

(i) Title

Opioids in advanced lung malignancy: A clinical audit of opioid prescription, patient education and safeguarding

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The authors declare no other affiliations or conflicts of interest. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors would like to thank Prof Ben Solomon and Dr Alexander for approval and extraction of data for patients enrolled in AURORA (AUstralian Registry and biObank of thoRAcic cancers) at Peter MacCallum Cancer Centre for use in this research.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the [Version of Record](#). Please cite this article as doi: [10.1111/imj.15354](https://doi.org/10.1111/imj.15354)

ABSTRACT

Background: Opioids have an important role in symptom management for people with advanced cancer. Clinical guidelines recommend patient education to ensure the safe use of opioids, however, no Australian studies have explored current education and safeguarding practices when opioids are initiated to advanced cancer patients.

Aims: To investigate risk assessment, safeguarding and education practices when opioids are first prescribed to advanced lung cancer patients

Methods: A retrospective medical record audit of outpatients with advanced non-small cell lung cancer seen at a tertiary Australian hospital between 1/1/2015 - 31/12/2019 and prescribed strong opioids for cancer-related symptoms.

Results: Of 1022 patients attending the lung cancer clinic, 205 were newly initiated on an opioid. Opioid-related risks including previous recreational drug use (28, 13.6%) and history of falls (16, 7.9%) were infrequently documented. Opioid-related safeguards and adverse effects management were variably instituted: written GP correspondence at opioid initiation (62, 30%), clinic follow-up (186, 91%) and laxative co-prescription (55, 26.8%). Most patients (137, 66.8%) received no documented opioid education on drug initiation. There was no association between age ($P=0.653$), number of comorbidities ($P=0.569$) or chronic alcohol use ($P=0.263$) and the provision of education on opioid initiation. Palliative care doctors or nurse practitioners were eight times more likely to document opioid education than medical oncologists (OR= 8.5, CI= 2.9-24.8, $P<0.0001$).

Conclusion: Guideline-recommended risk assessment, safeguards, and patient education were infrequently documented when opioids were initiated. Clinician training, decision assist prompts in electronic prescribing software and written education resources for patients may address these gaps in care.

Keywords: Opioid, Lung Neoplasms, Patient Education as Topic, Palliative Care

INTRODUCTION

Debilitating symptoms associated with advanced lung cancer are common. Pain is experienced by 66-78%,^{1,2} cough by 57%³ and breathlessness by 50%–87% of patients.⁴ Strong opioids are the mainstay of treatment for moderate to severe cancer-related pain.⁵ There is also some evidence to support the use of opioids to treat cough and breathlessness in people with lung cancer.⁶⁻⁸

Opioids are classified as Schedule 8 medications in Australia due to their potential to cause harm when used inappropriately.⁹ These medications are subject to strict prescribing regulations and are associated with side effects and risks that must be considered and discussed with patients on initiation. Predictable, common side effects such as constipation, nausea and drowsiness can be effectively managed with patient education and regular laxatives or anti-emetics.¹⁰ However, if patient education is not provided, side effects and other opioid-related concerns can limit the acceptance and effective use of opioids in people with cancer.¹¹

To ensure the safe and appropriate use of opioids, the *'Palliative care for adults: strong opioids for pain relief'* guideline by the UK National Institute for Health and Care Excellence (NICE)¹² and the *'Cancer pain management in adults'* guideline by Cancer Council Australia¹³ recommend that clinicians provide verbal and written information regarding the appropriate use of opioids, their side effects, the signs of toxicity, and safe storage. They also recommend risk assessment and education about patient concerns such as addiction.^{12,13} To

date, there are no Australian studies and limited international literature that have explored whether these recommendations are followed in clinical practice when initiating opioids in people with advanced cancer. This study of outpatients with advanced non-small cell lung cancer (NSCLC) aimed to understand:

