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Evolving Patterns of Care, Outcomes and Ongoing Challenges for Early-Stage Non-Small Cell Lung Cancer in the Immunotherapy Era: A Queensland Population-Based Study

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ABSTRACT

Introduction: This retrospective study describes contemporary patterns of care and outcomes for early-stage non-small cell lung cancer (NSCLC) in Queensland, Australia, with a focus on immunotherapy.

Methods: Population-based data for patients with NSCLC diagnosed at stages I-III between 2018 and 2022 were sourced from the Queensland Oncology Repository. Follow-up on treatment and mortality was available to 31 December 2024. Poisson models were used to determine patient and clinical characteristics associated with the treatments received. Differences in five-year observed survival were calculated from multivariable flexible parametric models.

Results: The study cohort comprised 4608 patients. Surgery alone was the most common treatment modality for stages I and II (55% and 27%, respectively), whereas 44% of patients with stage III disease had concurrent chemoradiotherapy without surgery. Just over half (53%) of this latter group were also treated with durvalumab. First Nations people were somewhat less likely to receive either surgery (relative likelihood = 0.95, 95% CI 0.91–1.00; $p = 0.04$) or chemotherapy (RL = 0.95, 95% CI 0.90–0.99; $p = 0.03$) compared to other Queensland residents. Five-year observed survival ranged from 17% (95% CI 11%–25%) for stage IIIC to 81% (95% CI 74%–87%) for stage IA1. Patients with unresected stage III disease who received concurrent chemoradiotherapy with subsequent durvalumab were 37% less likely to die from NSCLC within 5 years of diagnosis than chemoradiotherapy alone (hazard ratio = 0.63, 95% CI 0.51–0.78; $p < 0.001$).

Conclusions: Disparities in treatment for First Nation people with NSCLC require urgent attention. Durvalumab provides a survival advantage for unresectable stage III NSCLC within a real-world setting.

Abbreviations: CI, confidence interval; CRT, chemoradiotherapy; CT, chemotherapy; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; NSCLC, non-small cell lung cancer; RL, relative likelihood; RT, radiotherapy; SES, socioeconomic status; TNM, tumor, node, metastasis.

1 | Introduction

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for approximately 85% of all lung cancer cases worldwide [1, 2]. Between 40% and 50% of NSCLC patients are diagnosed at an advanced stage after the disease has metastasized [3, 4], when the chance of cure is remote. In contrast, for early-stage NSCLC (referred to here as stages I, II, and III at diagnosis) where the cancer is more localized, it is potentially curable.

Treatment for early-stage NSCLC has historically revolved around surgery, radiation therapy, and chemotherapy, often used in combination depending on the stage and location of the tumor [5–7]. If resectable and medically operable, complete surgical resection remains the gold standard for early-stage NSCLC, offering the best chance for cure [8]. Although most commonly used for stages I and II, surgery can also be an important treatment modality for selected cases with stage III NSCLC [9]. This space is rapidly evolving, with adjuvant [10], neoadjuvant [11] and perioperative [12–14] strategies now adding immune checkpoint inhibitors to traditional treatment modalities.

For those diagnosed with unresectable or inoperable stage III NSCLC, definitive radiation with concurrent chemotherapy was the historically established treatment [9]. In 2017, the PACIFIC study [15, 16] demonstrated that the addition of consolidation immunotherapy with durvalumab, an anti-PD-L1 antibody, significantly improved survival, thus becoming the new standard of care [9].

We have published population-based information relating to patterns of care and outcomes for early-stage NSCLC in Queensland immediately prior to the immunotherapy era (2011–2017) [17]. In the current study, patterns of care and survival for the period 2018–2022 are examined, during which time consolidation durvalumab for unresectable stage III NSCLC was approved and reimbursed in Australia (1 March 2020). Thus, our study includes an evaluation of the use of durvalumab and its impact on outcomes.

2 | Material and Methods

This study was carried out in accordance with Section 82 of the Queensland Hospital and Health Boards Act (2011) [18], which allows access to identifiable information stored within the Queensland Oncology Repository to members of the Queensland Cancer Control Safety and Quality Partnership. Separate approval from a human research ethics committee for the study was therefore not required.

The Queensland Oncology Repository contains extensive information on patient demographics, cancer diagnoses, deaths, and treatments, for the purposes of directing and assessing cancer control efforts at a whole-of-population level. A central element of the Queensland Oncology Repository is its sophisticated patient matching engine, which is designed to accurately identify and link records belonging to the same individual across multiple, diverse data sources, including the Queensland Cancer Register, the Queensland Hospital Admitted Patient Data Collection (covering all patients from both public and licensed private hospitals and private day surgeries throughout the state), and the Registry of Births, Deaths, and Marriages. A combination of deterministic rules and probabilistic algorithms is then used to compare patient demographic information such as name (including any aliases), date of birth and residential address. By calculating match scores and applying defined thresholds, the system determines whether records should be linked, flagged for manual review, or kept distinct to ensure data integrity.

Patients eligible for inclusion in the study were residents of Queensland aged 15 years and over who were diagnosed with early-stage primary NSCLC between 2018 and 2022. Information on mortality was complete through to 31 December 2024, allowing a potential minimum of 2 years of follow-up per patient. Treatments (categorized as surgery, radiotherapy, chemotherapy, and immunotherapy (durvalumab)) were only considered in the study if they commenced within 1 year of the date of diagnosis. Note that radiotherapy includes external beam only. Radiotherapy and chemotherapy were categorized according to whether they were given concurrently (i.e., overlapping treatment dates), sequentially (where chemotherapy commenced within 45 days of radiotherapy ending, or vice versa), as distinct therapies (both treatments given but there were more than 45 days between the end of one and start of the other) or only one or the other was administered. Note that oral systemic agents were not recorded within the Queensland Oncology Repository, and so for the purposes of this study, chemotherapy refers to intravenous systemic therapy only.

