Clinical and Translational Radiation Oncology 50 (2025) 100873

Contents lists available at ScienceDirect

Clinical and Translational Radiation Oncology

journal homepage: www.sciencedirect.com/journal/clinical-and-translational-radiation-oncology

Original Research Article

Health care system factors associated with receipt of treatment and treatment intent in stage III non-small cell lung cancer: A population-based study in Ontario

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ARTICLE INFO

Keywords:
Lung cancer
Treatment patterns
Quality of care
Access to care
Health services research

ABSTRACT

Purpose: Stage III non-small cell lung cancer (NSCLC) is a heterogeneous disease, with a spectrum of anatomic extent, health status, and treatment approaches. Receipt of treatment and its intent should be independent of health system factors where care quality is optimal. We investigated the degree that modifiable health system factors are associated with receipt of treatment and treatment intent in stage III NSCLC in a large, universal health system.

Methods: This was a population-based, retrospective cohort study with health administrative data from Ontario, Canada, 2010–2018 for those aged $\geq$ 20 years, with AJCC 7 or 8 stage III NSCLC. We explored health system factors associated with NSCLC treatment: region of residence, diagnostic interval, travel distance, advanced radiation (e.g. IMRT, VMAT) and systemic therapy treatment volumes, and year of treatment (treatment era). The relative risk (RR) of (1) any treatment versus no treatment, and (2) palliative versus non-palliative treatment was determined, using multivariable stepwise Poisson regression models. We adjusted for patient, disease, and treatment factors.

Results: We identified 7,093 people with stage III NSCLC between 2010 and 2018. There were no health system factors associated with receipt of treatment versus no treatment in adjusted analysis. The major health system factor associated with palliative intent was region of residence (RR: Region ranges from 0.88 to 1.67, $p < 0.001$). Stratifying by era (2010–2012 vs. 2013–2015 vs. 2016–2018), there was an increase in receipt of curative treatment and use of advanced radiotherapy techniques and immunotherapy over time, but regional variation of treatment intent was similar.

Conclusions: Region of residence emerged as the major health system factor associated with treatment intent for stage III NSCLC. This variation remained, even as advances in radiotherapy and systemic therapy were adopted. Our study suggests possible opportunities to improve care outcomes by addressing unexplained regional variation in care.

Introduction

Stage III non-small cell lung cancer (NSCLC) is a heterogeneous disease, portending a spectrum of anatomic extent (primary tumor, nodal disease), patient performance status, and treatment approach (surgery and/or combined-modality therapy), and frequently requires tertiary care-level multidisciplinary services [1]. Modern advances in cancer care, including immunotherapy [2], as well as conformal radiotherapy techniques such as volumetric modulated arc radiotherapy (VMAT) [3,4], have led to tangible benefits in toxicity and survival. Patients with stage III NSCLC are typically considered for some combination of these treatments [3]. Whether patients are treated for curative-

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https://doi.org/10.1016/j.ctro.2024.100873
Received 4 June 2024; Received in revised form 20 September 2024; Accepted 5 October 2024
Available online 10 October 2024

or palliative-intent, or treated at all, is ideally based on patient- and disease-centered factors alone, such as performance status, medical co-morbidity, lung function, and patient preference. Therefore, whether cancer-directed therapy decisions are solely based on patient- and disease-centered factors is a measure of health care system quality [21].

We lack sufficient information on the impact of health system factors, such as treating health region, travel distance, wait times, and treatment delay for stage III NSCLC as a whole, including on the highest level decisions of treatment versus no treatment, and choice of treatment intent. Identified system factors associated with treatment choice should spur policy change, to reduce barriers in accessing less toxic and potentially life-prolonging therapy for patients with stage III NSCLC. Limited evidence suggests that for selected subgroups of NSCLC, health system factors, such as expertise at presenting cancer center and use of radiotherapy [5], access to multidisciplinary care and use of multi-modality therapy [6], and neighbourhood of residence and treatment choice in stage I disease [7], are associated with treatment received.

The primary objective of this population-based retrospective cohort study of stage III NSCLC treated in Ontario from 2010 to 2018 is to identify what modifiable health care system factors are associated with choice of treatment and intent. Here we investigate the following decisions: 1) treatment versus no treatment and 2) palliative-only versus curative treatment. We hypothesize that diagnostic interval, increasing adoption of advanced radiotherapy techniques, travel distance,

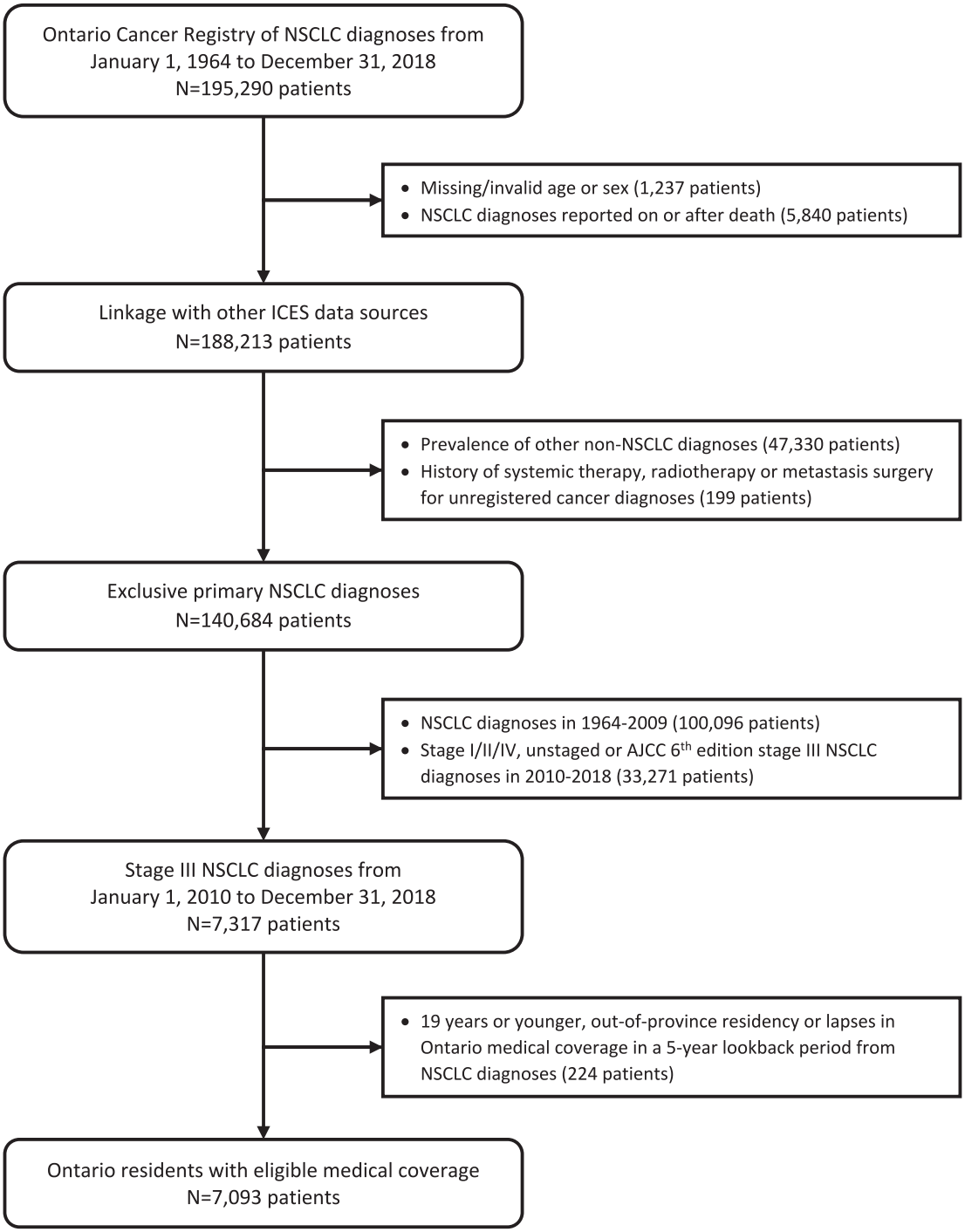

Fig. 1. Identification of study cohort patients diagnosed with stage III non-small cell lung cancer (NSCLC) in Ontario.

