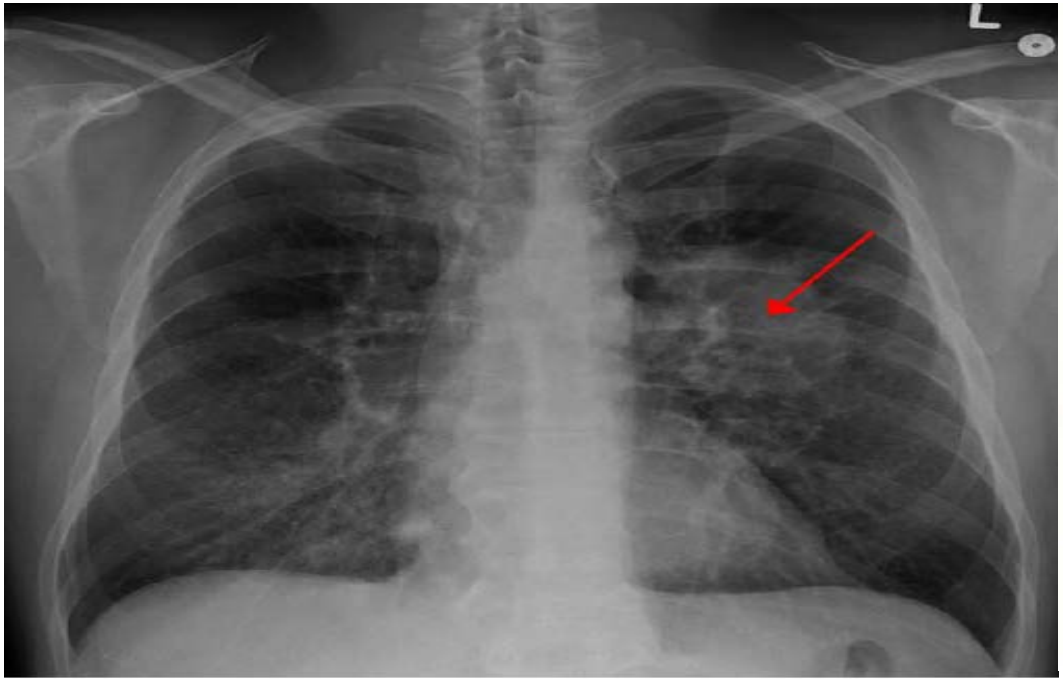
KCE REPORT 266S

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

QUALITY INDICATORS FOR THE MANAGEMENT OF LUNG CANCER – SUPPLEMENT

SUPPLEMENT — TECHNICAL FICHES FOR INDICATORS



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HEALTH SERVICES RESEARCH

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- **The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.**
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LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
2D	Two-dimensional
3D	Three-dimensional
95% CI	95% Confidence interval
ACE-27	Adult Comorbidity Evaluation-27
ALK	Anaplastic lymphoma kinase
ATC	Anatomical Therapeutical Chemical
AUC	Area under the curve
AZ	Algemeen ziekenhuis (general hospital)
BCR	Belgian Cancer Registry
cI, cII, etc	Clinical stage I, clinical stage II, etc.
CIRS	Cumulative illness rating scale
CT	Computed tomography
DDD	Defined daily dose
DICA-DLSA	Dutch Institute for Clinical Auditing – Dutch Lung Surgery Audit
DLCO	Diffusing capacity of the lung for carbon monoxide
EBUS	Endobronchial ultrasound
EGFR	Epidermal growth factor receptor
EORTC	European Organisation for Research and Treatment of Cancer
EPAAC	European Partnership Action Against Cancer
EUS	Endoscopic ultrasonography
FEV1	Forced expiratory volume in 1 second
FNA	Fine needle aspiration
GDG	Guideline development group
GRADE	Grades of Recommendation Assessment, Development and Evaluation

HIV/AIDS	Human immuno-deficiency virus / Acquired immune deficiency syndrome
HR	Hazard ratio
ICD-10-CM	International Classification of Diseases, 10th Revision, Clinical Modification
IGZ	Inspectie voor de Gezondheidszorg (The Netherlands)
IHC	Immunohistochemistry
IKNL	Integraal Kankercentrum Nederland
IMA – AIM	InterMutualistisch Agentschap – Agence Intermutualliste
IMRT	Intensity-modulated radiotherapy
INSZ – NISS	National Number for Social Security
K	Kappa statistic
KCE	Belgian Health Care Knowledge Centre
KSZ – BCSS	Kruispuntbank van de Sociale Zekerheid – Crossroads Bank for Social Security - Banque Carrefour de la Sécurité Sociale
maxSUV	Maximum standardized uptake value
MDT	Multidisciplinary team
MOC – COM	Pathological stage I, etc.
MRI	Magnetic resonance imaging
MZG – RHM	Minimale Ziekenhuisgegevens – Résumé Hospitalier Minimum
NA	Not applicable
NHS	National Health Service (United Kingdom)
NICE	National Institute for Health and Care Excellence (United Kingdom)
NOS	Not otherwise specified
NPV	Negative predictive value
NSCLC	Non small cell lung cancer
OR	Odds ratio

PET	Positron emission tomography
PFS	Progression free survical
PH	Proportional hazard
PPV	Positive predictive value
PS	Performance status
QI	Quality indicator
RIZIV – INAMI	Rijksinstituut voor ziekte-en invaliditeitsverzekering – Institut National d'Assurance Maladie Invalidité
ROC	Receiver Operating Characteristic
RT	Radiotherapy
SCLC	Small cell lung cancer
Se	Sensitivity
SIGN	Scottish Intercollegiate Guidelines Network
Soncos	Stichting Oncologische Samenwerking (The Netherlands)
Sp	Specificity
TBNA	Transbronchial needle aspiration
TKI	Tyrosine kinase inhibitor
TNM	Tumour – Node – Metastasis
UCL	Université catholique de Louvain
UK	United Kingdom
US(A)	United States (of America)
UZ	Universitair ziekenhuis (academic hospital)
VA	Alveolar volume
WHO	World Health Organization
X	Missing stage

SUPPLEMENT: TECHNICAL FICHES

1 SURVIVAL AFTER DIAGNOSIS OF LUNG CANCER

1.1 1-year observed and relative survival (S-1 and S-2)

1.1.1 Documentation sheet

Title	1-year survival after a diagnosis of lung cancer 1-year observed survival 1-year relative survival
Rationale	Treatment of lung cancer aims to prolong survival and improve quality of life. Observed survival reflects the proportion of patients still alive at a certain time point after the diagnostic of cancer, whether they died from a cancer-related cause or not. On the contrary, relative survival can be used as a measure of cancer survival, excluding the effect arising from different background mortalities. This is calculated as the ratio of the observed survival to the expected survival (=survival that would be expected if the cancer patients had the same age and sex specific mortality in each period as the general population). These two indicators are commonly accepted indicators of the effectiveness of a country's healthcare system to screen, early detect and treat patients with cancer. For the majority of cancers, a survival after a five-year time span after diagnosis is generally accepted as an indicator of cure. As lung cancer has one of the worst vital prognoses, one year time is also admitted as an indicator of effectiveness of care.
Type of QI	Outcome
Calculation	(A) The 1-year observed survival is computed using the Kaplan Meier survival function. This is the same as the proportion of patients alive 1 year after incidence date if there is no censoring (lost to follow-up) in the data. (B) The 1-year relative survival is computed as the 1-year observed survival for the population diagnosed with the specified type of cancer (= proportion of people surviving 1 year after the diagnosis), divided by the 1-year expected survival of a comparable group from the general population residing in Belgium. The relative survival is expressed as a percentage, and estimates the excess mortality that can be attributed to the cancer. A 100% 1-year relative survival indicates that patients who were diagnosed with cancer had a similar mortality rate than the general population of the same age, sex, calendar year and Region. Included in analysis: all lung cancer patients (except those with multiple tumours)
Data source	Belgian Cancer Registry (BCR): incidence years 2010-2011 Kruispuntbank - Banque Carrefour for mortality data (vital status of patients diagnosed with cancer): until 31 December 2014. IMA data for subgroup analyses