- 1) The prevalence of new opioid prescription for pain, breathlessness and/or cough
- 2) Whether clinicians evaluated and documented individual patient risks for adverse outcomes when opioids were first prescribed
- 3) Whether guideline-recommended opioid education and safeguards were provided when opioids were first prescribed
- 4) Whether clinical practice regarding opioid education and safeguards varies by prescriber specialty

METHODS

Study Design and Setting

A retrospective medical record review of patients attending the lung tumour clinic at the Peter MacCallum Cancer Centre (PMCC) in Melbourne between 1 January 2015 and 31 December 2019 was performed. This multidisciplinary clinic provides long-term cancer care from thoracic surgeons, radiation and medical oncologists, palliative care clinicians and specialist nurses. Ethics approval was granted for the study from the Peter MacCallum Cancer Centre Human Research Ethics Committee (reference no. LNR/58322/PMCC-2019).

Study Population

Medical records were included if patients had a diagnosis of stage III or IV NSCLC and were newly initiated on strong opioids for cancer-related pain, breathlessness or cough. We chose this population due to their high symptom burden and therefore likelihood of opioid

prescription. Records of patients who were started on an opioid in the community for symptom crisis management and received rapid follow-up in the lung clinic were also included. The medical records of patients with other co-existing malignancies, those taking an opioid for a non-cancer indication, and those initiated on an opioid prior to the study period (chronic long-term use) or in the inpatient setting (where opioid education could not be easily assessed) were excluded.

Data Collection

Data were extracted from the Australian Registry and biobank of thoracic cancers (AURORA) and the electronic medical record (EMR). Patient demographics, comorbidities, cancer type and stage, and risks factors for an opioid-related adverse outcome (including previous drug use, history of falls, and renal or liver function impairment) were recorded. The opioid(s) prescribed, dose, route, indication, prescriber speciality and data on laxative prescription were collected from clinic visits. Records were examined for documentation of opioid education provided to patients on opioid initiation and during follow up. This included education regarding the correct use of opioids, their side effects, signs of opioid toxicity, safe storage, and addiction. The institution of the following safeguards at opioid initiation was also recorded: correspondence with the patient's general practitioner (GP) regarding opioid initiation, and a follow-up appointment.

Data Analysis

Data were analysed using SPSS Statistics version 26 and are presented descriptively. The Chi square test was used to compare categorical variables and Student's t test was used to compare continuous numerical variables, with logistic regression used to explore any positive associations.

RESULTS

Patients' characteristics

One thousand and twenty-two patients' medical records were screened, with 205 medical records included (Figure 1). The mean age of patients was 66 years (SD=10.7) and 52% were male (Table 1). The majority of patients had stage IV NSCLC (157; 77%) and a mean of 2.8 comorbidities (SD=2.2) and 3.2 medications (SD=2.9).

Patients with stage IV NSCLC were almost twice as likely to be initiated on an opioid compared to those with stage III NSCLC (OR=1.7, CI=1.1-2.5, $P=0.012$). Patients initiated on an opioid were almost four times more likely to have died during follow up than patients who were not initiated on an opioid (OR= 3.7, CI= 2.5-5.4; $P<0.0001$). There was no association between opioid initiation and age, gender, number of comorbidities, living arrangements, ethnicity or history of alcohol use.

Opioid characteristics

Opioids were most likely to be initiated for pain (79.0%) (Table 2). Opioid indication, route and the specific drug prescribed changed significantly over time ($P<0.0001$). There were increases in both extended release opioid ($P<0.0001$) and immediate release opioid ($P<0.0001$) dosing requirements over time. The clinical specialty of the opioid prescriber was: medical oncology (108, 52.7%), radiation oncology (47, 22.9%), hospital palliative care (doctors or nurse practitioners) (19, 9.3%), cardiothoracic surgery (2, 1.0%), community palliative care (2, 1.0%) and other specialties (GP, Respiratory Physician etc.) (27, 13.2%). After opioid initiation, the median number of lung cancer clinic follow-up appointments where the patient remained on an opioid was 8 (IQR= 4-16).