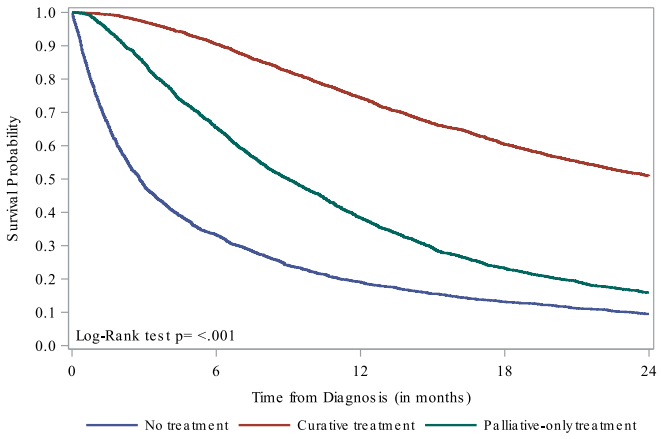

Fig. 2. Overall survival, by type of treatment, for cohort patients diagnosed with stage III non-small cell lung cancer (NSCLC) in Ontario.

treatment volume, and regional variation in practice patterns will be associated with treatment intent.

Methods

Study design and population

Ontario is one of the largest of the 10 sovereign, subnational jurisdictions (provinces) in Canada, legally responsible for the administration health care [8]. Its population is approximately 15.6 million, spread out over ~ 415,000 sq. mi [9]. The system of health care in Ontario provides universal, comprehensive, portable, and accessible publicly-administered health insurance [10] for residents of Ontario, with health care delivered almost entirely by non-governmental agencies via a single-payer model. Most care of patients with stage III NSCLC is highly centralized within the province.

We report the findings of this population-based retrospective cohort study of patients diagnosed with stage III NSCLC in Ontario from January 2010 to December 2018. NSCLC diagnoses were identified through the Ontario Cancer Registry (OCR) (starting from January 1, 1964) using the combination of specified ICD-O-3 morphology and topography codes for the bronchus and lung body site, as previously referenced [11]. ICES is an independent, non-profit research institute which houses a comprehensive high-quality collection of health administrative claims and billing data in the province of Ontario, whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health care system evaluation and improvement. Patients with other non-NSCLC diagnosis, lacking a valid provincial health card or continuous coverage (5-year lookback from date of diagnosis), staged according to AJCC 6th edition, age < 20 years, and non-Ontario place of residence at time of diagnosis, were excluded. This study was approved by the Queen's University Health Sciences Research Ethics Board (ONGY-592–21) and follows the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) guidelines (Appendix 7).

Data sources

The OCR is a population-based tumor registry, administered by Ontario Health Cancer Care Ontario (OH CCO), which passively collects cancer data on residents of Ontario through pathology reporting, hospital records, OH CCO treatment centres, and death records, including disease stage. Demographic information, including date of birth, sex, and postal code, was obtained from the Registered Persons Database (RPDB), a repository for all Ontario residents who are eligible for the Ontario Health Insurance Plan (OHIP). General health, health care system, and treatment data were abstracted from multiple administrative databases (Appendix 1). Chronic diseases and conditions were identified with ICES-derived datasets based on validated algorithms. These datasets were linked using unique encoded identifiers and analyzed at ICES.

Classification of variables

We stratified our study cohort into 1) those who did and did not receive cancer-directed treatment of any kind and 2) those who received palliative-only or curative-intent treatment. To determine which *health system* factors were associated with choice of treatment intent, we collected and controlled for *patient* and *disease* factors which could be associated with treatment choice in turn.

Patient and disease factors

We included *patient factors* ([20,21], Appendix 6) such as age, sex, neighbourhood income quintile, rurality, area-level smoking rates, Elixhauser comorbidity index score, and presence of comorbidities including asthma, chronic obstructive pulmonary disease (COPD), hypertension, congestive heart failure (CHF), dementia, and chronic kidney disease. *Disease factors* (Appendix 6) included histology, anatomic (lobar) tumor location, overall stage, TNM stage according to the 7th or 8th edition of the AJCC staging manual, and factors related to treatment in patients who received treatment including receipt of systemic therapy, radiotherapy, or cancer surgery, designated as palliative- or curative intent (including (neo)adjuvant treatments). Subtypes of systemic therapy included cytotoxic, immunotherapy, targeted therapy, or trial/other therapy. Subtypes of radiotherapy were designed as either "basic" or "advanced" (if IMRT, VMAT, stereotactic, brachytherapy, or ≥ 5 fields). Subtypes of cancer surgery included thoracic tumor resection or metastasis surgery (in those patients initially treated for curative intent). Completion of an ESAS assessment, consultation to a palliative care, geriatric, or medical oncology specialist (Appendix 2), healthcare utilization prior to diagnosis (e.g., ward admission, emergency department-only visit), and receipt of a PET scan were also considered disease factors.

Health system factors

Year of treatment (referred to as treatment era) was considered a health system factor, as patterns of practice, newer technologies, and new evidence and standards of care are adopted over time. **Health region of residence** was defined as a system factor, assuming that after adjustment for patient and disease factors, residual variation was primarily system-related, and would be modifiable given the province's single-payer universal health care system. Region of residence was designated based on a patient's postal code of residence at time of diagnosis. Individual health regions are anonymized in our publication due to privacy regulations. A **diagnostic interval** was calculated by referring to the first dedicated chest imaging within three months prior to diagnosis. The nearest regional cancer centre within a health region was also designated using the patient's individual postal code. **Distance** was calculated based on "as-the-crow-flies" distance and estimated shortest driving distance using the Open Source Routing Machine (OSRM) API with OpenStreetMap [22]. This was done for the nearest regional cancer centre, nearest cancer centre with radiotherapy, and nearest cancer centre with thoracic surgery. **Treatment volume** at the nearest cancer centre over the prior year to date of diagnosis was determined using ALR/NDFP as applicable, designated as systemic therapy or radiotherapy, and by systemic therapy regimen (cytotoxic chemotherapy, immunotherapy, targeted) and radiotherapy type (basic, advanced). This was determined based on the number of patients with stage III NSCLC treated with a particular modality, at the particular regional cancer centre, in the previous year to date of diagnosis, but

Table 1
Socio-demographics, general health, and disease characteristics for cohort patients diagnosed with stage III non-small cell lung cancer (NSCLC) in Ontario.