Technical definition	*For subgroup analyses:* Surgery with curative intent: billing codes (IMA) in Table 74 (appendix) Radiotherapy with curative intent: biling codes (IMA) in Table 75 (appendix) Chemotherapy: billing codes (IMA) in Table 76 (appendix) Targeted therapy: billing codes in Table 77 (appendix)
Subgroup analyses	1. For all lung cancer patients: by patient and tumour characteristics 2. For patients with NSCLC: a. by patient and tumour characteristics b. by treatment modality received (exclusive categories: surgical resection with curative intent, (chemo)radiotherapy with curative intent, chemotherapy including targeted treatment, no treatment). 3. For patients with NSCLC and surgical resection with curative intent: by patient and tumour characteristics Patient characteristics include: sex, age group, measures of comorbidities and patient frailty (performance status, history of cardiovascular diseases, history of respiratory diseases, history of diabetes, days in hospital in the year preceding incidence date) Tumour characteristics include: histological (sub)type, stage (clinical, pathological, combined), tumour sublocalisation.
Sensitivity analyses	Median survival time
Benchmarking	Analyses per centre all NSCLC patients (per diagnostic centre) subgroup of operated patients (per centre of surgery) subgroup of primary radiotherapy (per centre of radiotherapy) subgroup of primary chemotherapy/targeted treatment (per by centre of chemotherapy (diagnostic centre)) Observed survival: Adjust for case-mix: age, sex, histology, stage, comorbidity, performance status
International indicator	See Table 1.

Table 1 – Observed and 1-year survival: international results

Author	Period covered	Country	Results
Longkanker in Beeld	1989-2011	The Netherlands	1-year relative survival for all lung cancer patients exceeded 40% in 2011 (taken from graph). Results for NSCLC and SCLC separately appear to be similar to the Belgian results.
National Lung Cancer Audit Report	2013	UK	Crude median survival for all lung cancer patients is 232 days. For stage 3 NSCLC patients, crude median survival is 293 days.

1.1.2 Results

1.1.2.1 Survival of patients diagnosed with lung cancer (any type)

Table 2 – 1-, 2-, and 3-year observed and relative survival, median survival, by tumour and patient characteristics, all lung cancer patients

		Observed survival (%)			Relative survival (%)			Median observed survival (months)
Characteristics	N at risk	**1-year**	2-year	3-year	**1-year**	2-year	3-year	
Overall	12 839	**43.9**	27.1	20.3	**45.3**	28.7	22.2	9.5
Sex								
Female	3 786	**49.9**	33.4	25.8	**50.9**	34.6	27.1	12.0
Male	9 053	**41.4**	24.4	18.1	**43.0**	26.2	20.0	8.8
Age group								
0-49 years	643	**53.8**	36.6	30.1	**53.9**	36.7	30.3	13.6
50-59 years	2 419	**51.5**	32.9	25.6	**51.9**	33.4	26.2	12.6
60-69 years	3 889	**49.4**	31.4	24.1	**50.1**	32.3	25.2	11.7
70-79 years	3 884	**40.7**	24.7	18.2	**42.2**	26.7	20.5	8.6
80 years and more	2 004	**27.0**	13.1	7.5	**30.1**	16.2	10.5	4.6
Histological type								
Non-small cell lung cancer	9 817	**46.4**	29.6	22.4	**47.8**	31.3	24.3	10.3
Small cell lung cancer	2 004	**33.7**	14.3	9.4	**34.7**	15.0	10.1	8.1
Other specified lung cancer	1 018	**39.9**	27.3	21.7	**42.7**	30.9	25.8	6.8
Combined stage								
I	1 721	**86.3**	73.0	62.9	**89.0**	77.6	68.9	>36.0
II	955	**72.1**	54.5	45.0	**74.5**	57.8	49.1	29.2

		Observed survival (%)			Relative survival (%)			Median observed survival (months)
III	2 639	**52.4**	30.8	21.1	**54.1**	32.6	22.9	12.8
IV	5 275	**26.5**	9.3	4.7	**27.4**	9.9	5.1	6.0
X (unknown)	2 249	**30.2**	17.4	12.9	**31.4**	18.7	14.2	5.3

Source: BCR

Discussion Table 1

The majority of the patients diagnosed with lung cancer will not survive the first year after diagnosis: the 1-year observed survival is 43.9%, and drops to 20.3% at 3-years (Table 1). This poor prognosis is partly explained by the fact that most patients are diagnosed when cancer is metastasized, and those patients have the worst prognosis (stage IV, 26.5% survival at 1 year). The type of lung cancer being an important prognostic factor (NSCLC: 46.4% survival at 1 year, SCLC: 33.7%), all following results will be further presented on the population with NSCLC separately.

Relative survival shows very similar results (45.3% at 1 year, 22.2% at 3 years), indicating that the mortality is almost entirely attributable to the lung cancer, and not to the underlying natural mortality rate of the population.

Median survival for this population is 9.5 months overall.

Benchmarking these results with those of other countries

Benchmarking national survival rates with those of other countries is a difficult exercise. Results from the EUROCARE studies are currently the most reliable source of information.

EUROCARE is the largest cooperative study of population-based cancer survival in Europe, started under the initiative of two Italian Institutes (www.eurocare.it). Their last publication assesses the 5-year survival for the ten most common cancers, including lung cancer, in 29 European countries, for patients diagnosed between 1999 and 2007.[1 2]

In the EUROCARE-5 study, the European mean age-standardised 5-year survival for lung cancer was the **poorest of the ten cancers studied** (**13·0%**), and was better for women than for men. **Geographical differences were small**, compared to other cancers, varying from **9·0%** in the UK and Ireland to **14·8%** in **Central Europe** (6 countries, including Belgium, with the limitation that data originated exclusively from Flanders, because at the time there was no national registry). Among the 6 countries from Central Europe, Belgium showed the **third highest survival rate (15.4%)** after Austria (16.7%) and Germany (15.6%). European 5-year survival increased slightly from 11·6% in 1999–2001 to 13·4% in 2005–07, with similar trends in each country.[1 2] One year survival age standardised in EUROCARE was 39% overall. Age standardised overall 1 year survival for Belgium in the same report was 44.8 %. Age adjusted 3 year survival was 17.1 %.

The next study, EUROCARE-6, is already scheduled and will continue the activity of surveillance and the comparison between survival and care of cancer patients across Europe, initiated with EUROCARE-1,-2,-3, -4, and -5. The EUROCARE-6 will update the study database by including data of patients diagnosed to 2012 and followed up to 2013 or later.

