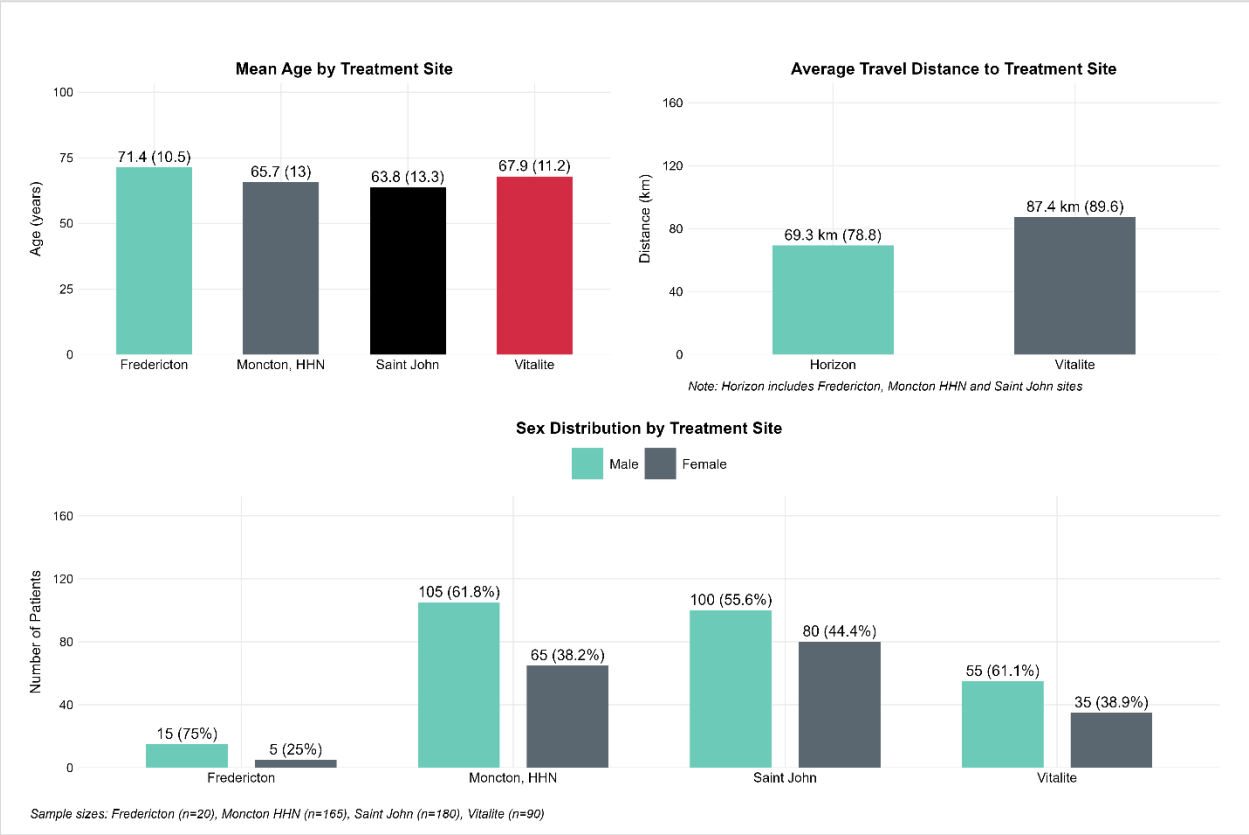
	Hazard Ratio (SE)	P-Value	95% Confidence Interval
Moncton HHN	2.44 (0.95)	0.022	1.14 - 5.22
Saint John	1.64 (0.94)	0.385	0.54 - 5.04
Average travel distance to treatment site	1.00 (0.00)	0.538	1.00 - 1.00
Had radiation treatment	1.13 (0.22)	0.533	0.77 - 5.57
Had HSCT	0.71 (0.27)	0.364	0.34 - 1.48

Supplemental Table 4. Cox Proportional Hazards Model Predicting Death in 5-Year Follow-Up, Regimen of Longest Duration (n=460)

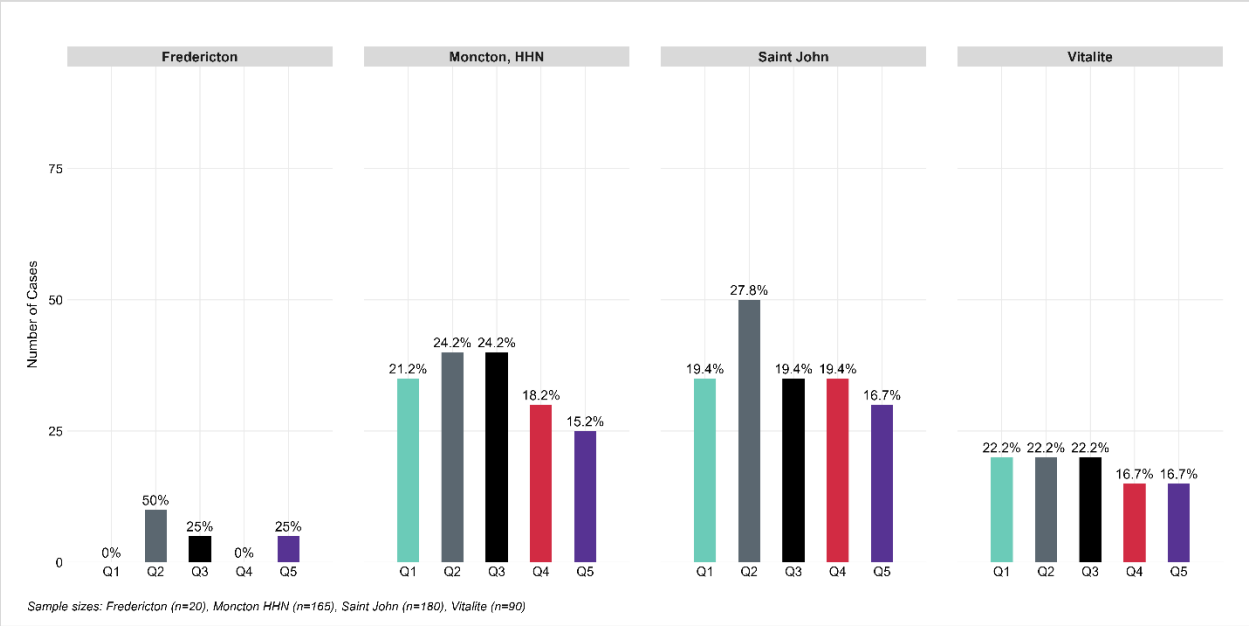
	Hazard Ratio (SE)	P-Value	95% Confidence Interval
Covariates			
Age at diagnosis	1.05 (0.01)	0.000	1.03 - 1.07
Stage at diagnosis (ref: Stage 1)			
Stage 2	0.66 (0.24)	0.254	0.33 - 1.35
Stage 3	0.85 (0.31)	0.651	0.41 - 1.73
Stage 4	1.61 (0.50)	0.127	0.87 - 2.97
Stage unspecified	0.90 (0.49)	0.849	0.31 - 2.60
Missing Stage	1.08 (0.31)	0.798	0.62 - 1.88