Opioid-related risk assessment, safeguards and education

When initiating an opioid, history of previous recreational drug use or falls was documented in 28 (13.6%) and 16 (7.9%) patients respectively (Table 3). Written correspondence with the GP with information about opioid initiation occurred in 62 patients (30.2%). Medical oncologists were almost three times more likely to write to the GP regarding opioid initiation than a palliative care doctor or nurse practitioner (OR=2.9, CI=1.1-7.8, $P=0.038$). A follow-up appointment was provided to the majority of patients (186; 90.7%).

Education about opioids at the time they were initiated was infrequently documented by clinicians (Figure 2). One hundred and thirty-seven patients (66.8%) had no documented education on opioid initiation and 77 patients (38%) had no documented education at subsequent appointments. Palliative care doctors or nurse practitioners were eight times more likely to document opioid education than medical oncologists (OR=8.5, CI=2.9-24.8, $P<0.0001$). There was no association between the provision of opioid education and patient age, number of comorbidities, and history of chronic alcohol use. Men were almost four times more likely to receive education about opioid side effects on opioid initiation compared to women (OR=3.8, CI=1.4-10.9, $P=0.011$).

DISCUSSION

This is the first Australian study to explore whether education and safeguards are provided and documented when strong opioids are initiated to manage symptoms associated with advanced lung cancer. Although opioids were commonly prescribed, and many patients were at increased risk for adverse events (due to being older, living alone, having multiple comorbidities, and using multiple medications), there was infrequent documentation of an

opioid risk assessment or patient education. Moreover, many patients did not have any opioid education documented at subsequent clinic visits despite significant changes in opioid indication, route, drug type and dose. The provision of opioid education and safeguarding differed by clinical specialty; palliative care doctors or nurse practitioners were more likely to provide opioid education than medical oncologists but less likely to write to the GP on opioid initiation. This study highlights gaps in current practice that need to be addressed to ensure the safe and appropriate use of opioids amongst advanced cancer patients. This is especially crucial in the context of growing concerns about opioid-related harm in Australia and the “*opioid epidemic*” in the United States.¹⁴ Clinicians have a responsibility to provide patient-focused education with documentation of individualised opioid-related risk assessment, education and safeguards (figure 3).

Nevertheless, we need better understanding of the barriers to provision and documentation of opioid education and safeguards to outpatients. Previous studies have found that education and counselling tend to be under-reported in the medical record when compared to other domains of medical care,¹⁵ and perhaps clinician attitudes towards documentation of this information are a relevant factor. While these issues may be discussed during patient consultations, many clinicians may not consider the importance of recording these discussions.¹⁶ Lack of familiarity with the recommendations for education in current guidelines may also play a role in this gap in patient-centred care.¹⁷ To overcome these barriers, some clinicians may benefit from focused training on common opioid-related adverse effects and potential harms, with particular focus on what constitutes effective patient education, safeguarding and documentation practices.

However, lack of time and a heavy workload are frequently cited factors affecting patient education and documentation practices.^{17,18} Emerging studies have demonstrated creative methods of education that do not increase clinician burden or disrupt workflow in the ambulatory setting. These include the use of an educational animation video and a brief web-based intervention which have improved opioid-related knowledge and practices. Novel modes of education delivery are a promising area for further research and may allow patients to access important education in their own time.^{19,20} Technology is ubiquitous in clinical practice, and the use of standardised forms, clinician-assist prompts, and documentation templates in the EMR could play a useful role in improving the provision and documentation of guideline-recommended education and safeguards when prescribing opioids in a busy clinic environment.^{16,17} Nevertheless, we must be cautious to remain patient focused and avoid over-reliance on standardised protocols.