Patient Characteristics	Type of Treatment[a]			
	Total	No Treatment	Curative Treatment[b]	Palliative-Only Treatment
	N = 7,093	N = 1,557	N = 3,288	N = 2,248
Patient Factors				
Age				
Mean ± SD	69.84 ± 10.30	74.75 ± 9.99	66.81 ± 9.54	70.85 ± 10.09
Median (IQR)	70 (63–77)	76 (68–82)	67 (60–74)	72 (64–78)
20-64	2,145 (30.24 %)	265 (17.02 %)	1,287 (39.14 %)	593 (26.38 %)
65-69	1,215 (17.13 %)	207 (13.29 %)	661 (20.10 %)	347 (15.44 %)
70-74	1,301 (18.34 %)	234 (15.03 %)	620 (18.86 %)	447 (19.88 %)
75-79	1,098 (15.48 %)	273 (17.53 %)	429 (13.05 %)	396 (17.62 %)
80+	1,334 (18.81 %)	578 (37.12 %)	291 (8.85 %)	465 (20.69 %)
Sex				
Female	3,352 (47.26 %)	735 (47.21 %)	1,559 (47.41 %)	1,058 (47.06 %)
Male	3,741 (52.74 %)	822 (52.79 %)	1,729 (52.59 %)	1,190 (52.94 %)
Income quintile				
1 (Lowest)	1,771 (24.97 %)	414 (26.59 %)	764 (23.24 %)	593 (26.38 %)
2	1,679 (23.67 %)	376 (24.15 %)	788 (23.97 %)	515 (22.91 %)
3	1,327 (18.71 %)	294 (18.88 %)	612 (18.61 %)	421 (18.73 %)
4	1,201 (16.93 %)	235 (15.09 %)	580 (17.64 %)	386 (17.17 %)
5 (Highest)	1,093 (15.41 %)	231 (14.84 %)	539 (16.39 %)	323 (14.37 %)
Urban/rural residence				
Urban (RIO < 10)	4,075 (57.45 %)	860 (55.23 %)	1,867 (56.78 %)	1,348 (59.96 %)
Suburban (10 ≤ RIO < 40)	2,014 (28.39 %)	509 (32.69 %)	931 (28.32 %)	574 (25.53 %)
Rural (40 ≤ RIO)	898 (12.66 %)	167 (10.73 %)	445 (13.53 %)	286 (12.72 %)
Area-level lifetime experimental/abstinence smoking standardized rates[c]				
Higher than average	2,349 (33.12 %)	493 (31.66 %)	1,044 (31.75 %)	812 (36.12 %)
Typical average	2,765 (38.98 %)	602 (38.66 %)	1,342 (40.82 %)	821 (36.52 %)
Lower than average	1,979 (27.90 %)	462 (29.67 %)	902 (27.43 %)	615 (27.36 %)
Elixhauser comorbidity index[d]				
0	4,542 (64.03 %)	742 (47.66 %)	2,357 (71.68 %)	1,443 (64.19 %)
1-2	1,630 (22.98 %)	451 (28.97 %)	668 (20.32 %)	511 (22.73 %)
3+	921 (12.98 %)	364 (23.38 %)	263 (8.00 %)	294 (13.08 %)
Chronic conditions				
Asthma	1,201 (16.93 %)	297 (19.08 %)	505 (15.36 %)	399 (17.75 %)
COPD	3,762 (53.04 %)	968 (62.17 %)	1,583 (48.14 %)	1,211 (53.87 %)
Hypertension	4,371 (61.62 %)	1,091 (70.07 %)	1,865 (56.72 %)	1,415 (62.94 %)
CHF	814 (11.48 %)	306 (19.65 %)	229 (6.96 %)	279 (12.41 %)
Dementia	332 (4.68 %)	189 (12.14 %)	60 (1.82 %)	83 (3.69 %)
CKD[e]	754 (10.63 %)	249 (15.99 %)	233 (7.09 %)	272 (12.10 %)
Disease Factors				
Histology/morphology				
Neoplasms, NOS	595 (8.39 %)	475 (30.51 %)	41 (1.25 %)	79 (3.51 %)
Epithelial neoplasms, NOS	1,360 (19.17 %)	322 (20.68 %)	522 (15.88 %)	516 (22.95 %)
Squamous cell neoplasms	2,321 (32.72 %)	407 (26.14 %)	1,101 (33.49 %)	813 (36.17 %)
Adenomas/adenocarcinomas	2,656 (37.45 %)	340 (21.84 %)	1,501 (45.65 %)	815 (36.25 %)
Other	161 (2.27 %)	13 (0.83 %)	123 (3.74 %)	25 (1.11 %)
Anatomic location				
Upper lobe	4,182 (58.96 %)	745 (47.85 %)	2,106 (64.05 %)	1,331 (59.21 %)
Middle lobe	295 (4.16 %)	70 (4.50 %)	130 (3.95 %)	95 (4.23 %)
Lower lobe	1,763 (24.86 %)	356 (22.86 %)	812 (24.70 %)	595 (26.47 %)
Main bronchus	412 (5.81 %)	90 (5.78 %)	167 (5.08 %)	155 (6.90 %)
Overlapping lesion/lung, NOS	441 (6.22 %)	296 (19.01 %	73 (2.22 %)	72 (3.20 %)
Best stage				
III/IIIA	4,770 (67.25 %)	1,094 (70.26 %)	2,442 (74.27 %)	1,234 (54.89 %)
IIIB/IIIC	2,323 (32.75 %)	463 (29.74 %)	846 (25.73 %)	1,014 (45.11 %)
T category				
TX/T0	229 (3.23 %)	87 (5.59 %)	66 (2.01 %)	76 (3.38 %)
T1/T1a/T1b/T1c	854 (12.04 %)	174 (11.18 %)	482 (14.66 %)	198 (8.81 %)

(*continued on next page*)

Table 1 (*continued*)

Patient Characteristics	Type of Treatment[a]			
	Total	No Treatment	Curative Treatment[b]	Palliative-Only Treatment
	N = 7,093	N = 1,557	N = 3,288	N = 2,248
T2/T2a/T2b	2,007 (28.30 %)	466 (29.93 %)	945 (28.74 %)	596 (26.51 %)
T3	1,727 (24.35 %)	359 (23.06 %)	826 (25.12 %)	542 (24.11 %)
T4	2,161 (30.47 %)	450 (28.90 %)	916 (27.86 %)	795 (35.36 %)
N category				
NX/N0	711 (10.02 %)	166 (10.66 %)	356 (10.83 %)	189 (8.41 %)
N1	602 (8.49 %)	74 (4.75 %)	423 (12.86 %)	105 (4.67 %)
N2	4,416 (62.26 %)	1,066 (68.46 %)	2,019 (61.41 %)	1,331 (59.21 %)
N3	1,248 (17.59 %)	230 (14.77 %)	436 (13.26 %)	582 (25.89 %)

Acronyms:
SD, standard deviation; IQR, interquartile range; RIO, Rurality Index for Ontario; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; CKD, chronic kidney disease; NOS, not otherwise specified.
Notes:
a. Type of treatment was measured within a 2-year lookforward period from NSCLC diagnosis; column percentages may not sum to 100% due to missing data.
b. Patients who received curative/adjuvant treatment may eventually receive palliative treatment.
c. Smoking status was collected from survey respondents in the 2015–2017 Canadian Community Health Survey (CCHS) data; area-level age-sex standardized rates were computed with the 2016 Ontario census division (CD) geography and population
d. Elixhauser comorbidity index was measured within a 5-year lookback period from NSCLC diagnosis; total comorbidity score excluded indices for lymphoma, metastatic cancer and solid tumor without metastases.
e. CKD was measured with an average estimated glomerular filtration rate of < 60 mL/min/1.73 m^2 from multiple laboratory tests within a 1-year lookback period from NSCLC diagnosis.

without exclusion for patients who may have had another non-NSCLC diagnosis.

Statistical analysis

Descriptive statistics by treatment intent were generated for all patient, disease, and health care system factors. Overall survival was depicted using Kaplan-Meier methods. Multivariable Poisson regression analysis was performed to estimate the association between identified patient, disease, and health system factors and the choice of treatment and intent. Unadjusted and adjusted stepwise models were derived. The adjusted model excluded treatment volume of specific types of systemic therapy and radiotherapy due to the presence of statistical interactions with health region of residence. The stepwise adjusted analysis used a 0.2 significance level for model entry and 0.1 significance level for model exclusion of variables used in the unadjusted analyses. As a sensitivity analysis, Poisson regression analyses were implemented on the study cohort stratified by treatment era. A p-value of < 0.05 was considered statistically significant. Data analyses were performed using the SAS software (version 9.4, SAS Institute, Cary, NC).

Results

Cohort description

In total, 7,093 patients met our pre-specified selection criteria for stage III NSCLC in Ontario between January 1, 2010 and December 31, 2018 (Fig. 1). Overall, 22.0 % of patients did not receive treatment, while 46.4 % and 31.7 % received curative and palliative-only treatment, respectively. Overall survival (OS) was significantly worse in the no treatment group (2-year OS [95 % Confidence Interval {CI}]: 9.5 % [8.1–11.0 %]), compared with the curative (2-year OS: 50.9 % [49.2–52.6 %]) and palliative-only groups (2-year OS: 15.9 % [14.5–17.5 %]) ($p < 0.001$) (Fig. 2).

Patient and disease factors

A detailed description of our results can be found in Tables 1-3 and Appendices 3–5. The median age at diagnosis was 70 (interquartile range [IQR] 63–77) (Table 1). 36.0 % of patients had an Elixhauser comorbidity index of ≥ 1, highest in the no treatment group (52.3 %). 53.0 % of patients had COPD, highest in the no treatment group (62.2 %). Overall, 32.8 % were stage IIIB/IIIC, with a greater proportion (45.1 %) in the palliative-only group (Table 1).

In the treatment group, the number of patients who received immunotherapy and advanced radiotherapy increased over time (Fig. 3A, Fig. 3B, Fig. 3C). 65.2 % of patients had a PET scan, which was highest in the curative group (88.0 %). 69.4 % of patients who received radiotherapy received advanced radiotherapy (e.g., VMAT/IMRT). In the curative group, most (76.7 % and 84.5 %) were treated with chemotherapy and radiotherapy, respectively (Table 2). About one-third had a thoracic tumour resection, 75.8 % of whom received cytotoxic chemotherapy.

In adjusted analyses, advanced age remained a moderate predictor for not receiving treatment, and amongst those treated it was a strong predictor of palliative-only treatment (Table 3). Advanced stage subcategory (IIIB-IIIC vs. III/IIIA) was not predictive of the choice of treatment versus no treatment, but among those treated was strongly predictive of palliative-only treatment. Other patient and disease factors in the multivariable model are shown in Table 3.