Female (ref: Male)	0.95 (0.17)	0.787	0.68 - 1.35
Location of Residence (ref: Moncton)			
Bathurst	1.60 (0.63)	0.239	0.73 - 3.47
Campbellton	0.57 (0.49)	0.515	0.11 - 3.09
Edmundston	2.20 (2.19)	0.429	0.31 - 15.47
Fredericton	2.40 (1.39)	0.129	0.77 - 7.46
Miramichi	1.54 (0.56)	0.237	0.75 - 3.13
Saint John	2.52 (1.25)	0.062	0.96 - 6.66
Income Quintile (ref: Q1)			
Q2	0.95 (0.24)	0.849	0.58 - 1.58
Q3	1.10 (0.28)	0.712	0.67 - 1.80

	Hazard Ratio (SE)	P-Value	95% Confidence Interval
Q4	0.95 (0.25)	0.834	0.56 - 1.59
Q5	1.05 (0.29)	0.865	0.61 - 1.81
Comorbidities			
Acute myocardial infarction	1.74 (0.58)	0.98	0.90 - 3.35
Heart failure	1.37 (0.45)	0.333	0.72 - 2.61
Hypertension	0.56 (0.10)	0.001	0.40 - 0.79
Ischemic Heart Disease	0.68 (0.18)	0.141	0.41 - 1.14
Stroke	0.89 (0.30)	0.730	0.47 : 1.71
Chronic obstructive pulmonary disease	0.92 (0.20)	0.717	0.60 - 1.42
Diabetes	1.15 (0.23)	0.485	0.77 - 1.71