A multidisciplinary approach to opioid education may prove effective, although the evidence for this is conflicting. For instance, structured nurse-led education interventions have successfully improved cancer pain management in ambulatory settings.²¹ Pharmacists may also assist in providing medication-specific education; however, they may lack access to the patient's medical record thereby limiting continuity of care and individualised education. Notably, opioid prescriptions prescribed in the outpatient setting may not be filled in hospital pharmacies. According to the literature, rates of medication counselling in community pharmacies vary from 8 to 100%²² and numerous factors including busyness and lack of privacy have been shown to influence whether medication counselling is provided to patients in this setting.²³ Furthermore, while nurses and pharmacists are often responsible for providing education on discharge medication in the inpatient setting, a recent study has

shown patients newly prescribed opioids in hospital received minimal opioid counselling on discharge according to patient and pharmacy records.²⁴ Thus, if the responsibility to provide opioid education is shifted from the prescriber to another healthcare professional, there is a significant risk that it will not be provided.

Ultimately, the legal and clinical responsibility for providing personalised medication education falls on the prescriber,²⁵ so any education provided by another professional should only serve to supplement prescriber education. Simple, standardised written opioid education resources that are customisable may be a low-cost way to reinforce verbal opioid education to patients by clinicians.²⁶ Other health care professionals, including nurses or pharmacists, can then use this resource to deliver supplementary education that is consistent with information provided by the prescriber.

When initiating opioid therapy, medical oncologists were more likely to safeguard patients via written correspondence with the patient's GP. However, medical oncologists were less likely to provide opioid specific education compared to palliative care clinicians. A similar difference in education provision was reported in a set of studies where oncologists were less likely to institute routine patient education about pain management than palliative care physicians.^{27,28} One explanation for our findings may be that palliative care specialists have more specialised training in symptom management and are more likely to undertake a primary role in opioid titration and monitoring.²⁹ They also may have more time during appointments to dedicate to opioid-related education. Medical oncologists must dedicate the majority of appointment time to cancer management.²⁹ We note that the increased rate of GP correspondence by medical oncologists may relate to the longer time interval of follow up for

each patient, whereas palliative care teams see individual patients more frequently. Palliative care clinicians are also more likely to liaise with community palliative care teams to oversee patients on opioids in the community rather than the GP, although this data was not collected in our study.

Notably, a number of studies over the last decade have put a spotlight on the differences in content of oncology and palliative care consultations, and the benefits of early integration of palliative care into the routine management of advanced cancer patients have been demonstrated repeatedly.³⁰⁻³² Our findings suggest that the increased provision of patient education by palliative care clinicians may play a role in explaining some improvements in patient outcomes and should be investigated in future studies.

This study has some limitations. The findings from this single-centre audit may not be generalizable to wider clinical practice at other health services. This retrospective study is also limited by its reliance on accurate documentation by medical practitioners in the patient's medical record to understand current practice. ECOG (Eastern Cooperative Group) performance status was rarely documented at opioid initiation and thus could not be included in this study.

Future studies should gather qualitative data to better understand current practices at opioid initiation, and clinician barriers to the provision and documentation of guideline-recommended risk assessment, patient education and safeguards. Health care organisations should encourage and support the training of clinicians to improve opioid specific knowledge and clinical practice. Future quality improvement projects should consider optimal strategies

for efficient and effective verbal opioid education in the outpatient setting and development of customisable written education that can support patient understanding of their medications.

CONCLUSION

Opioids were commonly initiated for pain and towards the end of life in advanced lung cancer outpatients. Despite guidelines and the ubiquity of opioid prescription in advanced cancer patients, this study highlights the current gaps in the provision and documentation of patient education and safeguarding when opioids are prescribed. Opportunities to enhance clinical practice include focussed clinician training, a multidisciplinary approach to the provision of individualised opioid education and safeguards to patients and caregivers, and the development of standardised written documentation templates and education materials to supplement verbal opioid education.

DISCLOSURES AND ACKNOWLEDGMENTS

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors declare no conflicts of interest. The authors would like to thank Prof Ben Solomon and Dr Alexander for approval and extraction of data for patients enrolled in AURORA (**AU**stralian **R**egistry and **biO**bank of **thoRA**cic cancers) at Peter MacCallum Cancer Centre for use in this research.

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FIGURE LEGENDS

Figure 1. Study flow diagram

NSCLC, non-small cell lung cancer

Figure 2. Opioid-related patient education provided on initiation

†Education about the use of extended-release opioid was not applicable in 100 patients in whom it was not prescribed. Education about the use of an immediate-release opioid was not applicable in 18 patients in whom it was not prescribed.