These encouragingly good results should however be interpreted with some caution. As it happens, the authors mention in the discussion that Belgian survival data for rapidly fatal cancers (i.e. oesophagus, lung, pancreas, pleura, and liver cancer) were unexpectedly high (this was also the case for Austria, Croatia, Germany and Poland), suggesting difficulties with ascertainment of vital status.[1, 2] This is unlikely tough, as Belgian Cancer Registry has a direct link with the Crossroad Bank of Social Security (Kruispuntbank van de Sociale Zekerheid / Banque Carrefour de la Sécurité Sociale), and receives exact dates of death. A possible explanation (based

on internal discussion with experts at the Cancer Registry) might be a small underreporting of patients with very poor prognosis to the Belgian Cancer Registry. Patients diagnosed at advanced stage, unfit for any treatment and for whom there is not even a pathological confirmation are less likely to be reported, resulting in an overestimation of the national survival rate. Another explanation, which is to be confirmed with data, might be that patients are more aggressively treated in Belgium.

1.1.2.2 All patients diagnosed with NSCLC

Table 3 – 1-year observed survival, by tumour and patient characteristics, and HR from multivariate Cox PH model (all NSCLC patients)

Characteristics	Observed survival (%)			Results from multivariate Cox PH model on death at 1 year			
	N at risk	Median survival (months)	1 year	Hazard ratio (95%CI)	Lower Limit	Upper limit	p-value
Overall							
Overall	9 817	10.3	46.4	---	---	---	---
Sex							<.0001
Female	2 913	13.1	52.2	0.83	0.78	0.88	
Male	6 904	9.5	43.9	ref			
Age group							<.0001
0-49 years	547	14.5	55.2	ref			
50-59 years	1 931	13.1	52.7	ref			
60-69 years	3 058	12.5	51.4	1.11	1.03	1.20	
70-79 years	2 981	9.3	43.2	1.37	1.27	1.49	
80 years and more	1 300	5.0	28.7	1.91	1.74	2.10	
Sublocalisation							0.0002

Characteristics	Observed survival (%)			Results from multivariate Cox PH model on death at 1 year			
	N at risk	Median survival (months)	1 year	Hazard ratio (95%CI)	Lower Limit	Upper limit	p-value
C340 Main bronchus	501	7.1	34.9	ref			
C341 Upper Lobe, lung	3 669	12.8	51.8	0.80	0.71	0.90	
C342 Middle Lobe, lung	344	12.1	50.0	0.76	0.63	0.92	
C343 Lower Lobe, lung	1 930	12.3	50.7	0.83	0.74	0.95	
C349 Lung, NOS	3 373	7.8	39.3	0.90	0.80	1.01	
Combined stage							
I	1 415	--	88.4	ref			<.0001
II	826	32.8	73.8	2.36	1.93	2.90	
III	2 073	13.0	53.2	4.62	3.91	5.46	
IV	3 987	6.1	28.2	9.11	7.76	10.69	
X	1 516	4.8	30.5	9.38	7.89	11.14	
Histological subtype							<.0001
Adenocarcinoma	5 152	10.8	47.4	ref			
Squamous cell carcinoma	3 144	11.5	49.2	1.00	0.94	1.07	
Other subtypes	1 521	7.4	37.0	1.34	1.25	1.45	
WHO performance status							<.0001
0 – Asymptomatic	1 172	27.9	69.4	ref			

Characteristics	Observed survival (%)			Results from multivariate Cox PH model on death at 1 year			
	N at risk	Median survival (months)	1 year	Hazard ratio (95%CI)	Lower Limit	Upper limit	p-value
1 – Symptomatic but completely ambulatory	5 279	12.0	50.0	1.33	1.19	1.49	
2 – Symptomatic, <50% in bed during the day*	994	4.4	23.6	2.37	2.09	2.70	
3 – Symptomatic, >50% in bed, but not confined to bed*	362	1.8	11.3	4.02	3.49 1.25	4.65 1.62	
4 – Confined to bed	114	1.5	15.8				
Missing	1 896	8.6	42.3	1.42	1.25	1.62	
Chronic respiratory disease**							0.0664
No	7 048	10.2	46.2	ref			
Yes	2 769	10.6	46.7	1.06	1.00	1.13	
Cardiovascular disease**							0.5424
No	4 317	11.6	49.1	ref			
Yes	5 500	9.5	44.3	1.02	0.96	1.08	
Diabetes mellitus**							0.0002
No	8 497	10.6	47.2	ref			
Yes	1 320	8.4	41.2	1.16	1.07	1.26	
Days of hospitalisation one year before incidence date lung cancer							0.0001
None	7 222	10.3	46.2	ref			
1-5 days	1 484	12.0	50.0	0.99	0.92	1.07	

Characteristics	Observed survival (%) N at risk	Median survival (months)	1 year	Results from multivariate Cox PH model on death at 1 year Hazard ratio (95%CI)	Lower Limit	Upper limit	p-value
6-15 days	640	10.6	47.3	1.05	0.94	1.18	
More than 15 days	471	6.8	36.9	1.32	1.17	1.49	

**WHO performance status level 3 and 4 are taken together in the multivariate Cox PH model*
***identified based on pharma consumption*

Discussion

One year survival results and prognostic factors for NSCLC patients are presented in Table 3. Overall, 1-year survival was 46.4%, with the following prognostic factors: sex (being male has a worse prognosis), age (being older), WHO performance status, sub-localisation (main bronchus), stage, subtype. Of the three comorbidity measures, diabetes is the most predictive of 1 year mortality. Chronic respiratory disease only shows a moderate effect on one year mortality, while cardiovascular disease is not predictive (after adjustment for all other factors).

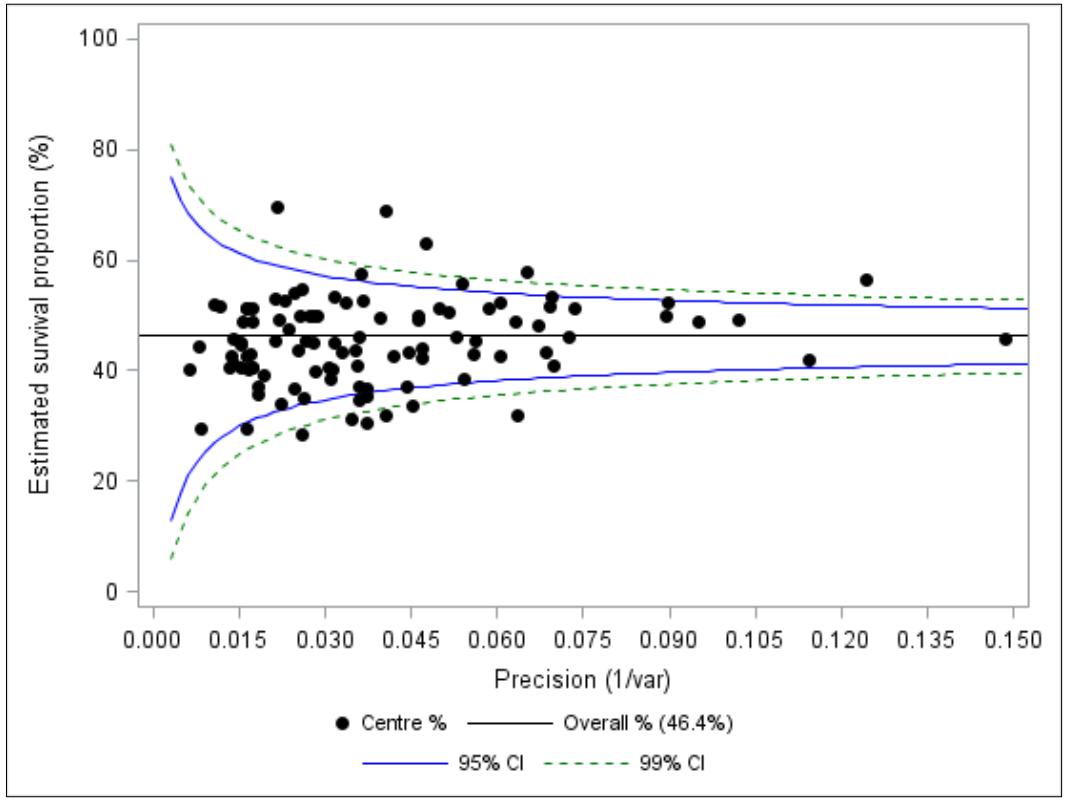
Days of hospitalisation in the year before the incidence date, shows worse survival for patients hospitalized more than 15 days during the year preceding the incidence date (probably pointing to poor general health).