Common regimen (ref: R-CHOP)			
R-CHOP variants	1.37 (0.52)	0.411	0.65 - 2.88
Less intensive R-CHOP regimens	3.32 (2.15)	0.065	0.93 - 11.82
Salvage therapies	3.46 (0.87)	0.000	2.12 - 5.66
High dosage therapies	3.97 (2.36)	0.021	1.24 - 12.76
Other regimens	3.15 (1.70)	0.033	1.09 - 9.06
Single agent therapies	0.81 (0.29)	0.551	0.40 - 1.64
Atypical drug combinations for lymphoma	1.70 (0.72)	0.205	0.75 - 3.89
Treatment sites (ref: Vitalité)			
Fredericton	1.76 (1.25)	0.425	0.44 - 7.06
Moncton HHN	1.83 (0.62)	0.077	0.94 - 3.56
Saint John	1.15 (0.65)	0.810	0.38 - 3.47
Average travel distance to treatment site	1.00 (0.00)	0.62	1.00 - 1.00
Had radiation treatment	1.13 (0.21)	0.521	0.78 - 1.63
Had HSCT	0.63 (0.24)	0.228	0.29 - 1.34

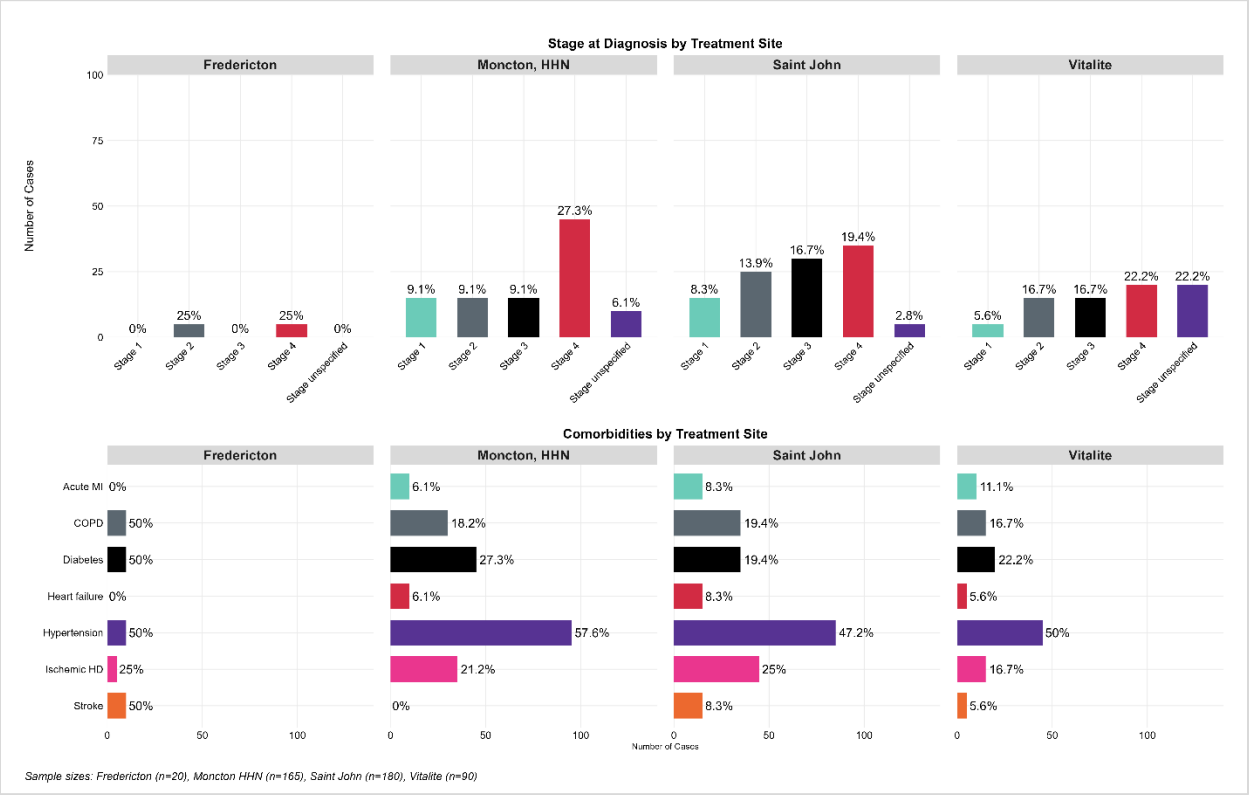
Supplemental Figure 1. DLBCL Treatment Cohort Characteristics by Treatment Site (n=455).