‡Education data could not be accessed for the following clinician specialties: General Practitioners, Community Palliative Care, Respiratory Physicians.

Figure 3. Practice points when prescribing opioids for cancer-related symptoms

Adapted from 'Recommendations for communication and self-management' from 'Cancer Pain Management in Adults' guideline by Cancer Council Australia¹³

TABLES

Table 1. Patients' characteristics

Variable	Opioid initiated (n=205§)	No opioid initiated (n=366)	P-value
Age†	66.1 ± 10.7	67.9 ± 11.4	0.188
Gender			0.147
Male	107 (52.2%)	214 (58.5%)	
Diagnosis			0.031
NSCLC stage III	47 (22.9%)	120 (32.8%)	
NSCLC stage IV	157 (76.6%)	242 (66.1%)	
Mixed cancer type ¶	1 (0.5%)	4 (1.1%)	
Living arrangement§			0.644
Alone	44 (21.5%)	71 (19.4%)	
With adult carer	121 (59.0%)	228 (62.3%)	
With adult non-carer	13 (6.3%)	18 (4.9%)	
With children only	26 (12.7%)	37 (10.1%)	
Comorbidities			
Cardiovascular	83 (40.5%)	146 (39.9%)	0.889
Respiratory	62 (30.2%)	115 (31.4%)	0.771
Diabetes mellitus	32 (15.6%)	52 (14.2%)	0.650
Renal insufficiency	11 (5.4%)	11 (3.0%)	0.160
Number of comorbidities†	2.8 ± 2.2	3.0 ± 2.5	0.095
Number of medications†	3.2 ± 2.9	3.2 ± 3.0	0.820
Smoking history§			0.573

Never smoked	53 (25.9%)	104 (28.4%)	
Ex-smoker	116 (56.6%)	208 (56.8%)	
Current smoker	36 (17.6%)	53 (14.5%)	
Pack years ‡	41.5 (23.25-54)	40.0 (20.0-60.0)	0.127
History of chronic alcohol use	25 (12.2%)	29 (7.9%)	0.094
Ethnicity			0.150
White/Caucasian	171 (83.4%)	280 (76.5%)	
Asian	29 (14.1%)	74 (20.2%)	
Other	5(2.5%)	12 (3.3%)	
Patient Status §			0.0001*
Alive	49 (23.9%)	195 (53.3%)	
Deceased	155 (75.6%)	166 (45.4%)	

Data reported as counts with frequencies, means† with standard deviation, or medians‡ with IQR.

§ Living Status was not documented in one patient who was initiated on an opioid and twelve patients who were not. Smoking status was not documented in one patient who was not initiated on an opioid. Patient Status includes one patient who was initiated on an opioid and five patients who were not that were lost to follow-up or discharged.

¶Mixed cancer type included patients with mixed histology of advanced NSCLC with SCLC or mesothelioma.

Table 2. Opioid characteristics

Variable	At initiation of opioid	At most recent clinic visit while on opioid	P-value
Opioid indication	n=205	n=170‡	<0.0001*
Pain	162 (79.0%)	143 (84.1%)	
Dyspnoea	8 (4.0%)	7 (4.1%)	
Cough	12 (6.0%)	3 (1.8%)	
Pain and cough	9 (4.4%)	5 (2.9%)	
Pain and dyspnoea	5 (2.4%)	8 (4.7%)	
Cough and dyspnoea	7 (3.4%)	3 (1.8%)	
Pain and dyspnoea and cough	2 (1.0%)	1 (0.6%)	
Opioid route	n=205	n=169‡	<0.0001*
Oral	197 (96.1%)	149 (88.2%)	
Continuous subcutaneous infusion	0 (0.0%)	2 (1.2%)	
Transdermal	8 (3.9%)	18 (10.7%)	
Extended-release opioid	n=105‡	n=151‡	<0.0001*
Morphine	21 (20.0%)	52 (34.4%)	
Oxycodone	75 (71.4%)	72 (47.7%)	
Hydromorphone	1 (1.0%)	7 (4.6%)	
Fentanyl	5 (4.8%)	15 (9.9%)	
Buprenorphine	3 (2.9%)	4 (2.6%)	
Methadone	0 (0.0%)	1 (0.7%)	
Extended-release OME daily dose (mg)†	n=105‡	n=151‡	<0.0001*