Table 4 presents survival results by primary treatment received. Results for patients operated are discussed in further details in the next section.

Table 4 – 1-, 2-, 3 -year observed survival, by treatment received (all NSCLC patients)

	Observed survival				
Treatment modality	N at risk	1-year	2-year	3-year	Median survival
Surgery	2,084	88.3	77.5	68.9	>36.0
(Chemo)RT	2,001	54.8	30.7	20.4	13.6
Chemo/target	3,692	35.8	14.0	6.6	8.3
NONE	2,040	14.3	8.0	5.5	1.8

Figure 1 – Observed 1-year survival for NSCLC patients (by diagnostic centre)



Note: Centres with less than 10 patients at risk were excluded from these analyses

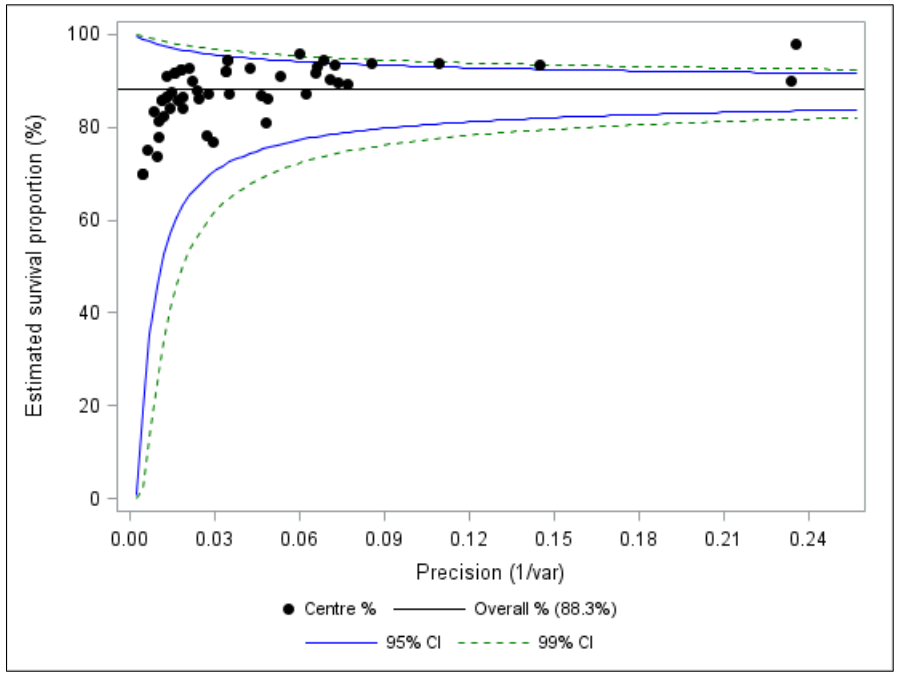
1.1.2.3 All patients diagnosed with NSCLC who underwent surgical intervention with curative intent

The analyses on the 1 year observed survival by tumor and patients characteristics for patients with NSCLC who underwent surgical internvention can be found in chapter "Volume-outcome" from the report.

Overall, one-year survival of NSCLC patients who underwent surgical intervention was 88.3%. Results for patients operated are discussed in further details in the next section. The following factors are predictive of 1–year survival: sex (male have worse prognosis), age (old people have worse prognosis), stage (1-year mortality increases with increasing stage), WHO performance status and the number of days of hospitalisation one year

before incidence date (see analyses in chapter volume outcome of the report).

Figure 2 – Observed 1-year survival for NSCLC patients who underwent surgical interventions with curative intent (by centre of surgery)



Note: 6 centres with less than 20 patients at risk and having a survival of 100% (no death) were not represented for this analysis. This is because the precision, needed to position the datapoint for those centres on the X-axis of the graph, cannot be calculated when no event (death) is recorded.

Key Points

- **More than half of the patients diagnosed with lung cancer will not survive the first year after their diagnosis: the 1-year observed survival (all patients included) is 43.9%, and drops to 20.3% at 3-years.**
- **Results for international comparison are available from the EUROCARE-5 study (5-year survival, 29 European countries, patient diagnosed between 1999 and 2007). Among the 6 countries from Central Europe, Belgium showed high survival rates compared to other countries. These encouragingly good results should however be interpreted with some caution, as there may have been some underreporting of patients with very poor prognosis to the Belgian Cancer Registry at that time.**
- **For NSCLC patients, 1-year survival was 46.4%, with the following prognostic factors: sex, age, WHO performance status, sublocalisation, stage, subtype, and the number of hospitalization days during the year preceding the incidence date.**
- **For patients who underwent surgical intervention, 1-year survival was 88.3%. The following factors are predictive of 1–year survival: sex, age, stage, WHO performance status and the number of hospitalization days one year before incidence date.**