Health system factors

Over time, more patients received treatment (75.5 % in 2010–2012, 77.7 % in 2013–2015, and 81.4 % in 2016–2018), and the proportion receiving curative treatment was highest in the most recent era (43.9 % in 2010–2012, 44.9 % in 2013–2015, and 50.8 % in 2016–2018) (Table 2, Fig. 3A,Fig. 3B,Fig. 3C). The median driving distance to nearest regional cancer centre was 26.7 km (IQR 9.1–69.9).

In our stepwise adjusted model, there were no health system factors associated with choice of treatment versus no treatment (Table 3). However, in our adjusted model of factors associated with palliative-only versus curative treatment, health system factors associated with palliative-only treatment were: shorter diagnostic interval, lower immunotherapy treatment volume, and health region of residence (RR estimates ranging from 0.88 to 1.67) (Table 3).

Given that we observed increased receipt of treatment over time, as well as increasing proportions of curative treatment, advanced radiotherapy techniques, and use of immunotherapy, we hypothesized that the regional variation in use of curative treatment should also diminish

Table 2
Treatment and health system characteristics for cohort patients diagnosed with stage III non-small cell lung cancer (NSCLC) in Ontario.

Patient Characteristics	Type of Treatment[a]			
	Total	No Treatment	Curative Treatment[b]	Palliative-Only Treatment
	N = 7,093	N = 1,557	N = 3,288	N = 2,248
Disease Factors				
Time (in months) from diagnosis to first curative/palliative treatment				
Mean ± SD	2.18 ± 2.17	N/A	2.13 ± 1.75	2.26 ± 2.66
Median (IQR)	1.71 (1.12–2.56)	N/A	1.81 (1.22–2.60)	1.57 (0.95–2.50)
Curative/palliative treatment				
Systemic therapy	3,449 (48.63 %)	N/A	2,522 (76.70 %)	927 (41.24 %)
Radiotherapy	4,748 (66.94 %)	N/A	2,778 (84.49 %)	1,970 (87.63 %)
Metastasis surgery	128 (1.80 %)	N/A	100 (3.04 %)	28 (1.25 %)
Curative treatment				
Thoracic tumour resection	1,049 (14.79 %)	N/A	1,049 (31.90 %)	0 (0.00 %)
Concurrent chemoradiation without thoracic surgery	1,610 (22.70 %)	N/A	1,610 (48.97 %)	0 (0.00 %)
Concurrent chemoradiation with thoracic surgery	248 (3.50 %)	N/A	248 (7.54 %)	0 (0.00 %)
Curative/palliative chemotherapy regimen				
Cytotoxic	3,283 (46.29 %)	N/A	2,493 (75.82 %)	790 (35.14 %)
Immunotherapy (±chemotherapy)	501 (7.06 %)	N/A	325 (9.88 %)	176 (7.83 %)
Targeted	346 (4.88 %)	N/A	171 (5.20 %)	175 (7.78 %)
Trial/other	31 (0.44 %)	N/A	19 (0.58 %)	12 (0.53 %)
Curative/palliative specific-type radiotherapy				
2-field	1,904 (26.84 %)	N/A	566 (17.21 %)	1,338 (59.52 %)
3-field	437 (6.16 %)	N/A	238 (7.24 %)	199 (8.85 %)
4-field	206 (2.90 %)	N/A	136 (4.14 %)	70 (3.11 %)
5/more field	166 (2.34 %)	N/A	123 (3.74 %)	43 (1.91 %)
IMRT/FIF/tomography	1,548 (21.82 %)	N/A	1,249 (37.99 %)	299 (13.30 %)
Stereotactic	304 (4.29 %)	N/A	227 (6.90 %)	77 (3.43 %)
VMAT	1,035 (14.59 %)	N/A	836 (25.43 %)	199 (8.85 %)
Other	317 (4.47 %)	N/A	138 (4.20 %)	179 (7.96 %)
Curative/palliative simplified-type radiotherapy[c]				
Basic	2,513 (35.43 %)	N/A	926 (28.16 %)	1,587 (70.60 %)
Advanced	2,891 (40.76 %)	N/A	2,281 (69.37 %)	610 (27.14 %)
Metastasis surgery				
Intracranial tumour resection	108 (1.52 %)	N/A	86 (2.62 %)	22 (0.98 %)
Spinal cord compression	24 (0.34 %)	N/A	17 (0.52 %)	7 (0.31 %)
Diagnostic imaging[d]				
PET scan	4,627 (65.23 %)	454 (29.16 %)	2,893 (87.99 %)	1,280 (56.94 %)
Comprehensive assessment[e]				
Palliative care consultation	1,710 (24.11 %)	503 (32.31 %)	344 (10.46 %)	863 (38.39 %)
Geriatric consultation	126 (1.78 %)	68 (4.37 %)	23 (0.70 %)	35 (1.56 %)
Medical oncology consultation	3,409 (48.06 %)	351 (22.54 %)	1,814 (55.17 %)	1,244 (55.34 %)
ESAS assessment	4,649 (65.54 %)	396 (25.43 %)	2,601 (79.11 %)	1,652 (73.49 %)
Health utilization prior to diagnosis[f]				
Inpatient hospitalization	705 (9.94 %)	266 (17.08 %)	235 (7.15 %)	204 (9.07 %)
Inpatient hospitalization with ICU admission	127 (1.79 %)	54 (3.47 %)	47 (1.43 %)	26 (1.16 %)
ED-only visit	2,194 (30.93 %)	555 (35.65 %)	890 (27.07 %)	749 (33.32 %)
Health System Factors				
Treatment Era				
2010-2012	2,595 (36.59 %)	636 (40.85 %)	1,138 (34.61 %)	821 (36.52 %)
2013-2015	2,291 (32.30 %)	510 (32.76 %)	1,029 (31.30 %)	752 (33.45 %)
2016-2018	2,207 (31.12 %)	411 (26.40 %)	1,121 (34.09 %)	675 (30.03 %)
Place of residence (LHIN)				
A	374 (5.27 %)	88 (5.65 %)	179 (5.44 %)	107 (4.76 %)
B	476 (6.71 %)	93 (5.97 %)	251 (7.63 %)	132 (5.87 %)
C	756 (10.66 %)	163 (10.47 %)	358 (10.89 %)	235 (10.45 %)
D	444 (6.26 %)	113 (7.26 %)	159 (4.84 %)	172 (7.65 %)

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Table 2 (*continued*)