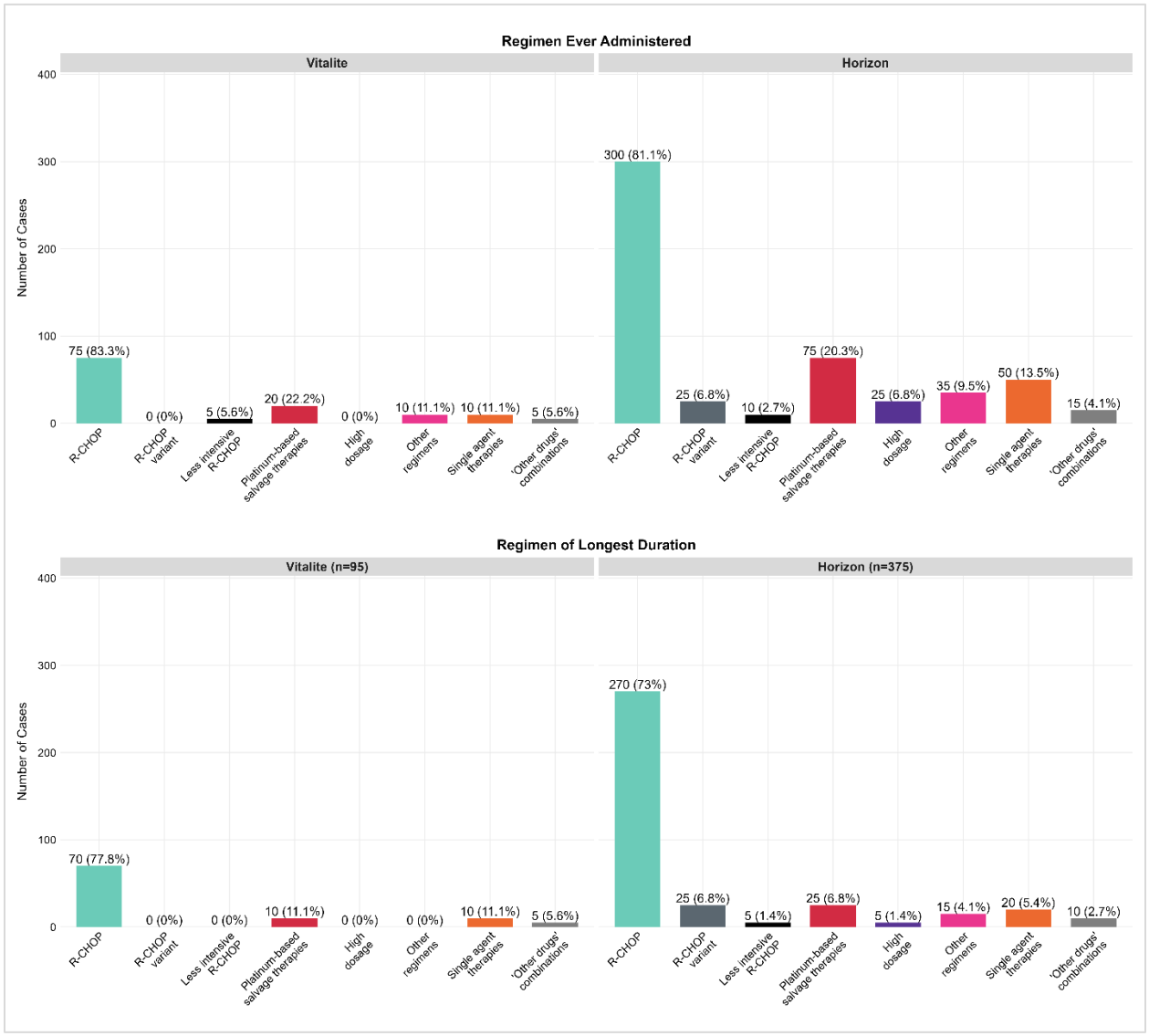
Supplemental Figure 2. DLBCL Treatment Cohort Neighbourhood Income Quintile by Treatment Site (n=455).