Morphological subtype was categorized as adenocarcinoma, squamous cell carcinoma or other carcinomas, based on the 2021 World Health Organization Classification of Lung Tumors [19] (see Supplementary Table 1 for full details). Stage at diagnosis was assigned using the 8th edition of the TNM staging system [20]. If there was more than one notification of stage (clinical and/or pathological) received for the same person, the staging category recorded was determined by an automated approach that gave higher priority to information that was likely to be of better quality (e.g., pathological results would generally take precedence over clinical results to determine stage).

Other key demographic and clinical characteristics of interest were: sex; age group; First Nations status (self-reported as an Aboriginal and/or Torres Strait Islander person); remoteness of residence [21]; area-based socio-economic status [22]; number of comorbidities [23]; and performance status [24] (measured at baseline). The categories and definitions for each of these variables are outlined in Supplementary Table 2.

2.1 | Data Analyses

To determine the features associated with different patterns of care, generalized linear models were fitted to all patients in the study cohort using a Poisson distribution and log link function, with broad types of treatment (i.e., any treatment, surgery, radiotherapy or chemotherapy) as the independent variable. A similar model was fitted specifically to patients who received concurrent chemoradiotherapy for unresectable stage III NSCLC to examine the utilization of durvalumab. The models were adjusted

for each of the key personal and clinical characteristics (as outlined above). Results were expressed in terms of the relative likelihood (RL) of receiving a particular type of treatment compared to the reference category within each covariate.

Five-year observed survival was estimated using the Kaplan–Meier method, with equality of the survival curves evaluated by the log-rank test. Survival time by substage at diagnosis was calculated from the date of diagnosis until the date of death from any cause, the end of the study period (31 December 2024), or 5 years after diagnosis, depending on which of these events occurred first. A separate survival analysis was performed for unresectable stage III cases who received concurrent chemoradiotherapy by whether they went on to receive durvalumab. Survival time for this subgroup was calculated from 4 months after the commencement of chemotherapy and radiotherapy rather than from the date of diagnosis, to better compare against the inclusion criteria of the landmark PACIFIC study, where patients received durvalumab following concurrent chemoradiotherapy if they did not have any evidence of progressive disease [15].

Differences in survival by key personal and clinical characteristics were calculated by fitting multivariable flexible parametric survival models, stratified by stage at diagnosis and including adjustment for the type of treatment received. Flexible parametric modeling has several advantages over traditional proportional hazards survival models, such as allowing for changes in the hazard ratio over time [25]. Models were fitted separately for stage III NSCLC according to whether or not surgery was performed and for those who received concurrent chemoradiotherapy. A multivariate fractional polynomial model was also run to determine which covariates to retain in the final model (set at the 20% level of significance). Outcomes with respect to the reference category for each remaining covariate were expressed as the adjusted excess mortality hazard ratio (HR) at 5 years after diagnosis.

The selected reference group for each of the personal and clinical characteristics was generally the most common category and/or the characteristic associated with better survival. Point estimates are presented along with 95% confidence intervals (95% CIs) and *p*-values where relevant. All analyses were conducted using Stata/MP for Windows version 18.0 (StataCorp LLC, College Station, Texas).

3 | Results

3.1 | Study Cohort

Early-stage disease represented 41% of all patients in Queensland diagnosed with NSCLC between 2018 and 2022 ($n = 4608$ of 11 259), following exclusion of those with unknown stage ($n = 1427$, 13%) or who initially presented with metastases ($n = 5224$, 46%) – Supplementary Figure 1. Most cases included in the study cohort were diagnosed based on histology ($n = 3783$, 82%) or cytology ($n = 616$, 13%). The remainder were diagnosed by clinical investigations such as radioscopy or endoscopy ($n = 132$, 3%), clinical examination only ($n = 71$, 2%), or where the basis of diagnosis was not stated ($n = 6$, 0.1%).

Half of all patients were diagnosed at stage I ($n = 2296$, 50%), 17% ($n = 763$) at stage II and 34% ($n = 1549$) at stage III. Most cases ($n = 3528$, 77%) were staged on the basis of pathological or clinical stage only. Where both types of staging were available, 77% were concordant ($n = 832$ of 1080); that is, pathological and clinical stage were discordant for only 5% of patients in the study cohort ($n = 248$ of 4608).

There were slightly more males overall ($n = 2411$, 52%) and the median age at diagnosis was 71 years old (interquartile range 64–77 years old). Among the subset of 648 patients with stage III disease who had concurrent chemoradiotherapy without surgery and who survived a minimum of 120 days from the commencement of treatment, 56% ($n = 364$) were male with a median age of 67 years (interquartile range 61–73 years).

Highly significant differences ($p < 0.001$) were seen for several of the personal and clinical characteristics within the entire study cohort after stratification by stage at diagnosis (Table 1). Females (52%) outnumbered males among stage I patients, compared to 42% females among those with stage III disease. Patients aged 70 years and over at diagnosis accounted for 51% of stage III disease compared to 58% for both stage I and stage II. The percentage of patients from major cities varied from 70% for stage I to 65% for stages II and III. Living in a socio-economically disadvantaged area was lowest for stage I and highest for stage III (28% vs. 34%, respectively). Adenocarcinoma comprised 64% of stage I cases compared to 47% for stages II and III. There were no clear differences by stage at diagnosis for First Nations status, number of comorbidities or performance status.

3.2 | Patterns of Care

Details of the patterns of care within 1 year of diagnosis by stage at diagnosis are shown in Figure 1 and Supplementary Table 3. Overall, 92% of the study cohort had some form of treatment recorded. Almost half (48%) had surgery, including 33% who had surgery only. Chemotherapy was given to 35% and radiotherapy to 47%, with 24% receiving both. Less than 4% of patients received all three treatment modalities.

The most frequent treatment pathway for both stage I and II involved surgery (64% and 59%, respectively), including 55% for stage I and 27% for stage II who had surgery only. For stage III disease, 44% of patients had concurrent chemoradiotherapy without surgery whereas 18% had surgical treatment with or without chemotherapy and/or radiotherapy. Radiotherapy alone was the next most common type of treatment for all disease stages (24% for stage I, 18% for stage II and 12% for stage III). Those who did not receive any treatment within the first year following their diagnosis varied from 5% for stage I and 6% for stage II to 13% for stage III NSCLC.