2 QUALITY OF DATA REPORTING TO BELGIAN CANCER REGISTRY

2.1 TNM reported to the BCR (DR-1)

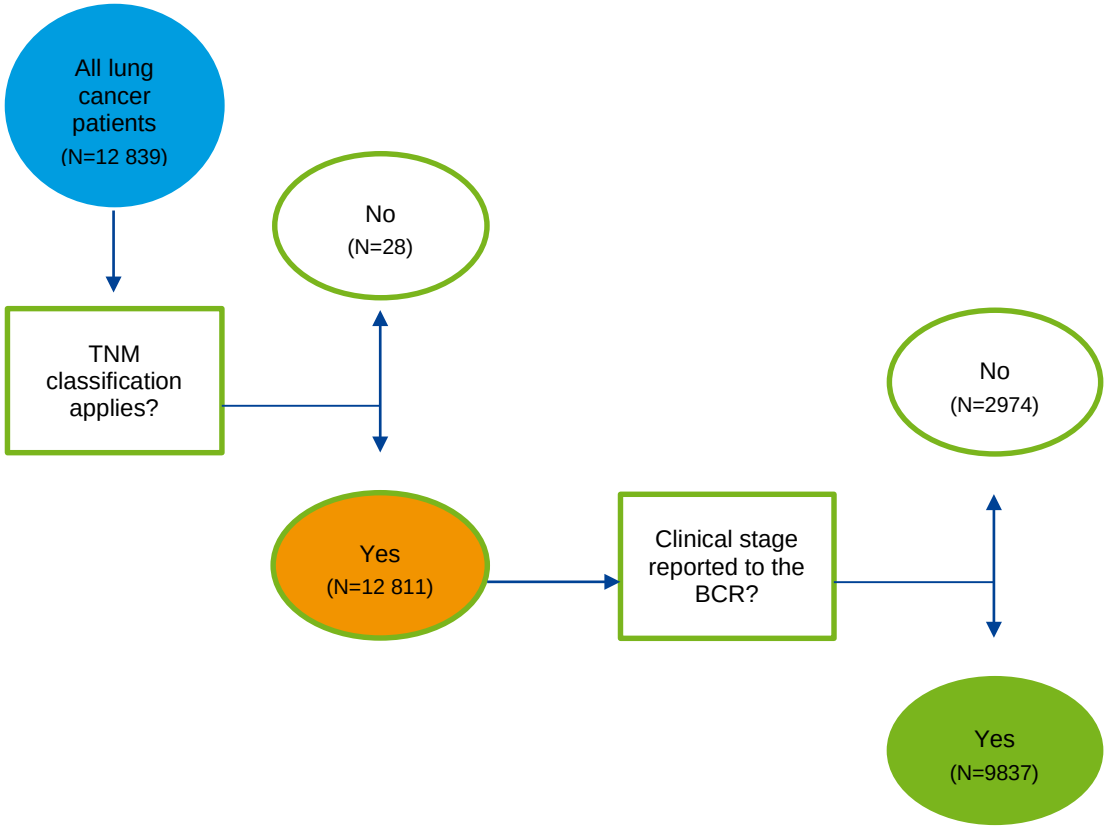
2.1.1 Documentation sheet

Title	A) Proportion of lung cancer patients who have their cTNM stage reported to the Belgian Cancer Registry (BCR) B) Proportion of patients treated with surgery with curative intent who have their pTNM stage reported to the BCR
Rationale	The staging process is an essential step of the clinical pathway, as further treatment (or no treatment) decisions are based on this information. Cancer registration to the Belgian Cancer Registry is mandatory for all new diagnoses of cancer, but completeness of information is still far from achieved. This indicator is not per se a quality indicator, but gives an indication of the quality of data which are transferred to the BCR.
Type of QI	Process
Calculation	Indicator A: Numerator: number of lung cancer patients who have their cTNM reported to the BCR Denominator: all patients diagnosed with lung cancer Indicator B: Numerator: number of lung cancer patients treated with surgery with curative intent, who have their pTNM reported to the BCR Denominator: number of lung cancer patients treated with surgery with curative intent Exclusion: tumours for which TNM classification does not apply. The TNM classification applies to carcinomas of the lung, including Non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC) and bronchopulmonary carcinoid tumours. It does not apply to sarcomas and other rare tumours.
Target	95%
Data source	BCR
Technical definition	Diagnostic of lung cancer: ICD-10 code C34 (BCR) (Table 103 in appendix)
Limitations	The indicator is a combination of reporting and effectively determining the stage. Therefore, the cause of low reporting rates may be unclear. Low rates indicate either poor quality of care (the information is not known at the centre) or poor coordination to transfer the information to the BCR. Staging may not be performed because patients are unfit for treatment, the proportion for whom this is the case is not known.

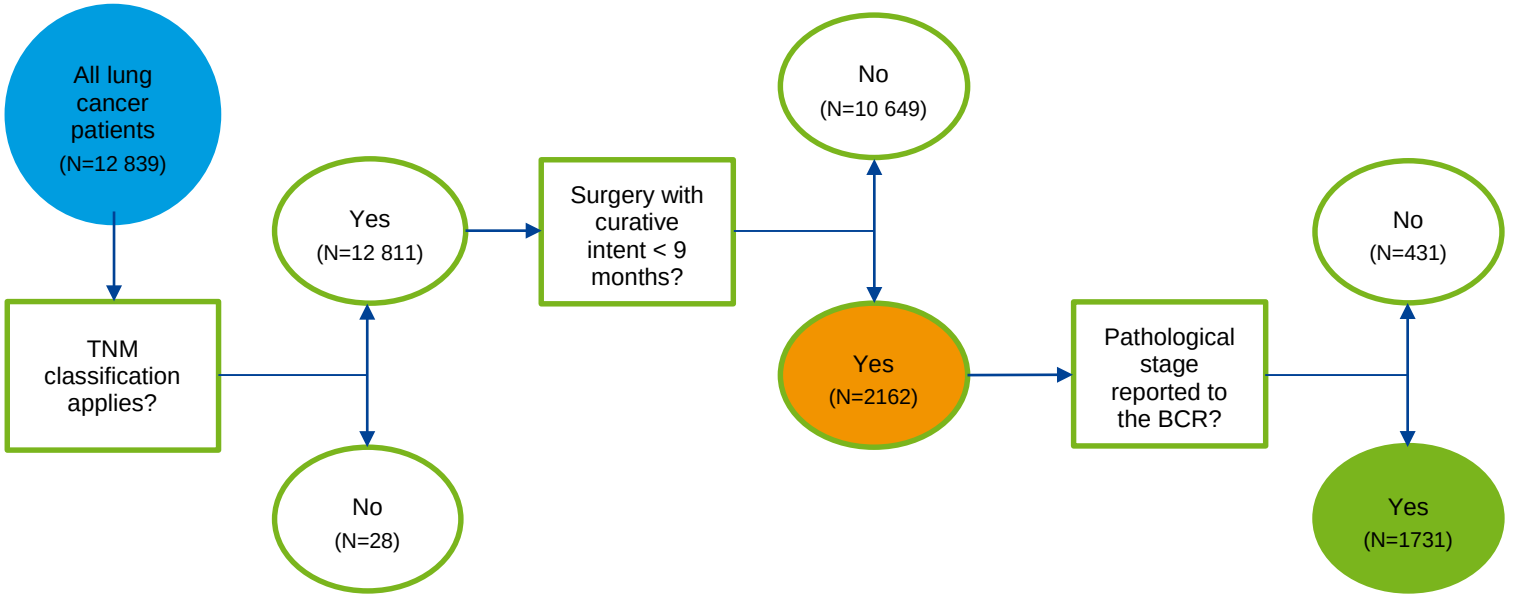
Subgroup analyses	By type of lung cancer (NSCLC, SCLC)
Sensitivity analyses	With exclusion of patients who received no active treatment within 9 months after incidence
Benchmarking	Diagnostic centre
International indicator	It is an indicator that is rather specific to the Belgian context, information flow in different countries is organised in a different way.

2.1.2 *Flowchart*

A)



B)


All lung cancer patients (N=12 839)
TNM classification applies?
Yes (N=12 811)
No (N=28)
Surgery with curative intent < 9 months?
No (N=10 649)
Yes (N=2162)
Pathological stage reported to the BCR?
No (N=431)
Yes (N=1731)