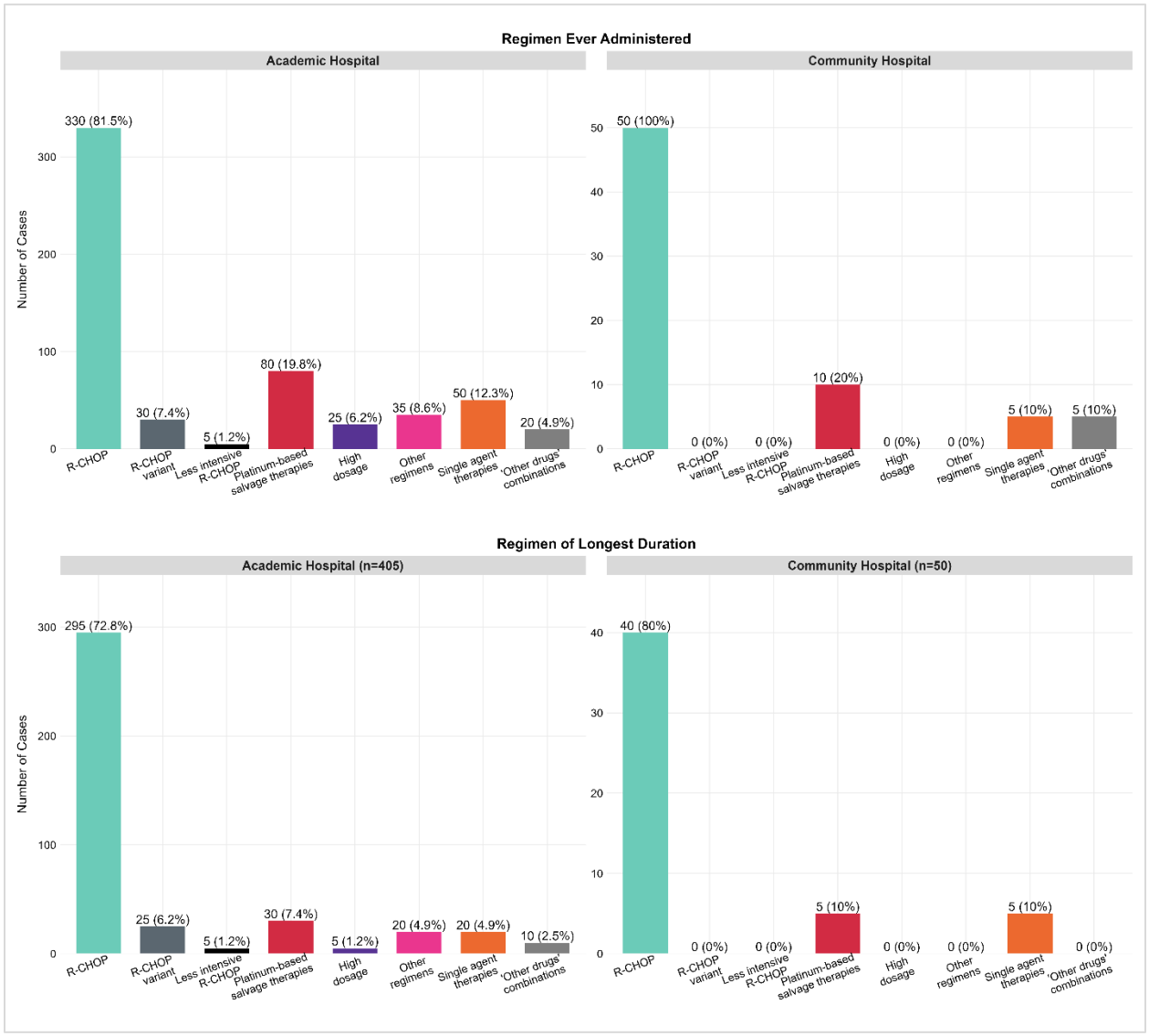
Supplemental Figure 3. DLBCL Treatment Cohort Stage at Diagnosis and Comorbidities by Treatment Site (n=455).