3.3 | Characteristics Associated With Any Recorded Treatment

Following adjustment for other factors including stage at diagnosis, patients with poor performance status were 9% less likely to receive any recorded treatment compared to those with good

TABLE 1 | Key characteristics of early-stage NSCLC patients by stage at diagnosis, Queensland, 2018–2022.

	Stage I ($N=2296$)		Stage II ($N=763$)		Stage III ($N=1549$)		Total ($N=4608$)	
Characteristic	***n***	**Col%**	***n***	**Col%**	***n***	**Col%**	***n***	**Col%**
Sex ($p<0.001$)								
Males	1103	48.0	412	54.0	896	57.8	2411	52.3
Females	1193	52.0	351	46.0	653	42.2	2197	47.7
Age group at diagnosis ($p<0.001$)								
<60 years	276	12.0	89	11.7	252	16.3	617	13.4
60–69 years	695	30.3	228	29.9	508	32.8	1431	31.1
70–79 years	1000	43.5	322	42.2	577	37.2	1899	41.2
≥80 years	325	14.2	124	16.2	212	13.7	661	14.3
First Nations status ($p=0.09$)								
Aboriginal and/or Torres Strait Island	68	3.0	32	4.2	64	4.1	164	3.6
Other Queensland resident	2228	97.0	731	95.8	1485	95.9	4444	96.4
Residential location ($p=0.005$)								
Major city	1608	70.0	499	65.4	1008	65.1	3115	67.6
Inner regional	471	20.5	183	24.0	352	22.7	1006	21.8
Outer regional/remote/very remote	217	9.5	81	10.6	189	12.2	487	10.6
Area-based socioeconomic status ($p<0.001$)								
Advantaged	218	9.5	52	6.8	94	6.1	364	7.9
Middle SES	1446	63.0	464	60.8	927	59.8	2837	61.6
Disadvantaged	632	27.5	247	32.4	528	34.1	1407	30.5
Number of comorbidities ($p=0.13$)								
None	1128	49.1	356	46.7	701	45.3	2185	47.4
One	640	27.9	213	27.9	446	28.8	1299	28.2
Two or more	528	23.0	194	25.4	402	25.9	1124	24.4
Performance status ($p=0.22$)[a]								
Good (ECOG score 0–1)	1217	53.0	476	62.4	977	63.1	2670	57.9
Poor (ECOG score 2–4)	138	6.0	62	8.1	138	8.9	338	7.3
Unknown	941	41.0	225	29.5	434	28.0	1600	34.7
Morphological subtype ($p<0.001$)								
Adenocarcinoma	1475	64.2	361	47.3	725	46.8	2561	55.6
Squamous cell carcinoma	435	19.0	249	32.6	518	33.4	1202	26.1
Other carcinomas	386	16.8	153	20.1	306	19.8	845	18.3

Abbreviations: NSCLC, non-small cell lung cancer; SES, socio-economic status.
[a]*p*-value excludes "Unknown" category.

performance status (RL = 0.91 compared to good performance status, 95% CI 0.89–0.94; $p<0.001$) – Figure 2. Being aged 80 years or over (RL = 0.94 compared to under 60 years old, 95% CI 0.93–0.96; $p<0.001$) and having stage III disease (RL = 0.96 compared to stage I, 95% CI 0.95–0.97; $p<0.001$) were also significant determinants for not receiving treatment. Further analysis revealed the demographic and clinical characteristics, which were associated with a significantly decreased or increased likelihood of receiving any surgery, chemotherapy or radiotherapy (see Supplementary Figure 2a–c). In particular, Aboriginal and/or Torres Strait Islander people with early-stage NSCLC were 5% less likely to be treated with either surgery (RL = 0.95, 95% CI 0.91–1.00; $p=0.04$) or chemotherapy (RL = 0.95, 95% CI 0.90–0.99; $p=0.03$) than other Queensland residents.