	15 (15.0-30.0)	45 (30.0-80.0)	
Immediate-release opioid	n=187‡	n=157‡	<0.0001*
Morphine	72 (38.5%)	71 (45.2%)	
Oxycodone	114 (61.0%)	78 (49.7%)	
Hydromorphone	1 (0.5%)	7 (4.5%)	
Buprenorphine	0 (0.0%)	1 (0.6%)	
Immediate-release OME single dose (mg)†	n=187‡	n=156‡	<0.0001*
	7.50 (5.0-7.5)	7.5 (5.0-10.0)	

Data reported as counts with frequencies or medians† with IQR

‡Indication for the most recent opioid was unknown in thirty-five patients. Route for the most recent opioid was unknown in thirty-six patients. Initial extended-release opioid type and dose was not applicable in one hundred patients (not prescribed). Most recent extended-release opioid type and dose was not applicable in fifty-four patients (no extended-release opioid prescribed, or type and dose data unavailable). Initial immediate-release opioid dose and opioid type was not applicable in eighteen patients (not prescribed). Most recent immediate-release opioid dose was not applicable in forty-nine patients (not prescribed or dose data unavailable). Most recent immediate-release opioid type was not applicable in forty-eight patients (not prescribed or type unavailable).

*Statistically significant ($P < 0.05$)

OME, Oral Morphine Equivalent

Table 3. Documentation of opioid-related risks and safeguards

Variable	Result (n=205†)
History of previous drug use	
Yes	6 (2.9%)
No	22 (10.7%)
Not documented	177 (86.3%)
History of falls	
Yes	12 (5.9%)
No	4 (2.0%)
Not documented	189 (92.2%)
Biochemical results	
eGFR‡‡	90 (76.75-90)
Abnormal LFTs ‡	73 (50.3%)
Correspondence to GP on opioid initiation	
No	115 (56.1%)
Yes	62 (30.2%)
Unknown, opioid started by external specialty§	28 (13.7%)
Follow-up	
Follow up appointment	186 (90.7%)
Community palliative care	14 (6.8%)
GP	3 (1.5%)
Other	2 (1.0%)
Co-prescription of laxatives	
Yes	55 (26.8%)

No	120 (58.5%)
Unknown	30 (14.6%)

Data reported as counts with frequencies or medians with IQR†

‡eGFR data was unavailable for fifty-seven patients (n=148). LFT results were unavailable for sixty patients (n=145).

eGFR, estimated glomerular filtration rate; LFTs, Liver Function Tests; GP, General Practitioner