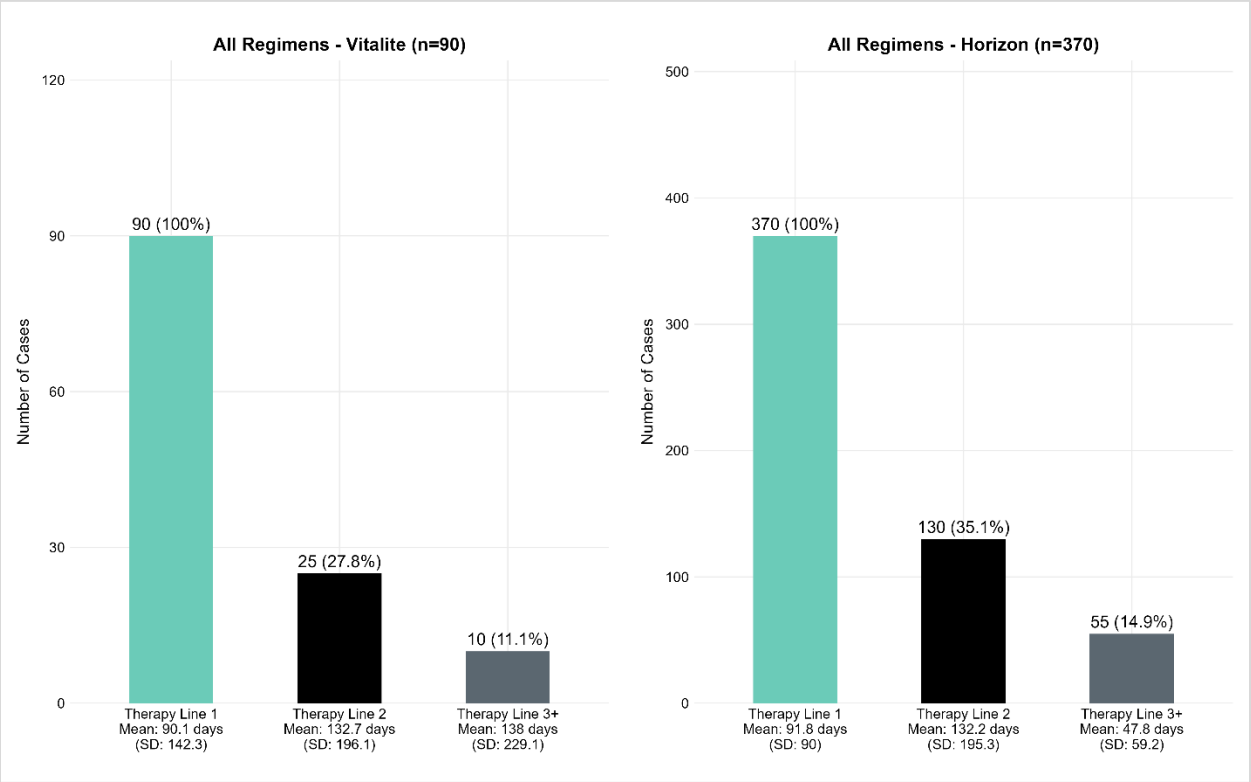
Supplemental Figure 4. Chemotherapy Regimens, Ever Administered and of Longest Duration, by Treatment Site (n=455).