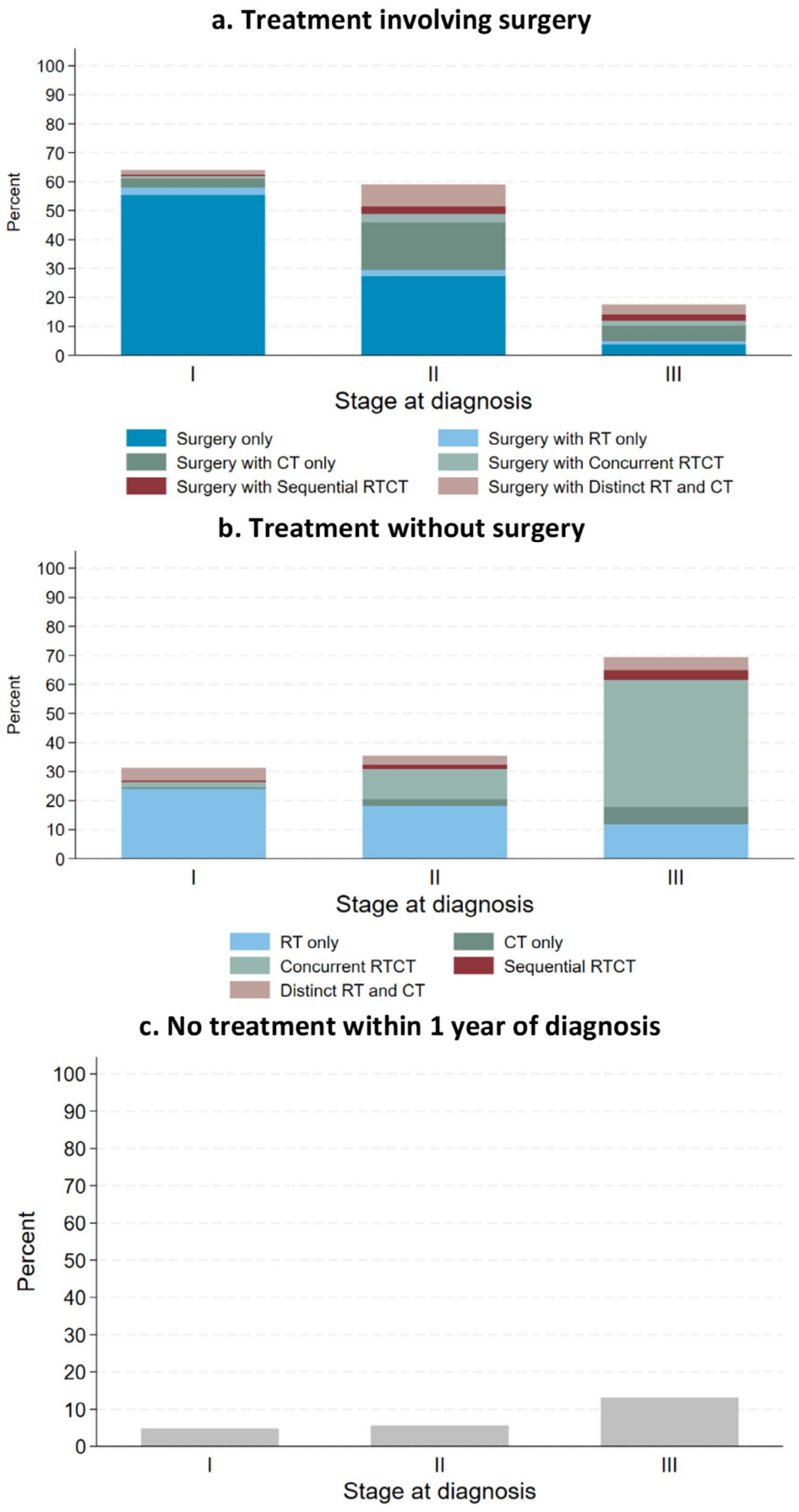

FIGURE 1 | Legend on next page.

FIGURE 1 | Type of treatment within 1 year of diagnosis by stage at diagnosis for early-stage NSCLC, Queensland, 2018–2022. CT—chemotherapy; RT—radiotherapy. *Source*: Excludes oral CT. RT and/or CT given within 1 year of diagnosis. Concurrent CRT – dates of the treatments overlap. Sequential CRT—one therapy is commenced within 45 days of the other ending, in either order. Distinct RT and CT – both treatments given in any order but there were more than 45 days between end of one and start of the other.

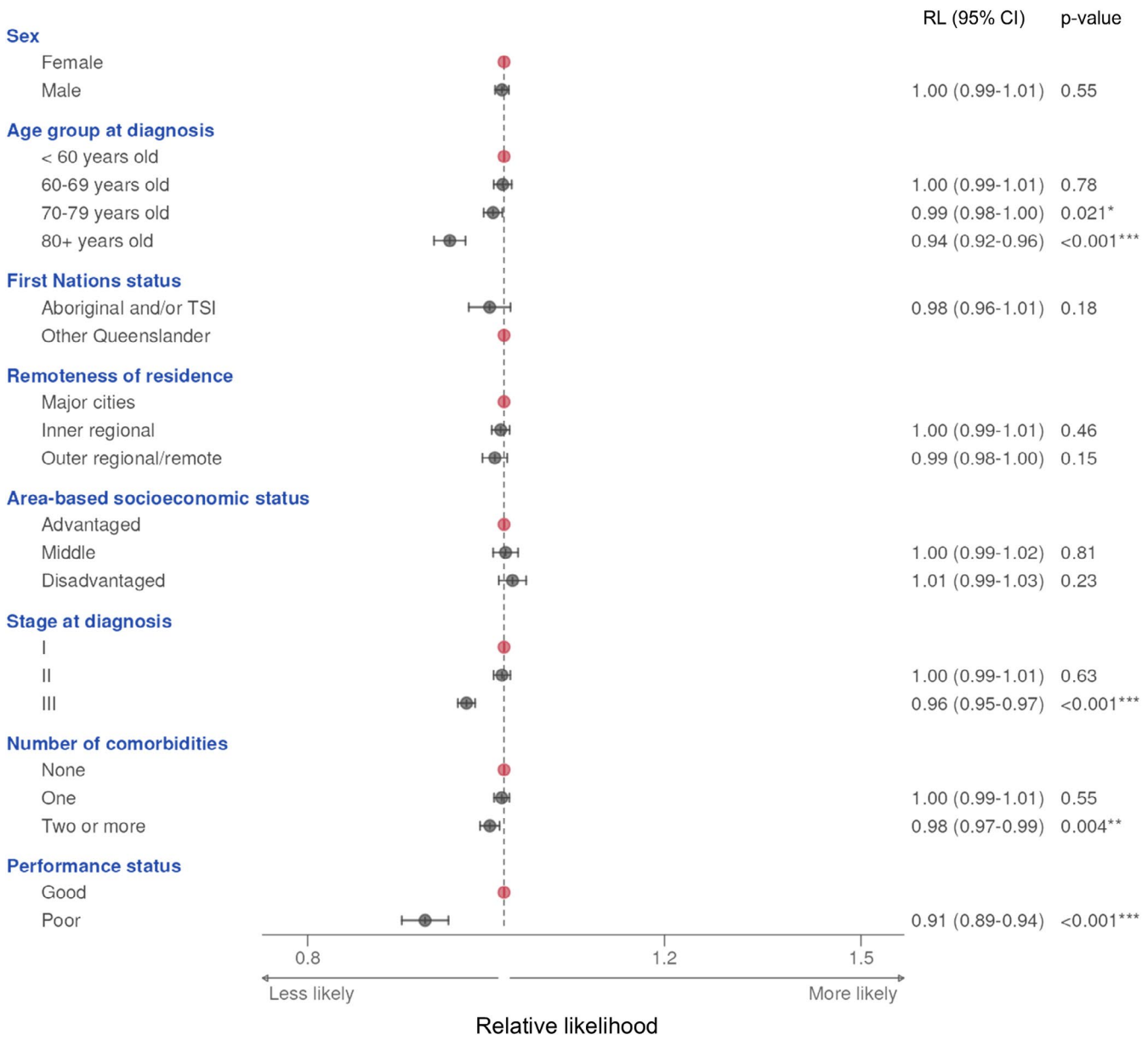

FIGURE 2 | Relative likelihood of receiving any type of treatment within 1 year of diagnosis for NSCLC, Queensland, 2018–2022. *Source*: Red dots signify reference category. Excludes oral chemotherapy.