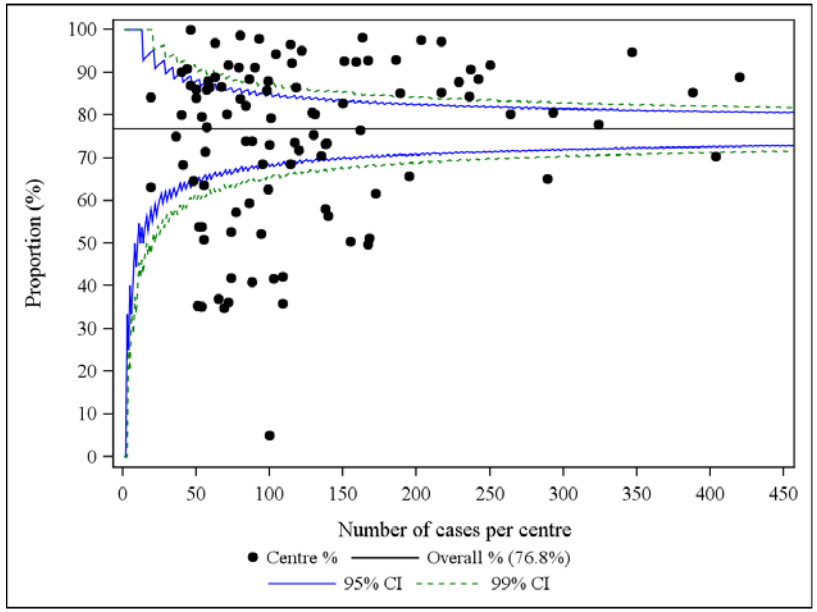
2.1.3 Results

Table 5 – Proportion of lung cancer patients who have their cTNM reported to the BCR, by type of lung cancer

Characteristic	Denominator	Numerator	Proportion (%)
Overall	12 811	9837	76.8
Histological type			
Non-small cell lung cancer	9817	7588	77.3
Small cell lung cancer	2004	1421	70.9
Other specified lung cancer	990	828	83.6

Source: BCR

Figure 3 – Proportion of lung cancer patients who have their cTNM reported to the BCR, by diagnostic centre



Note: 110 patients were not shown in the figure because they could not be assigned to a diagnostic centre.
Source: BCR

Table 6 – Sensitivity analysis: proportion of lung cancer patients who have their cTNM reported to the BCR versus proportion of lung cancer patients with active treatment who have their cTNM reported to the BCR

Characteristic	Denominator	Numerator	Proportion (%)
Overall	12 811	9837	76.8
Only patients with active treatment	10 080	7946	78.8

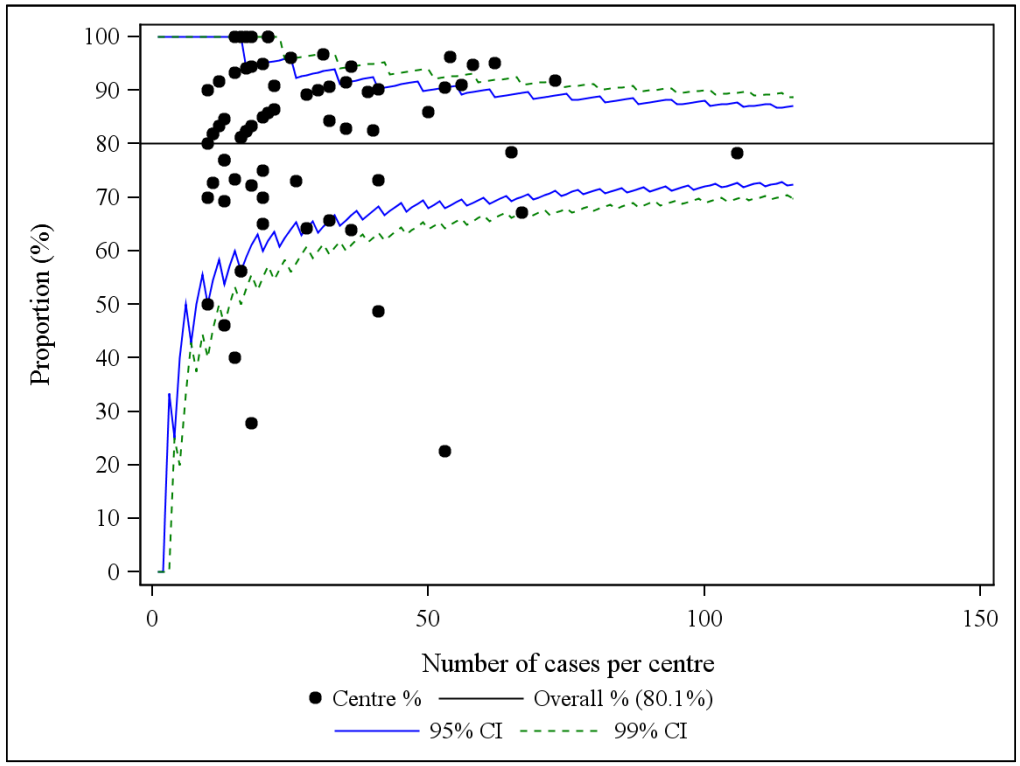
Source: BCR

Table 7 – Proportion of lung cancer patients treated with surgery with curative intent, who have their pTNM reported to the BCR, by type of lung cancer

Characteristic	Denominator	Numerator	Proportion (%)
Overall	2162	1731	80.1
Histological type			
Non-small cell lung cancer	2084	1700	81.6
Small cell lung cancer	47	30	63.8
Other specified lung cancer	31	1	3.2

Source: BCR

Figure 4 – Proportion of lung cancer patients treated with surgery with curative intent, who have their pTNM reported to the BCR, by diagnostic centre



Note 1: 1 patient was not shown in the figure because he/she could not be assigned to a diagnostic centre.
Note 2: 31 centres were not displayed because the denominator was smaller than 10.
Source: BCR

2.1.4 Discussion

Table 5 shows the proportion of lung cancer patients who have their cTNM reported to the BCR. The proportion is somewhat lower for small cell lung cancer. Reasons for this are unclear. The funnel plot shows that there is a large variability between centres, much larger than could be expected by mere coincidence (overdispersion). In a considerable proportion of centres there is large room for improvement. One explanation may be that some centres do not seem to know that both clinical and pathological stage need to be reported, or do not find it important to report the clinical stage when they know that the pathological stage is reported.

Table 6 shows the proportion of lung cancer patients treated with surgery with curative intent, who have their pTNM reported to the BCR, by type of lung cancer. The proportion is lower for small cell cancer, but the numbers in this group are small. It is somewhat puzzling that in the group other specified lung cancer only one pathological TNM was reported. Variability is lower than for the clinical stage, it may be that if centres are able to determine the pathological stage, they also report it in a more consistent way. Given the fact that in principle it is always possible to determine the pathological TNM stage of cancers in patients that underwent surgery, there is also ample room for improvement here.

Although some similar indicators are reported in the literature,[3, 4] differences in the way data collection systems are organised make it difficult to compare these reporting rates internationally.

Key Points

- **Reporting of clinical TNM stage is suboptimal (78%), and variable between centres.**
- **Reporting of pathologicalTNM stage in different centres is more consistent and proportions are similar.**
- **For both clinical and pathological TNM stage in different centres there is clear room for improvement.**
- **Underreporting of TNM stage has important consequences for the other quality indicators, because TNM stage is a crucial parameter in the evaluation of quality (patient selection, definition of indicators, case mix adjustment for outcomes,..)**