Patient Characteristics	Type of Treatment[a]			
	Total	No Treatment	Curative Treatment[b]	Palliative-Only Treatment
	N = 7,093	N = 1,557	N = 3,288	N = 2,248
E	1,042 (14.69 %)	195 (12.52 %)	456 (13.87 %)	391 (17.39 %)
F	347 (4.89 %)	91 (5.84 %)	162 (4.93 %)	94 (4.18 %)
G	557 (7.85 %)	107 (6.87 %)	247 (7.51 %)	203 (9.03 %)
H	159 (2.24 %)	40 (2.57 %)	81 (2.46 %)	38 (1.69 %)
I	475 (6.70 %)	111 (7.13 %)	217 (6.60 %)	147 (6.54 %)
J	638 (8.99 %)	131 (8.41 %)	370 (11.25 %)	137 (6.09 %)
K	308 (4.34 %)	60 (3.85 %)	137 (4.17 %)	111 (4.94 %)
L	993 (14.00 %)	254 (16.31 %)	452 (13.75 %)	287 (12.77 %)
M	175 (2.47 %)	38 (2.44 %)	82 (2.49 %)	55 (2.45 %)
N	349 (4.92 %)	73 (4.69 %)	137 (4.17 %)	139 (6.18 %)
Diagnostic interval[d]				
Chest X-ray/CT scan	6,843 (96.48 %)	1,492 (95.83 %)	3,181 (96.75 %)	2,170 (96.53 %)
Time (in weeks) from first chest X-ray/CT scan to diagnosis				
Mean ± SD	4.99 ± 3.78	4.52 ± 4.11	5.40 ± 3.63	4.70 ± 3.71
Median (IQR)	4.6 (1.9–7.9)	3.8 (0.2–7.9)	5.1 (2.6–8.0)	4.1 (1.6–7.3)
Cancer centre location[g]				
Driving distance (in km) from residence to nearest regional cancer centre				
Mean ± SD	49.93 ± 65.58	52.06 ± 67.80	49.58 ± 64.60	48.98 ± 65.43
Median (IQR)	26.7 (9.1–69.9)	28.6 (9.0–72.5)	27.3 (9.4–69.8)	24.8 (8.9–69.2)
As-the-crow-flies distance (in km) from residence to nearest regional cancer centre				
Mean ± SD	39.47 ± 54.34	41.48 ± 56.19	38.79 ± 51.43	39.07 ± 57.10
Median (IQR)	19.0 (6.3–56.2)	19.8 (6.4–60.2)	19.7 (6.4–55.7)	17.2 (6.1–54.6)
As-the-crow-flies distance (in km) from residence to nearest radiotherapy cancer centre				
Mean ± SD	33.97 ± 50.72	35.41 ± 52.35	33.62 ± 48.29	33.48 ± 53.00
Median (IQR)	15.4 (5.5–42.0)	16.0 (5.5–44.7)	15.7 (5.7–41.5)	14.6 (5.4–41.0)
As-the-crow-flies distance (in km) from residence to nearest thoracic surgery cancer centre				
Mean ± SD	41.19 ± 54.99	43.57 ± 56.89	40.60 ± 52.06	40.40 ± 57.71
Median (IQR)	19.6 (6.4–60.7)	21.4 (6.0–63.3)	20.7 (6.6–60.1)	17.3 (6.0–59.1)
Cancer centre treatment volume[h]				
Patient-level chemotherapy volume				
Mean ± SD	90.37 ± 40.81	89.07 ± 40.12	90.57 ± 40.48	90.96 ± 41.76
Median (IQR)	80 (60–120)	78 (60–119)	80 (61–119)	80 (59–121)
Patient-level immunotherapy (±chemotherapy) volume				
Mean ± SD	6.82 ± 13.14	5.81 ± 12.00	7.42 ± 13.88	6.63 ± 12.74
Median (IQR)	0 (0–6)	0 (0–3)	0 (0–8)	0 (0–6)
Patient-level targeted chemotherapy volume				
Mean ± SD	7.52 ± 8.29	6.99 ± 7.86	7.73 ± 8.54	7.59 ± 8.19
Median (IQR)	5 (2–10)	5 (2–10)	5 (2–10)	5 (2–10)
Patient-level radiotherapy volume				
Mean ± SD	108.91 ± 45.05	106.88 ± 43.68	108.18 ± 44.54	111.37 ± 46.63
Median (IQR)	101 (79–127)	100 (78–127)	101 (79–126)	102 (79–129)
Patient-level VMAT radiotherapy volume				
Mean ± SD	21.04 ± 35.67	17.85 ± 32.93	21.57 ± 35.69	22.46 ± 37.31
Median (IQR)	4 (0–24)	3 (0–16)	5 (0–25.5)	5 (0–25)
Patient-level basic radiotherapy volume				
Mean ± SD	56.35 ± 25.00	56.58 ± 24.52	54.35 ± 25.27	59.13 ± 24.66
Median (IQR)	54 (38–70)	53 (39–70)	51 (35–68)	56 (42–74)
Patient-level advanced radiotherapy volume				
Mean ± SD	62.38 ± 38.50	60.18 ± 37.28	63.46 ± 38.22	62.32 ± 39.67
Median (IQR)	58 (34–82)	57 (33–78)	59 (34.5–84)	57 (33–82)

Acronyms:
SD, standard deviation; IQR, interquartile range; IMRT, intensity-modulated radiation therapy; FIF, field-in-field; VMAT, volumetric modulated arc therapy; CT, computed tomography, PET, positron emission tomography; ESAS, Edmonton Symptom Assessment System; ICU, intensive care unit; ED, emergency department; LHIN, local health integration network; km, kilometres.
Notes:
a. Type of treatment was measured within a 2-year lookforward period from NSCLC diagnosis; column percentages may not sum to 100% due to missing data.
b. Patients who received curative treatment may eventually receive palliative treatment.
c. 2/3/4/direct-field treatment were classified as basic radiotherapy; 5/more-field, IMRT, FIF, tomography, stereotactic, VMAT or brachytherapy treatment were classified as advanced radiotherapy.
d. Chest X-ray and CT scans were measured within a 3-month lookback period from NSCLC diagnosis; PET scan was measured within a 3-month lookback and lookforward period from NSCLC diagnosis.
e. Palliative care, geriatric and medical oncology consultations were measured within a 3-month lookback and lookforward period from NSCLC diagnosis; ESAS assessment was measured within a 16-week lookback and lookforward period from NSCLC diagnosis.
f. Inpatient hospitalizations and ED-only visits were measured within a 3-month lookback period from NSCLC diagnosis.

g. Driving distance was measured with the shortest distance generated from the Open Source Routing Machine (OSRM) API with OpenStreetMap data between the postal code of residence and the geographic location of the regional cancer centre; as-the-crow-flies distance was measured with the haversine formula between the postal code of residence and the geographic locations of the regional, radiotherapy and thoracic surgery cancer centres; regional, radiotherapy and thoracic surgery cancer centre locations were obtained from Ontario Health; thoracic surgery cancer centres account for > 90 % of the thoracic cancer surgeries in the province.
h. Patient-level annual volume of chemotherapy/radiotherapy treatment was measured with all stage III NSCLC patients (who may have other non-NSCLC diagnoses) at the nearest regional cancer centre from their residence within a 1-year lookback period from NSCLC diagnosis.

over time (Fig. 3A,Fig. 3B,Fig. 3C). We thus performed a sensitivity analysis investigating regional variation in use of curative treatment, stratified by treatment era (Appendix 3–5). Relative variation in use of curative intent treatment remained similar between eras on multivariable analysis (e.g., 2010–2012 health region RR estimates ranging from for 0.83 to 1.52 and 2016–2018 RR estimates 0.73 to 1.34) (Fig. 4).

Discussion

Our population-based cohort study of over 7,000 patients with stage III NSCLC diagnosed in Ontario between 2010 and 2018 has revealed that, after adjustment for patient and disease factors, there remain important health care system-level factors associated with the ultimate treatment patients received. Our findings are relevant to other universal health care systems, and to those with private payers. Given the degree of variation seen in Ontario's single-payer system with clearly established guidelines, it is expected that the variation seen in this study represents a lower bound of system level variation in practice. Notably, our study reveals a large difference in the likelihood of receiving curative-intent treatment based on health region of residence. This association was maintained in an analysis stratified by treatment era. Our study also revealed that, despite controlling for related factors such as comorbidity, age remained a strong predictor of whether a patient received palliative-only treatment or no treatment at all. These have important implications for health system quality, where treatment received should principally be based on patient-centered factors.

While it is expected that predictors of treatment received such as stage and presence of comorbidities remained significant in our model, the residual effect of age alone must be accounted for. Our findings have been replicated in other publications by Miler et. al [12] and de Rijke et. al. [13]. This may be explained by unaccounted physician bias in treatment recommendations based on age, which has been documented elsewhere in the literature [14]. However, older adults may have different preferences for the aggressiveness of treatment compared to younger patients. Findings in the literature about patient preferences in older adults with lung cancer are mixed [15], though it appears that many older adults are willing to accept higher toxicity trade-offs if there is a large survival benefit [16,17]. Further research into patient-specific or provider-specific decision-making is warranted, such as through discrete choice experiment/analysis.

In our stepwise adjusted models, increasing immunotherapy volume at the nearest cancer centre, a marker of rapidity of uptake of new therapies, was associated with increased likelihood of receiving curative-intent treatment, as was increasing diagnostic interval. The magnitude of effect and statistical significance of treatment volume diminished over time in our era-based sensitivity analysis, suggesting that increasing adoption of modern techniques has qualified more patients for therapy they would not have otherwise received if treated in an earlier era. As for the diagnostic interval, the magnitude of this effect is minimal. It is likely explained by a shortened duration of work-up period in patients with a greater symptom burden from more advance disease with a poorer prognosis. It may also correlate with smaller cancer centre volume where local capacity for required diagnostic services (e.g., imaging, biopsy) is less strained compared to larger centres.