3.4 | Characteristics Associated With Receiving Durvalumab

A total of 406 patients (9%) from the overall study cohort were treated with durvalumab. Durvalumab was most commonly used for patients with stage III disease ($n = 366$, 90% of all those treated with durvalumab). Among the main target group for durvalumab (i.e., those diagnosed with stage III NSCLC who had concurrent chemoradiotherapy without surgery and who survived for at least 120 days following the commencement of treatment), 346 out of 648 (53%) subsequently received durvalumab, increasing from 36% during 2018 to 62% by 2022 (Supplementary Figure 3). Of this group, people aged 80 years and over (RL = 0.53 compared to under 60 years old, 95% CI 0.31–0.91; $p = 0.02$) and those from inner regional areas (RL = 0.75 compared to major cities, 95% CI 0.61–0.94; $p = 0.01$) were less likely to be treated with durvalumab (Figure 3). Conversely, patients living in outer regional or remote areas (RL = 1.37 compared to major cities, 95% CI 1.12–1.67; $p = 0.002$) had an increased likelihood of receiving durvalumab. Poor performance status was not a predictor of being treated with

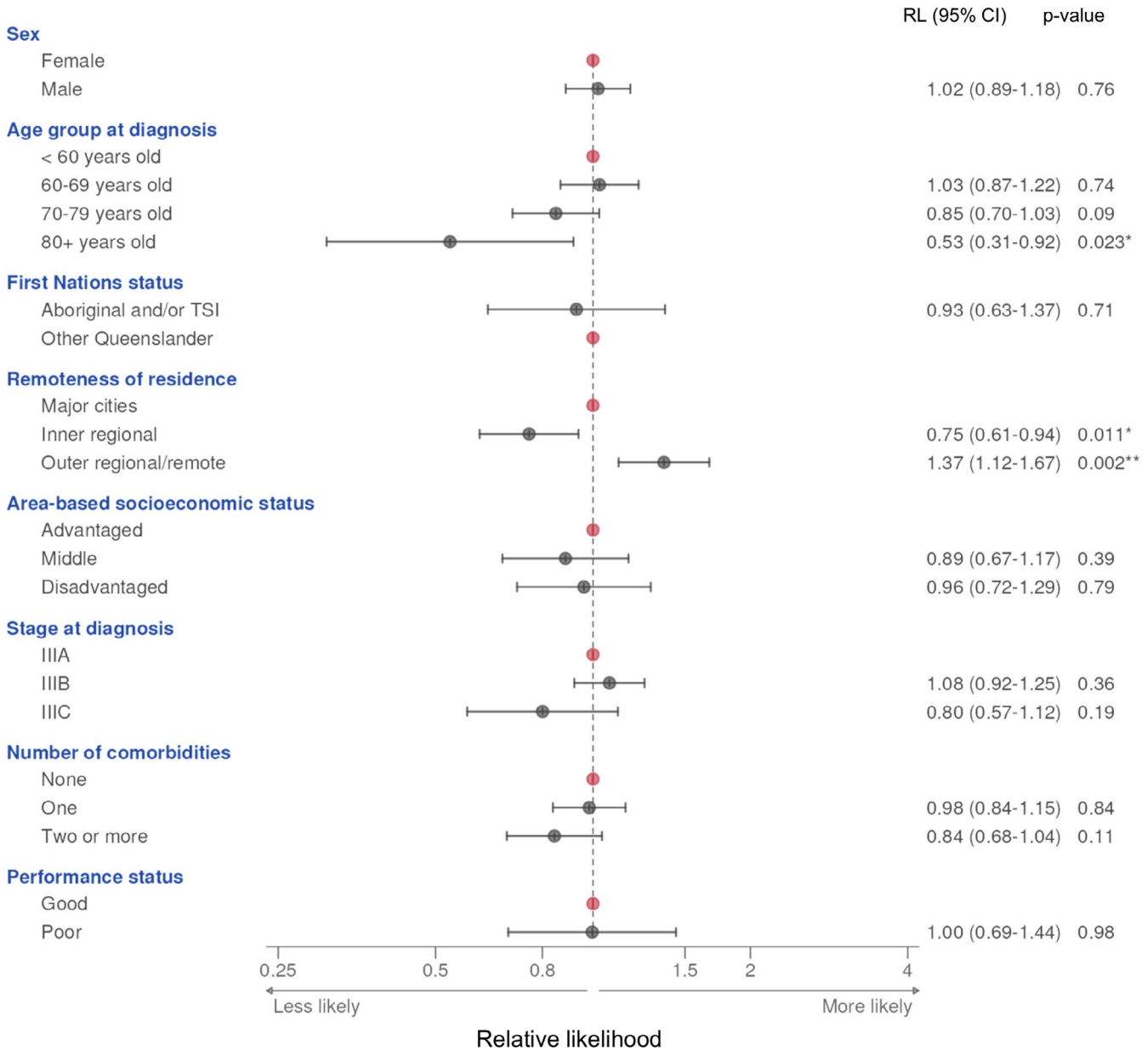

FIGURE 3 | Relative likelihood of receiving durvalumab for stage III NSCLC following combination chemotherapy/radiotherapy by selected patient and clinical characteristics, Queensland, 2018–2022. *Source*: Red dots signify reference category. Excludes patients who had surgery or those who died within 120 days of commencement of concurrent chemoradiotherapy.

durvalumab (RL = 1.00 compared to good performance status, 95% CI 0.69–1.44; $p = 0.98$).