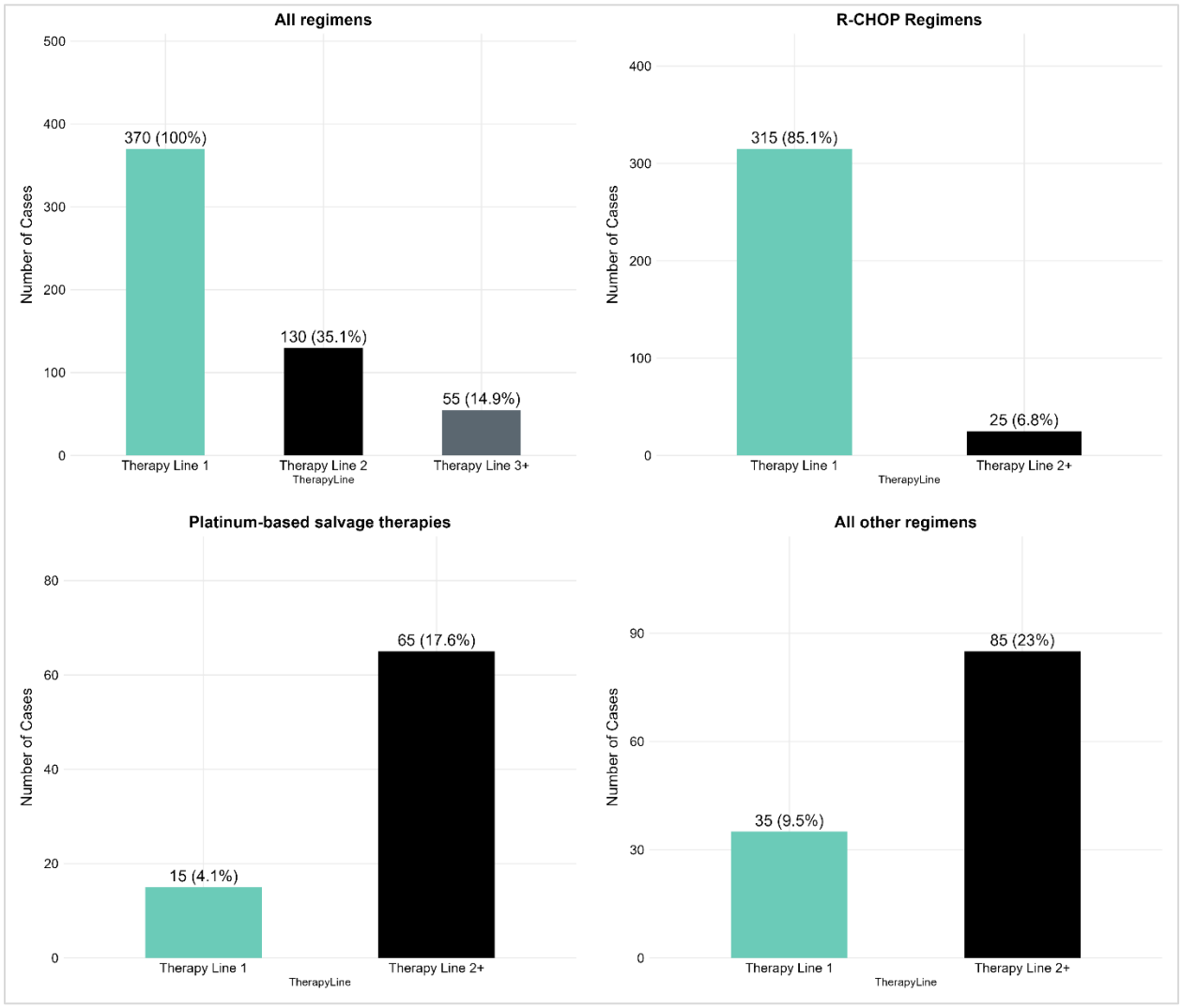
Supplemental Figure 5. Chemotherapy Regimens, Ever Administered and of Longest Duration, by Academic and Community Hospitals (n = 455).