3 QUALITY OF DIAGNOSIS AND STAGING

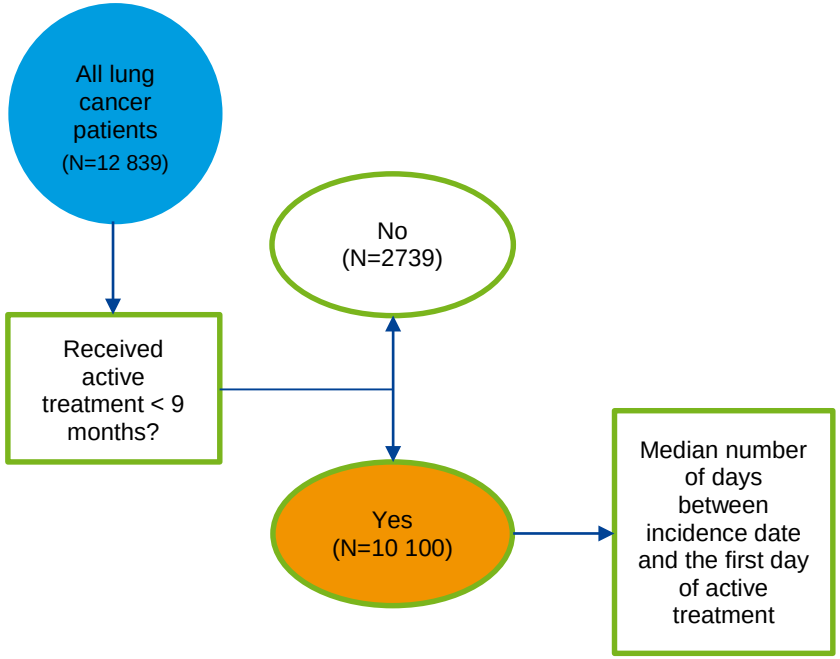
3.1 Median time from pathological diagnosis to first active treatment (DS-1)

3.1.1 Documentation sheet

Title	Time from incidence date to first active treatment (curative intent or palliative intent)
Rationale	Once the diagnosis and staging procedures have been completed and a decision of treatment has been taken, waiting time to first active treatment should be kept as low as medical and organisational reasons allow.
Type of QI	Process
Calculation	Median number of days between the incidence date and the first day of active treatment Included in analysis: all lung cancer patients who received treatment within 9 months after incidence date. Active treatment is defined as - surgery with curative intent - radiotherapy with curative intent (cat 2 to 4) - chemotherapy - targeted therapy - radiotherapy with palliative intent (cat 1)
Target	No target
Data source	BCR + IMA
Technical definition	Incidence date as registered in the BCR: date of first microscopic confirmation of malignancy, if not available, date of clinical diagnosis (In any case not later than start date of treatment). Active treatment: any surgery with curative intent (billing codes IMA in Table 74), radiotherapy with curative or palliative intent (IMA, Table 75, Table 100), chemotherapy (IMA, Table 76) or targeted therapy (IMA, Table 77) (see appendix)
Limitations	For oligo-metastatic patients, surgical resection of metastasis can explain delay.
Subgroup analyses	By histological type (NSCLC vs SCLC), by clinical stage and by treatment modality By referral status (patients referred to another centre or not)

Sensitivity analyses	Proportion of patients that exceed threshold of 4 weeks[5]
Benchmarking	Diagnostic centre
International indicator	Yes, similar indicators are used in Italy [6] the US [7] Canada [8, 9] and Catalonia, Spain, [5].

3.1.2 Flowchart



3.1.3 Results

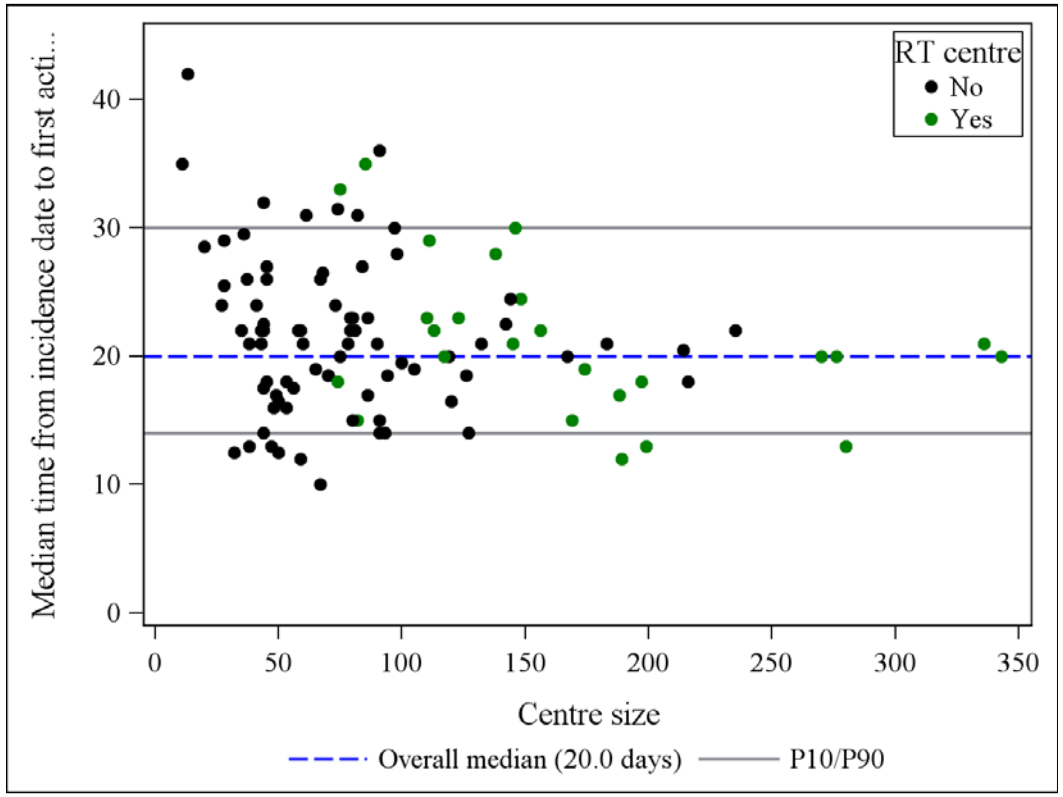
Table 8 – Time from incidence date to start of first active treatment by tumour and treatment characteristics, and referral status

Characteristic	Median number of days
Overall	20
Clinical stage	
I	32
II	28
III	22
IV	16
X	18
NA	33
Histological type	
Non-small cell lung cancer	22
Small cell lung cancer	12
Other specified lung cancer	37
Treatment modality	
Surgery	26
(Chemo)radiotherapy	22
Chemo-/Targeted therapy	17
No curative treatment (palliative RT)	16
Referral status	
Not referred to another centre	20
Referred to another centre	25

Characteristic	Median number of days
Unknown diagnostic or treatment centre	15

Source: BCR-IMA

Figure 5 – Time from incidence date to first active treatment (curative intent or palliative intent), by diagnostic centre (median number of days)