3.5 | Survival

The median follow-up time for all patients in the study was 37 months (interquartile range 22–57 months), including a median of 52 months (interquartile range 37–66 months) for those who had their follow-up censored. There were 2053 deaths from any cause (45% of the study cohort) recorded during the study period. Overall five-year observed survival for the study cohort was estimated to be 52% (95% CI 50%–54%), ranging from 17% (95% CI 11%–25%) for stage IIIC to 81% (95% CI 74%–87%) for stage IA1 (Figure 4).

Following multivariable adjustment, the type of treatment was seen to impact survival across all stage categories, except for patients with stage III disease who had surgery (see Supplementary Tables 4a–4d). Surgery by itself or in combination with either chemotherapy or radiotherapy alone was associated with better outcomes compared to most other treatment modalities for stage I and II disease. For example, patients who received radiotherapy alone were significantly more likely to die within 5 years of diagnosis compared to treatment with surgery only for both stage I (HR = 3.41, 95% CI 2.70–4.32; $p < 0.001$) and stage II (HR = 4.12, 95% CI 2.88–5.90; $p < 0.001$). For unresectable stage III NSCLC, there was a significant survival advantage for concurrent chemoradiotherapy compared to other treatment modalities, such as radiotherapy alone (HR = 2.59, 95% CI 2.14–3.14; $p < 0.001$).

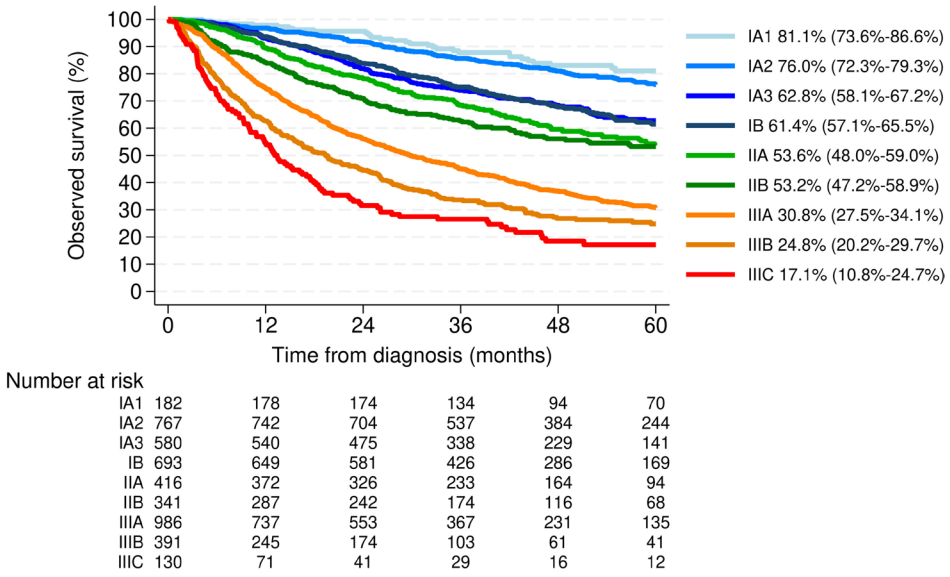

FIGURE 4 | Observed Kaplan–Meier survival curves by substage at diagnosis for early-stage NSCLC, Queensland, 2018–2022. *Source*: Follow-up for survival was available to 31 December 2024. Excludes patients with unknown substage.

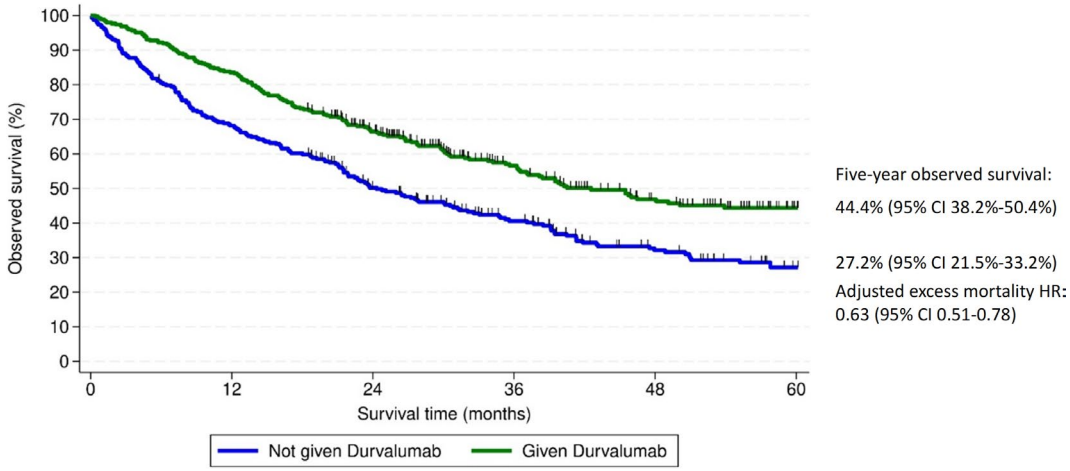

FIGURE 5 | Kaplan–Meier curves for observed survival for stage III NSCLC patients who had concurrent chemoradiotherapy by whether they received durvalumab, Queensland, 2018–2022. *Source*: Survival time was calculated from 120 days after concurrent chemoradiotherapy commenced. Follow-up for survival was available to 31 December 2024. Excludes patients who had surgery or those who died within 120 days of commencement of concurrent chemoradiotherapy.