The most significant finding of our study relates to the wide variation in the likelihood of receiving palliative-only treatment based on health region of residence. While we hypothesized that this effect should diminish over time, variability across health regions remained in our sensitivity analysis stratified by treatment era. As such, our findings contribute to growing literature that where a patient lives is associated with the type of treatment they receive. Factors outside of the patient's control, such as expertise at presenting cancer center and use of radiotherapy [5] and access to multidisciplinary care and use of multimodality therapy [6] have been associated with treatment received in NSCLC. Place of residence as a predictor of treatment received has also been a reported factor [7,18], as well as socioeconomic status (notably not a major factor in our study of a universal health care system), insurance status (in non-universal health care systems) [7], education level, and receipt of treatment at an academic/research hospital [19]. Our study is unique from these prior analyses because we investigate associations with curative-intent treatment of any kind rather than with a single modality, or only in unresectable patients, in patients with oncogenic driver mutations, or in early-stage patients. Within the Ontario health care system, the health region of residence is reflective of the treating regional cancer program. Evidence regarding the role of combined-modality therapies (of some kind) in stage III NSCLC is clear in terms of life-prolonging benefits for appropriately selected patients. Treating centres are not without evidence-based and consensus guidelines to inform treatment. Nevertheless, there may be variation in opinion of the importance of the benefits of curative over palliative treatment in patients with stage III NSCLC between regional cancer programs, or uncontrolled variation in patient preference between regions. In addition, the possibility that while some centres may systematically under-treat or emphasize palliative therapies, other centers may be offering curative therapy to unsuitable candidates, or over-treating. Under-treatment may result in shorter disease control and over-treatment may result in excessive toxicity, diminishing quality of life in patients with limited life expectancy. Notably, for decisions on treatment versus no treatment, there is no significant regional variation in practice, which could reflect the lack of ambiguity in outcome amongst patients where it is appropriate to consider no cancer-directed treatment. While some practice variability can be expected at the margins, the magnitude of the difference in treatment intent received by health region of residence in our modelling speaks to a variability in practice that should be understood and addressed if needed.

Proposals to address practice variability in offering curative-intent treatment could include increased emphasis on communities-of-practice, centralized or regional peer-review, more frequent or standardized multidisciplinary decision-making, and increased knowledge translation about the risks and benefits of therapy based on evidence-based guidelines. Efforts are already underway within OH CCO to standardize the therapeutic approach to cancer treatment across the province, especially as related to radiotherapy. Results of this study will be shared with each cancer centre to enable comparisons with anonymized data from peer centres across the province that could result in practice changes.

Limitations

Retrospective, population-based studies of this nature are inherently limited by residual confounding, though we regard the variables included in the analysis to be relevant and comprehensive. Some of our variables signal an association with treatment received that is likely a measure of an underlying coding standard (e.g., histology, location). Performance status was not perfectly accounted for in this analysis given this data was missing from the database, but variables that are reasonable proxies for it that we did include are comorbidities and Elixhauser index and instances of health care utilization such as hospitalization.

Table 3
Comparisons of type of treatment with socio-demographics, general health, disease, and health system characteristics for cohort patients diagnosed with stage III non-small cell lung cancer (NSCLC) in Ontario.

Patient Characteristics	Type of Treatment[a]							
	Any Treatment vs. No Treatment				Palliative-Only Treatment vs. Curative Treatment[b]			
	Unadjusted Analysis		Adjusted Analysis		Unadjusted Analysis		Adjusted Analysis	
	RR (95 % CI)	P-value	RR (95 % CI)	P-value	RR (95 % CI)	P-value	RR (95 % CI)	P-value
Patient Factors								
Age								
20-64 (Reference)								
65-69	0.94 (0.91–0.97)	<0.001	0.97 (0.95–1.00)	0.041	1.09 (0.98–1.22)	0.112	1.15 (1.04–1.26)	0.006
70-74	0.94 (0.91–0.96)	<0.001	0.98 (0.96–1.01)	0.241	1.33 (1.20–1.47)	<0.001	1.38 (1.26–1.51)	<0.001
75-79	0.85 (0.82–0.89)	<0.001	0.95 (0.92–0.98)	0.004	1.54 (1.39–1.70)	<0.001	1.54 (1.41–1.69)	<0.001
80+	0.65 (0.62–0.68)	<0.001	0.83 (0.80–0.87)	<0.001	1.97 (1.80–2.16)	<0.001	1.87 (1.71–2.03)	<0.001
Sex								
Female (Reference)								
Male	0.99 (0.97–1.02)	0.663			0.99 (0.93–1.06)	0.782		
Income quintile								
1 (Lowest) (Reference)								
2	1.01 (0.97–1.05)	0.639			0.90 (0.82–0.99)	0.032		
3	1.01 (0.97–1.05)	0.528			0.91 (0.83–1.00)	0.062		
4	1.05 (1.01–1.09)	0.010			0.92 (0.83–1.01)	0.085		
5 (Highest)	1.03 (0.99–1.08)	0.123			0.85 (0.77–0.95)	0.004		
Urban/rural residence								
Urban (RIO < 10)	0.96 (0.93–1.00)	0.032			1.08 (0.98–1.20)	0.131		
Suburban (10 ≤ RIO < 40)	0.91 (0.87–0.95)	<0.001			0.98 (0.88–1.10)	0.758		
Rural (40 ≤ RIO) (Reference)								
Area-level lifetime experimental/abstinence smoking rates[c]								
Higher than average	1.01 (0.98–1.04)	0.493			1.15 (1.07–1.25)	<0.001	1.18 (1.06–1.31)	0.003
Typical average (Reference)								
Lower than average	0.98 (0.95–1.01)	0.155			1.06 (0.98–1.16)	0.162	1.04 (0.95–1.14)	0.409
Elixhauser comorbidity index[d]								
0 (Reference)								
1-2	0.87 (0.84–0.90)	<0.001	0.95 (0.92–0.98)	<0.001	1.14 (1.05–1.23)	0.001		
3+	0.72 (0.68–0.76)	<0.001	0.88 (0.84–0.92)	<0.001	1.37 (1.25–1.50)	<0.001		
Chronic conditions								
Asthma (Yes vs. No)	0.96 (0.92–0.99)	0.018			1.11 (1.02–1.20)	0.015		
COPD (Yes vs. No)	0.90 (0.88–0.93)	<0.001			1.15 (1.08–1.23)	<0.001	1.11 (1.05–1.18)	0.001
Hypertension (Yes vs. No)	0.90 (0.88–0.93)	<0.001			1.18 (1.10–1.26)	<0.001		
CHF (Yes vs. No)	0.77 (0.73–0.82)	<0.001			1.40 (1.28–1.53)	<0.001	1.10 (1.01–1.20)	0.024
Dementia (Yes vs. No)	0.55 (0.49–0.63)	<0.001	0.78 (0.70–0.87)	<0.001	1.42 (1.23–1.65)	<0.001		
CKD[e] (Yes vs. No)	0.85 (0.80–0.89)	<0.001			1.36 (1.24–1.49)	<0.001		
Disease Factors								
Histology/morphology								

(*continued on next page*)

Table 3 (*continued*)