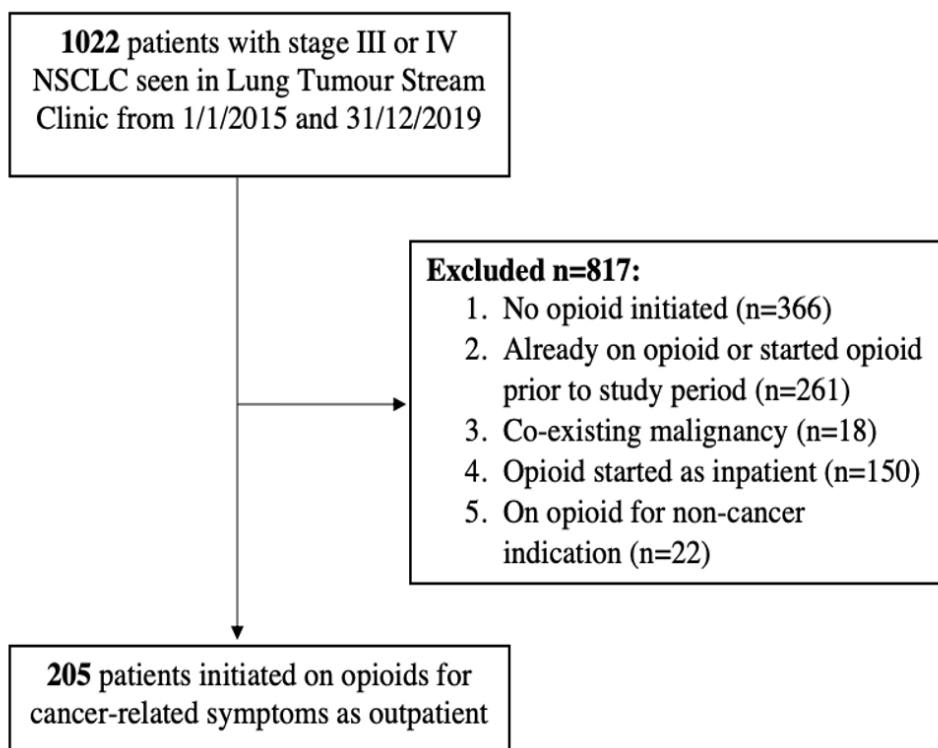


Figure 1. Study flow diagram
NSCLC, non-small cell lung cancer

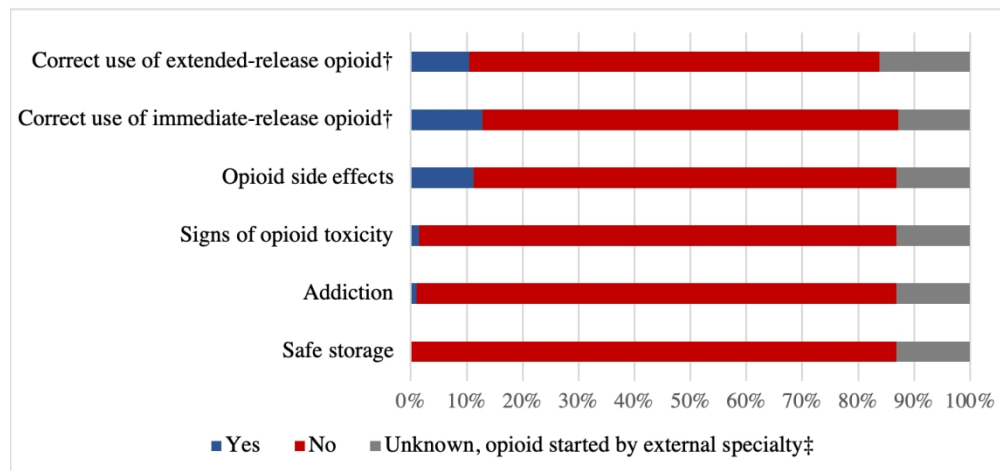


Figure 2. Opioid-related patient education provided on initiation

†Education about the use of extended-release opioid was not applicable in 100 patients in whom it was not prescribed. Education about the use of an immediate-release opioid was not applicable in 18 patients in whom it was not prescribed.

‡Education data could not be accessed for the following clinician specialties: GPs, Community Palliative Care, Respiratory Physicians.

1. Awareness of federal (PBS Criteria) and state-based (eg. SafeScript) opioid prescribing regulations
2. Actively screen and address patient risk factors for adverse events when prescribing opioids
3. Provide individualised, patient-focused verbal and written opioid education
 - Consider the use of patient education leaflets, documentation templates, checklists, and decision-assist prompts in the EMR
4. Adopt, where available, an interdisciplinary approach to opioid education and safeguarding
5. Maintain communication between primary and secondary health care providers
6. Consider early referral to Specialist Palliative Care

Figure 3. Practice points when prescribing opioids for cancer-related symptoms

Adapted from 'Recommendations for communication and self-management' from 'Cancer Pain Management in Adults' guideline by Cancer Council Australia¹³