Among patients with unresectable stage III NSCLC who had concurrent chemoradiotherapy and who survived for at least 120 days from their date of diagnosis, subsequent treatment with durvalumab resulted in a clear survival advantage. Three-year observed survival including all causes of death was estimated to be 57% (95% CI 51%–62%) for those who received durvalumab compared to 41% (95% CI 35%–46%) for those who did not, with corresponding five-year observed survival of 44% (95% CI 38%–50%) and 27% (95% CI 21%–33%), respectively ($p < 0.001$) – see Figure 5. Multivariable analysis on this subset of patients estimated that those who were treated with durvalumab were 37% less likely to die from NSCLC within 5 years of diagnosis relative to not receiving durvalumab (adjusted excess HR = 0.63, 95% CI 0.51–0.78; $p < 0.001$), as shown in Supplementary Table 5. The five-year survival differential for durvalumab was evident in both the 65–74 (HR = 0.55, 95% CI 0.38–0.77; $p < 0.001$) and over 75 years age groups (HR = 0.62, 95% CI 0.39–0.99; $p = 0.05$) but was not statistically significant for those aged under 65 (HR = 0.77, 95% CI 0.55–1.08; $p = 0.13$) – data not shown.

4 | Discussion

Our results provide contemporary information on patterns of care and outcomes for early-stage NSCLC at the population level, focused around the time immunotherapy targeting stage III disease became available. Some of the main findings from the current study include that: the type of treatment was a major prognostic factor even after accounting for substage at diagnosis; durvalumab dramatically improved survival among those with unresectable stage III NSCLC who received concurrent chemoradiotherapy; First Nations people were less likely to

receive certain treatments; and age group and remoteness of residence were influential in determining whether a person received durvalumab.

Our data reflect that surgical resection continued to be the mainstay of treatment for stages I and II NSCLC over the study period (i.e., diagnosis years 2018–2022). Almost two-thirds (64%) of the current cohort had surgery for stage I disease, slightly down compared to 68% in Queensland between 2011 and 2017 [17], and similar to the percentage reported in Canada for the period 2007–2015 (63%) [26]. The results for Queensland and Canada were also in close agreement for patients who received radiotherapy only for stage I disease (24% vs. 22% [26], respectively). In contrast, only 48% of stage I patients in The Netherlands between 2008 and 2018 received surgery and 40% were treated with radiotherapy alone [27]. Fewer patients in Queensland did not receive any treatment for stage I NSCLC (5%) compared to either Canada or The Netherlands (both 9%) [26, 27].

Some changes in patterns of care were observed for patients with stage II NSCLC in Queensland over time. Use of surgery increased slightly from 52% to 59% and radiotherapy only rose from 14% to 18% from 2011 to 2017 [17] to 2018–2022. Meanwhile, the percentage of stage II patients who did not receive any treatment within a year of their diagnosis decreased from 10% [17] to 6%. Addition of adjuvant, neoadjuvant or peri-operative immunotherapy to surgery and chemotherapy has recently been shown to significantly improve event-free survival for stage II disease [10, 11, 14] and is likely to become the standard of care for suitable patients moving forward, but was not relevant to the current cohort.

Comparisons with Queensland data for 2011–2017 [17] also revealed that surgery-based treatment increased from 13% to 18% between 2018 and 2022 for stage III NSCLC. Concurrent chemoradiotherapy continues as the definitive treatment for unresectable stage III disease [28, 29], rising from 38% [17] to 44% between the two study periods. The major development in the treatment for unresectable stage III NSCLC over the last decade has been the widespread introduction of consolidation immunotherapy with durvalumab following concurrent chemoradiotherapy. Use of durvalumab in Queensland varied across the study period, with a free medical access program in place from October 2017 to February 2019, followed by a free commercial access program, after which durvalumab was listed in the Pharmaceutical Benefits Scheme in March 2020. Consequently, the percentage of potentially eligible patients in our study who received durvalumab increased over time to around two-thirds during 2022. Ronden and colleagues [30] reported comparable population-level uptake of adjuvant durvalumab in The Netherlands from 2018 to 2019 (57% compared to an average of 53% in Queensland between 2018 and 2022), albeit in a smaller cohort. Although this uptake of durvalumab in Queensland may appear to be less than ideal, it must be remembered that the result reflects the real-world situation where not all patients with unresectable stage III NSCLC respond to concurrent chemoradiotherapy; consequently, the population-level denominator we used includes patients with both progressive and non-progressive disease rather than non-progressive disease only, as occurs in the corresponding clinical trial data [15]. We were limited by the fact that we cannot accurately identify those who are not progressing using the available data. Future integration and evaluation of restaging scan reports with artificial intelligence natural language processing will hopefully overcome this issue.

There was no difference in the likelihood of receiving durvalumab between patients with good and poor baseline performance status in our study cohort. Poor performance status at baseline due to disease can improve after concurrent chemoradiotherapy, thus allowing the future commencement of immunotherapy. We also note that a small number of patients in the study cohort diagnosed with stage I or II NSCLC received durvalumab. A probable explanation is that some of these patients may have had subsequent nodal recurrence (similar to clinical stage III) or developed new locally advanced malignancies (without updated staging being recorded) and were then treated with concurrent chemoradiotherapy and immunotherapy.

Five-year observed survival in our study cohort for patients with stage III NSCLC who received durvalumab (44%) aligned closely with the 43% reported survival from the PACIFIC trial [31]. Patients who did not receive durvalumab in Queensland appeared to slightly underperform compared to the control arm in the PACIFIC study (observed survival of 27% compared to 33%, respectively) [31], most likely because the present study included those with progressive disease following concurrent chemoradiotherapy. Our results for three-year observed survival for patients who had durvalumab were also somewhat lower than recently published data from the PACIFIC-R study [32] which involved over 1100 participants from 10 countries who were diagnosed with unresectable stage III NSCLC and were treated with durvalumab between September 2017 and December 2018 (57% compared to 63%, respectively); this difference may be due, at least in part, to the longer median follow-up time for the Queensland cohort (52 vs. 39 months among censored patients).