Patient Characteristics	Type of Treatment[a]							
	Any Treatment vs. No Treatment				Palliative-Only Treatment vs. Curative Treatment[b]			
	Unadjusted Analysis		Adjusted Analysis		Unadjusted Analysis		Adjusted Analysis	
	RR (95 % CI)	P-value	RR (95 % CI)	P-value	RR (95 % CI)	P-value	RR (95 % CI)	P-value
Other/neoplasms, NOS (Reference)								
Epithelial neoplasms, NOS	2.11 (1.90–2.33)	<0.001	1.53 (1.40–1.66)	<0.001	1.27 (1.07–1.50)	0.006	1.18 (1.02–1.36)	0.029
Squamous cell neoplasms	2.29 (2.07–2.53)	<0.001	1.60 (1.47–1.74)	<0.001	1.10 (0.93–1.29)	0.267	1.12 (0.97–1.29)	0.117
Adenomas/adenocarcinomas	2.41 (2.19–2.66)	<0.001	1.62 (1.49–1.75)	<0.001	0.91 (0.77–1.07)	0.258	1.03 (0.89–1.18)	0.733
Anatomic location								
Upper lobe	2.42 (2.11–2.77)	<0.001	1.56 (1.40–1.74)	<0.001	0.75 (0.63–0.88)	<0.001		
Middle lobe	2.25 (1.93–2.61)	<0.001	1.46 (1.29–1.65)	<0.001	0.80 (0.64–1.00)	0.052		
Lower lobe	2.35 (2.05–2.69)	<0.001	1.55 (1.39–1.72)	<0.001	0.82 (0.69–0.98)	0.026		
Main bronchus	2.31 (2.00–2.67)	<0.001	1.57 (1.40–1.76)	<0.001	0.95 (0.78–1.16)	0.607		
Overlapping lesion/lung, NOS (Reference)								
Best stage								
III/IIIA (Reference)								
IIIB/IIIC	1.03 (1.00–1.06)	0.024			1.65 (1.54–1.75)	<0.001	1.50 (1.42–1.59)	<0.001
Diagnostic imaging[f]								
PET scan (Yes vs. No)	1.66 (1.59–1.72)	<0.001	1.26 (1.22–1.30)	<0.001	0.42 (0.40–0.45)	<0.001	0.55 (0.52–0.59)	<0.001
Comprehensive assessment[g]								
Palliative care consultation (Yes vs. No)	0.87 (0.84–0.90)	<0.001	0.92 (0.89–0.94)	<0.001	2.24 (2.12–2.38)	<0.001	1.81 (1.71–1.92)	<0.001
Geriatric consultation (Yes vs. No)	0.61 (0.50–0.74)	<0.001	0.82 (0.71–0.95)	0.010	1.49 (1.20–1.86)	<0.001		
Medical oncology consultation (Yes vs. No)	1.33 (1.30–1.37)	<0.001	1.07 (1.04–1.09)	<0.001	0.99 (0.93–1.06)	0.858		
ESAS assessment (Yes vs. No)	1.76 (1.69–1.83)	<0.001	1.39 (1.34–1.44)	<0.001	0.82 (0.77–0.89)	<0.001	0.90 (0.84–0.96)	0.002
Health utilization[h]								
Inpatient hospitalization (Yes vs. No)	0.77 (0.73–0.82)	<0.001			1.15 (1.03–1.28)	0.011		
ED-only visit (Yes vs. No)	0.94 (0.92–0.97)	<0.001			1.19 (1.11–1.27)	<0.001	1.15 (1.08–1.22)	<0.001
Health System Factors								
Treatment Era								
2010-2012 (Reference)								
2013-2015	1.02 (0.99–1.06)	0.135			1.00 (0.92–1.08)	0.922		
2016-2018	1.08 (1.05–1.11)	<0.001			0.89 (0.82–0.96)	0.004		
Place of residence (LHIN)								
A (Reference)								
B	1.06 (0.98–1.14)	0.135			0.92 (0.75–1.13)	0.416	0.88 (0.73–1.05)	0.159
C	1.02 (0.95–1.09)	0.654			1.06 (0.88–1.27)	0.552	1.18 (0.99–1.41)	0.070
D	0.98 (0.90–1.06)	0.599			1.39 (1.16–1.68)	<0.001	1.67 (1.38–2.01)	<0.001
E	1.06 (1.00–1.14)	0.055			1.21 (1.02–1.44)	0.025	1.35 (1.16–1.57)	<0.001
F	0.97 (0.89–1.05)	0.461			0.99 (0.80–1.24)	0.950	1.13 (0.91–1.41)	0.258
G	1.05 (0.97–1.12)	0.219			1.16 (0.96–1.40)	0.123	1.25 (1.03–1.53)	0.023
H	0.98 (0.87–1.09)	0.672			0.93 (0.68–1.26)	0.638	1.10 (0.81–1.51)	0.534
I	1.01 (0.93–1.08)	0.891			1.06 (0.87–1.30)	0.551	1.28 (1.05–1.56)	0.014

(*continued on next page*)

Table 3 (*continued*)

Patient Characteristics	Type of Treatment[a]							
	Any Treatment vs. No Treatment				Palliative-Only Treatment vs. Curative Treatment[b]			
	Unadjusted Analysis		Adjusted Analysis		Unadjusted Analysis		Adjusted Analysis	
	RR (95 % CI)	P-value	RR (95 % CI)	P-value	RR (95 % CI)	P-value	RR (95 % CI)	P-value
J	1.05 (0.98–1.12)	0.195			0.74 (0.60–0.91)	0.005	0.94 (0.76–1.16)	0.551
K	1.05 (0.97–1.13)	0.271			1.22 (0.99–1.50)	0.057	1.23 (1.03–1.48)	0.026
L	0.97 (0.91–1.04)	0.409			1.04 (0.87–1.24)	0.699	1.36 (1.13–1.62)	0.001
M	1.02 (0.93–1.13)	0.684			1.09 (0.84–1.41)	0.519	1.19 (0.94–1.49)	0.148
N	1.03 (0.96–1.12)	0.411			1.35 (1.12–1.64)	0.002	1.35 (1.14–1.60)	<0.001
Diagnostic interval[f]								
Time from first chest X-ray/CT scan to diagnosis								
Per 1-week increase	1.01 (1.01–1.01)	<0.001			0.97 (0.96–0.98)	<0.001	0.99 (0.98–0.99)	0.001
Cancer centre location[i]								
As-the-crow-flies distance to nearest regional cancer centre								
Per 25-km increase	1.00 (0.99–1.00)	0.192			0.99 (0.98–1.01)	0.553		
As-the-crow-flies distance to nearest radiotherapy centre								
Per 25-km increase	1.00 (0.99–1.00)	0.388			0.99 (0.97–1.01)	0.341		
As-the-crow-flies distance to nearest thoracic surgery centre								
Per 25-km increase	0.99 (0.99–1.00)	0.123			0.99 (0.98–1.01)	0.402		
Cancer centre treatment volume[j]								
Patient-level immunotherapy (±chemotherapy) volume								
Per 100-person increase	1.19 (1.10–1.30)	<0.001			0.75 (0.58–0.97)	0.027	0.67 (0.53–0.85)	0.001
Patient-level advanced radiotherapy volume								
Per 100-person increase	1.05 (1.01–1.08)	0.005			0.95 (0.87–1.03)	0.222		

Acronyms:
RR, relative risk; CI, confidence interval; RIO, Rurality Index for Ontario; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; CKD, chronic kidney disease; NOS, not otherwise specified; CT, computed tomography, PET, positron emission tomography; ESAS, Edmonton Symptom Assessment System; ED, emergency department; LHIN, local health integration network; km, kilometres.
Notes:
a. Type of treatment was measured within a 2-year lookforward period from NSCLC diagnosis.
b. Patients who received curative/adjuvant treatment may eventually receive palliative treatment.
c. Smoking status was collected from survey respondents in the 2015–2017 Canadian Community Health Survey (CCHS) data; area-level age-sex standardized rates were computed with the 2016 Ontario census division (CD) geography and population
d. Elixhauser comorbidity index was measured within a 5-year lookback period from NSCLC diagnosis; total comorbidity score excluded indices for lymphoma, metastatic cancer and solid tumor without metastases.
e. CKD was measured with an average estimated glomerular filtration rate of < 60 mL/min/1.73 m^2 from multiple laboratory tests within a 1-year lookback period from NSCLC diagnosis.
f. Chest X-ray and CT scans were measured within a 3-month lookback period from NSCLC diagnosis; PET scan was measured within a 3-month lookback and lookforward period from NSCLC diagnosis.
g. Palliative care, geriatric and medical oncology consultations were measured within a 3-month lookback and lookforward period from NSCLC diagnosis; ESAS assessment was measured within a 16-week lookback and lookforward period from NSCLC diagnosis.
h. Inpatient hospitalizations and ED-only visits were measured within a 3-month lookback period from NSCLC diagnosis.
i. As-the-crow-flies distance was measured with the haversine formula between the postal code of residence and the geographic locations of the regional, radiotherapy and thoracic surgery cancer centres; regional, radiotherapy and thoracic surgery cancer centre locations were obtained from Ontario Health; thoracic surgery cancer centres account for > 90 % of the thoracic cancer surgeries in the province.
j. Patient-level annual volume of chemotherapy/radiotherapy treatment was measured with all stage III NSCLC patients (who may have other non-NSCLC diagnoses) at the nearest regional cancer centre from their residence within a 1-year lookback period from NSCLC diagnosis.

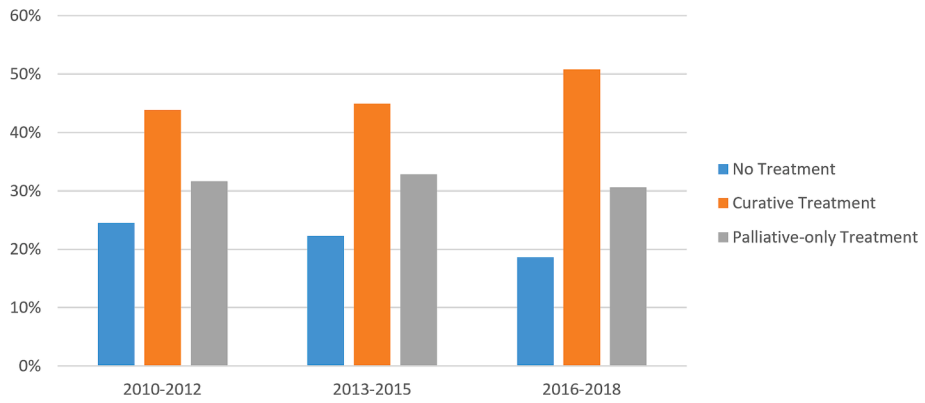

Fig. 3A. Types of treatment, by treatment era, for cohort patients diagnosed with stage III non-small cell lung cancer (NSCLC) in Ontario.