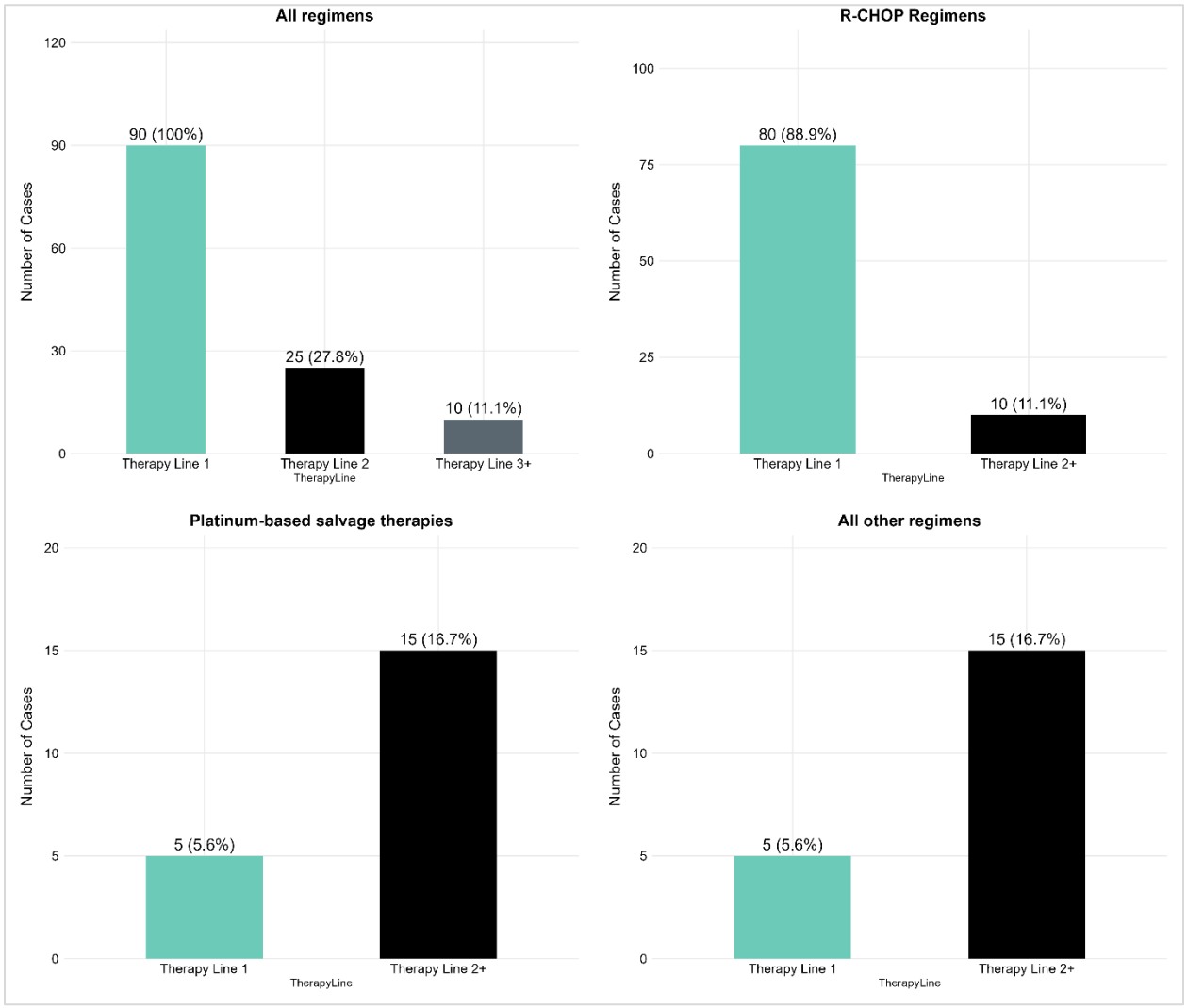
Supplemental Figure 6. Lines of Therapy and Treatment Duration Across All Regimens by Treatment Site (n=455).



Supplemental Figure 7. Chemotherapy Lines by Regimen Type, Horizon Health Network (n=370).



Supplemental Figure 8. Chemotherapy Lines by Regimen Type, Vitalité Health Network (n=90).



Supplemental Figure 9. Radiation Therapy and HSCT by Treatment Site (n=460).