Lung cancer is the most commonly diagnosed and leading cause of cancer-related death in First Nations Australians [33]. Furthermore, Aboriginal and Torres Strait Islander people are estimated to be 70% more likely to be diagnosed with lung cancer compared to other Australians [34], and a report by the Australian Institute of Health and Welfare on Indigenous cancer demonstrated poorer five-year relative survival rates from lung cancer of 11% compared to 16% for non-Indigenous Australians [35]. Previous studies in Australia have shown that Aboriginal and Torres Strait Islander people with lung cancer were significantly less likely to receive standard treatment, even after adjustment for covariates such as stage, age and comorbidities [36, 37]. The current results indicate that disparities in the management of NSCLC remain, with Aboriginal and Torres Strait Islander people around 5% less likely than other Queenslanders to be treated with surgery or chemotherapy after accounting for other demographic and clinical factors. Given the existing survival gap between First Nations and non-Indigenous Australians, urgent collaborative efforts from all stakeholders are required to fundamentally change the cancer ecosystem to address this inequity. It is anticipated that the Australian Cancer Plan [38] may provide a framework for the many system-wide and cultural changes that are needed.

Our finding that patients aged over 80 were less likely to receive durvalumab compared to those under 60 is possibly due to physical suitability related to frailty, and the need to undergo therapy for a further year. Although other studies [39, 40] have shown short-term survival following treatment with durvalumab is similar for patients over and under 70 years old, older patients are more prone to adverse events or deterioration from comorbidities. Causes for the difference in treatment with durvalumab by remoteness of residence are less clear and require further consideration.

Our study benefitted from the use of a comprehensive set of linked, population-based cancer information. Nonetheless, some limitations of our study data should be taken into consideration when interpreting the results. Details of patients' PD-L1 expression and mutational status that may be used to inform treatment decisions and interpret outcomes were not collected. Changes in patterns of care over time in Queensland need to be interpreted with due caution after moving from the 7th to the 8th edition of the TNM staging system for the current cohort. Measures such as stage and performance status are recorded at diagnosis/baseline, and may alter over the ensuing months, thus altering the likelihood of a person receiving a particular type of treatment (such as durvalumab). The first date of durvalumab treatment was not recorded in the Queensland Oncology Repository; instead, 4 months after commencement of concurrent chemoradiotherapy was used as the proxy start date for the durvalumab survival analysis. As mentioned above, in order for our results to be more directly comparable to the PACIFIC study we would need to have information on whether patients had a 'positive response or lack of progression' after chemoradiotherapy to then be eligible for durvalumab, which was not available. The PACIFIC trial also mandated patients to start durvalumab within 42 days of completion of chemoradiotherapy, whereas patients in our cohort may have started durvalumab at any time after chemoradiotherapy. Information on the number of cycles of durvalumab or duration of treatment was unavailable in the Queensland Oncology Repository.

In conclusion, the treatment landscape for early-stage NSCLC has evolved significantly in recent years. Most notably, the introduction of immunotherapy now offers new hope for patients, particularly those with unresectable tumors. These advances have not only improved survival rates but also expanded the range of treatment options, enabling a more personalized and effective approach to managing this complex disease.

Author Contributions

Conceptualization: Bryan Chan; Data curation: Tracey Guan; Formal analysis: Danny Youlden; Funding acquisition: Bryan Chan and Danica Cossio; Methodology: Danny Youlden; Project administration: Tracey Guan; Supervision: Bryan Chan, Danica Cossio and Jasotha Sanmugarajah; Writing (original draft): Danny Youlden and Bryan Chan; Writing (review and editing): Andrew Pattison, Tracey Guan, Danica Cossio and Jasotha Sanmugarajah.

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Conflicts of Interest

Bryan A. Chan declares the following financial interests/personal relationships which may be considered as potential conflicts of interest: AstraZeneca (consulting or advisory relationship), Daiichi Sankyo (consulting or advisory relationship), Merck Sharp and Dohme (consulting or advisory relationship), Roche (consulting or advisory relationship). Andrew Pattison declares the following financial interests/personal relationships which may be considered as potential conflicts of interest: AstraZeneca (payment for educational presentations). The other authors declare no conflicts of interest that could have appeared to influence the work reported in this paper.

Data Availability Statement

The unit record data used in this study are not publicly available to protect patient privacy and confidentiality. Deidentified data may be available from the corresponding author on reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Supplementary Figure 1** Flow diagram for selection of the study cohort for early-stage NSCLC, Queensland, 2018–2022. Percentages shown are of all NSCLC patients (all stages) diagnosed between 2018 and 2022. **Supplementary Figure 2** Relative likelihood of receiving different types of treatment within 1 year of diagnosis for NSCLC, Queensland, 2018–2022. Red dots signify reference category. **Supplementary Figure 3** Treatment with durvalumab following concurrent chemoradiotherapy for stage III NSCLC by year of diagnosis, Queensland, 2018–2022. Excludes patients who had surgery or those who died within 120 days of commencement of concurrent chemoradiotherapy. Information on whether the person responded to concurrent chemoradiotherapy is not available, and so the denominator will include patients with both progressive and non-progressive disease. Durvalumab was listed in the Australian Pharmaceutical Benefits Scheme in March 2020. **Supplementary Table 1** Incidence counts for morphological subtypes of NSCLC, Queensland, 2018–2022. **Supplementary Table 2** Definitions of demographic and clinical characteristics of interest. **Supplementary Table 3** Treatment details within 1 year of diagnosis by stage at diagnosis for early-stage NSCLC, Queensland, 2018–2022. **Supplementary Table 4a** Results of multivariable flexible parametric survival model for patients with stage I NSCLC, Queensland, 2018-2022[a]. **Supplementary Table 4b** Results of multivariable flexible parametric survival model for patients with

stage II NSCLC, Queensland, 2018-2022[a]. **Supplementary Table 4c** Results of multivariable flexible parametric survival model for patients with stage III NSCLC who had surgery, Queensland, 2018-2022[a]. **Supplementary Table 4d** Results of multivariable flexible parametric survival model for patients with stage III NSCLC who did not have surgery, Queensland, 2018-2022[a]. **Supplementary Table 5** Results of multivariable flexible parametric survival model for patients with stage III NSCLC who had concurrent chemoradiotherapy, Queensland, 2018-2022[a].