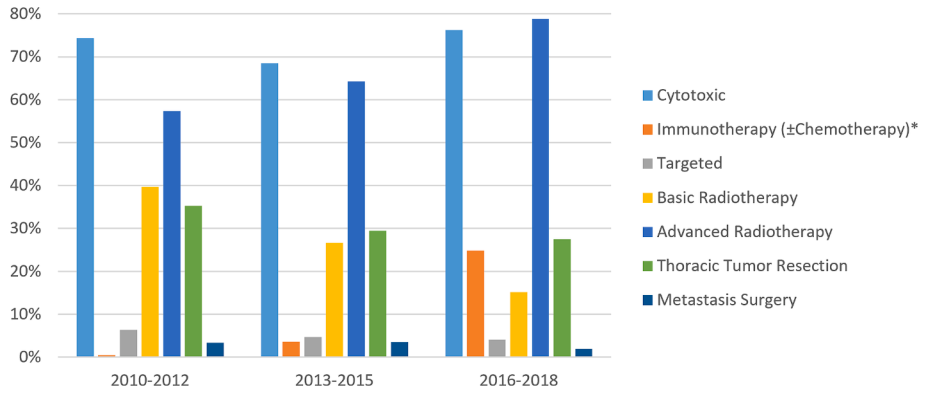

Fig. 3B. Types of treatment of curative patients, by treatment era, for cohort patients diagnosed with stage III non-small cell lung cancer (NSCLC) in Ontario**.** Notes: *Due to privacy regulations, small cells suppressed for 2010–2012 era of diagnosis.

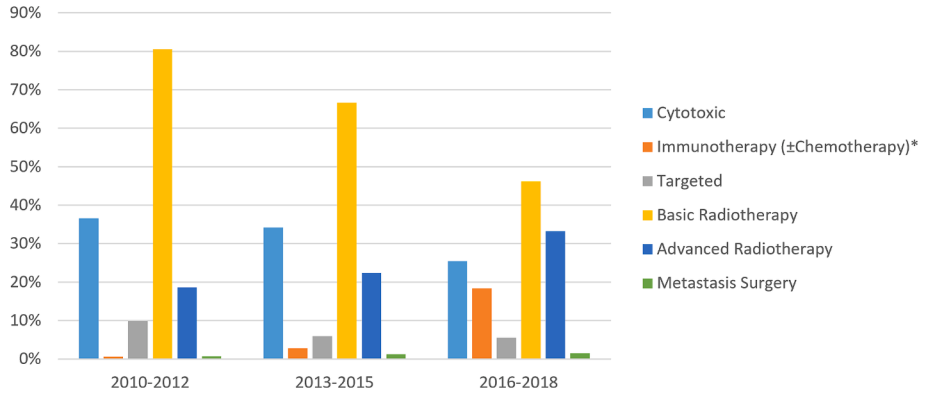

Fig. 3C. Types of treatment of palliative-only patients, by treatment era, for cohort patients diagnosed with stage III non-small cell lung cancer (NSCLC) in Ontario Notes: *Due to privacy regulations, small cells suppressed for 2010–2012 era of diagnosis.

Finally, patient preferences were not accounted for in our analysis, which is of course a major variable implicating treatment received. However, the magnitude of variation in intent of treatment received between health regions is unlikely to be explained by regional variation in patient preference. Nevertheless, our findings support the need for more analyses of patient- and provider-specific preferences, especially in older adults, such as through discrete choice experiments.

Conclusions

In this population-based cohort study of stage III NSCLC diagnosed and managed within a single-payer health care system in Ontario between January 2010 and December 2018, health region of residence was a major health system-level factor associated with treatment intent. Ensuring a consistent, standardized, evidence-based approach to offering curative-intent treatment is of paramount importance. Addressing system variation, where it exists, could include increased emphasis on communities-of-practice, centralized or regional peer-review, multidisciplinary decision-making, and knowledge translation. In addition, the patient-centeredness of decision making in older adults should be investigated.

Funding

T.P. Hanna holds a research grant provided by the Ontario Institute for Cancer Research through funding provided by the Government of

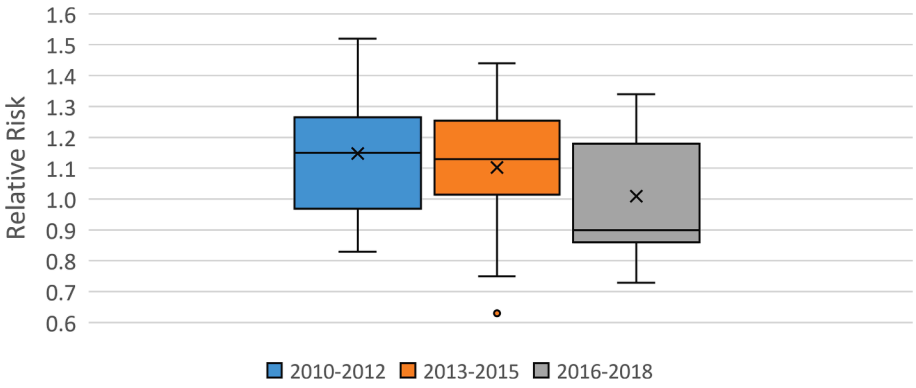

Fig. 4. Relative risk (RR) of palliative-only treatment vs. curative treatment by region of residence, stratified by treatment era, for the cohort of patients diagnosed with stage III non-small cell lung cancer (NSCLC) in Ontario. Relative risks from stepwise adjusted model. The box represents the RR interquartile range (IQR). The X within the box is the RR mean, and the horizontal bar within the box is the RR median. The horizontal bars at the end of the vertical bars represent the maximum and minimum values excluding outliers. The orange dot represents a lower outlier (value less than Q1 – 1.5xIQR). There were no upper outliers.

Ontario (#IA-035).

Author contribution

ST, PN, FYdM, and TH conceived the project. PN and TH performed data collection and statistical analysis. All authors contributed to data interpretation and writing, editing, and final preparation of the manuscript. TH had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: ST and PN do not declare any actual or possible conflicts of interest. AR declares previous honoraria from EISAI, Merk Sharp Dohme, AstraZeneca, and Bristol-Myers Squibb unrelated to the present work. FYdM declares previous honoraria from Cancer em foco and AstraZeneca unrelated to the present work. JP declares a current role as the Ontario Health Cancer Care Ontario (OH CCO) Provincial Head of the Radiation Treatment Program. TH declares a current role as the OH CCO Radiation Oncology Clinical Quality Lead for the Radiation Treatment Program.

Acknowledgements

This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health (MOH) and the Ministry of Long-Term Care (MLTC). This document used data adapted from the Statistics Canada Postal Code^{OM} Conversion File, which is based on data licensed from Canada Post Corporation, and/or data adapted from the Ontario Ministry of Health Postal Code Conversion File, which contains data copied under license from ©Canada Post Corporation and Statistics Canada. Parts of this material are based on data and/or information compiled and provided by: MOH, CIHI, Ontario Health (OH), Statistics Canada and IQVIA Solutions Canada Inc. The analyses, conclusions, opinions and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred.

Parts of this material are based on data and/or information compiled and provided by CIHI. However, the analyses, conclusions, opinions and statements expressed in the material are those of the author(s), and not necessarily those of CIHI. Parts of this material are based on data and information provided by OH. The opinions, results, view, and conclusions reported in this paper are those of the authors and do not necessarily reflect those of OH. No endorsement by OH is intended or should be inferred. Adapted from Statistics Canada, 2015 Canadian Community Health Survey – Annual Component (CCHS), March 2017; 2016 CCHS, September 2017; and 2017 CCHS, June 2018. This does not constitute an endorsement by Statistics Canada of this product. We thank IQVIA Solutions Canada Inc. for use of their Drug Information File.

Data sharing and availability

The dataset from this study is held securely in coded form at ICES. While legal data sharing agreements between ICES and data providers (e.g., healthcare organizations and government) prohibit ICES from making the dataset publicly available, access may be granted to those who meet pre-specified criteria for confidential access, available at www.ices.on.ca/DAS (email: das@ices.on.ca). The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctro.2024.100873.

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