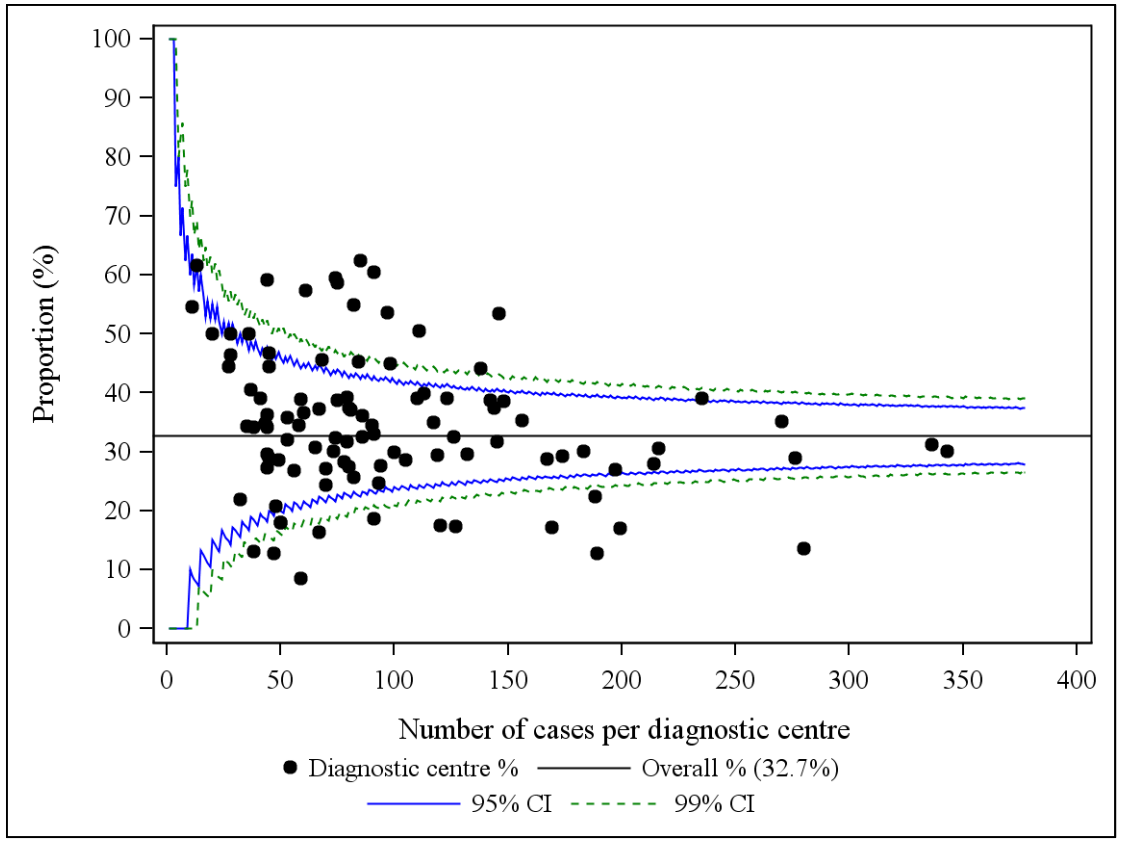
Note: 9 patients were not shown in the figure because they could not be assigned to a diagnostic centre.
Note: percentile 10 and percentile 90 are calculated on the median of the centres.
Source: BCR-IMA

Table 9 – Proportion of patients that exceed threshold of 4 weeks

Number of patients with active treatment within 9 months after incidence date	Number of patients with start active treatment after more than 4 weeks after incidence date
10 100	3299 (32.7%)

Source: BCR-IMA

Figure 6 – Proportion of patients that exceed threshold of 4 weeks, by diagnostic centre



Source: BCR-IMA

3.1.4 Discussion

A median delay of 20 days between incidence date and start date of active treatment is reported. There is a large variability across centres, with the scatter plot showing an asymmetry. A part of the smaller centres report larger median delay. Median delay increased for the lower stages and for surgical interventions, both may be linked: the lower the stage, the more likely it is that a surgical intervention takes place. Referral to another centre is associated with an increase in median delay of 5 days. A third of patients starts treatment after a delay higher than four weeks.

In a quality control programme in Italy, a time from pathological diagnosis to surgery of 50 days was reported, considered as poor performance against literature benchmarks of 28–35 days. A time from pathological diagnosis to chemotherapy of 26 days was reported, with a target ranging 14–21 days.[6] The Veterans Affairs Palo Alto Health Care System in the US reported median time from the initial suspicion of cancer to treatment was 84 days (interquartile range, 38–153 days), but it is difficult to compare this with our indicator.[7] In a Canadian setting (Alberta care registry) a median time from diagnosis to treatment of 41 days was reported, 90% started ≤ 115 days. [8] In Catalonia, Spain, median time from diagnosis to treatment reached 39 days, interquartile ranged from 17 days to 66 days, 57.9% >30 days. [5] The Belgian situation compares favorably to what is reported in the international literature, although the way the indicator is measured may be somewhat different.

Key Points

- **A median delay of 20 days between incidence date and start date of active treatment is reported, with a large variability across centres.**
- **A third of patients starts an active treatment after a delay of more than 4 weeks after incidence date.**

3.2 Pathological diagnosis and subtype (DS-2)

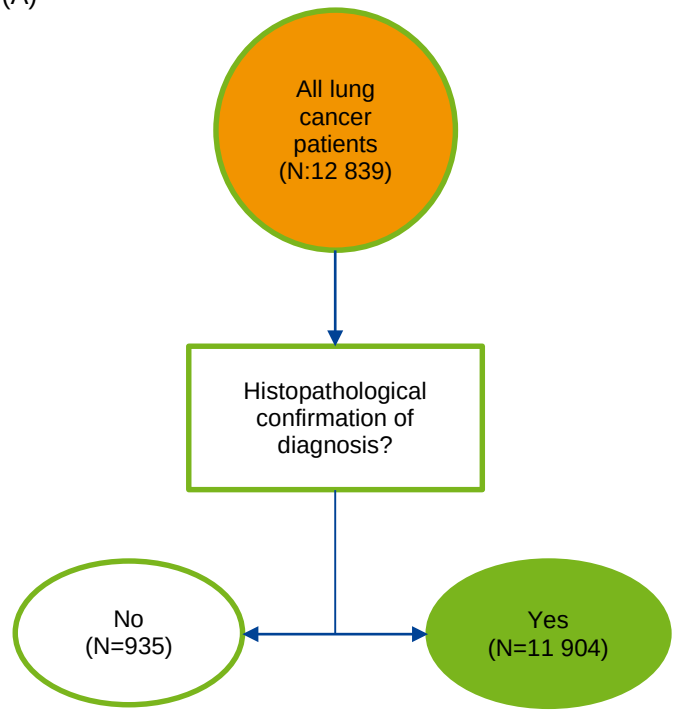
3.2.1 Documentation sheet

Title	**Proportion of lung cancer patients with histopathological confirmation of the diagnosis of lung cancer (indicator A),** **Proportion of lung cancer patients with histopathological confirmation of the diagnosis of lung cancer in whom the tumour type is identified (indicator B),** **Proportion of NSCLC patients for whom the subtype has been identified (indicator C)**
Rationale	Where possible patients should have a pathological diagnosis of lung cancer. A definitive diagnosis is valuable in helping inform patients and carers about the nature of the disease, the likely prognosis and treatment choice. Appropriate treatment of lung cancer depends on accurate diagnosis and distinction between histological types of lung cancer.
Type of QI	Process
Calculation	Indicator A: Numerator: number of lung cancer patients with histopathological confirmation of the diagnosis of lung cancer Denominator: all patients with a diagnosis of lung cancer Indicator B: Numerator: number of lung cancer patients who had tumour type identified (SCLC, NSCLC or other specified lung cancer) Denominator: all patients with a diagnosis of lung cancer with histopathological confirmation Indicator C: Numerator: number of NSCLC patients who had tumour subtype identified Denominator: all NSCLC patients
Target	SIGN put forward a target for this indicator of 75%, the tolerance level within this target takes account of the fact that it is not always appropriate, safe or possible to obtain a histological or cytological diagnosis due to the performance status of the patient or advanced nature of the disease. In patients where pathological diagnosis is appropriate this should be achieved wherever possible. However we do not have information to base a target on.
Data source	BCR
Technical definition	Diagnostic of lung cancer: ICD-10 code C34 (BCR) (Table 103 in appendix) Indicator A: Histopathology as basis of diagnosis (as reported to the BCR)

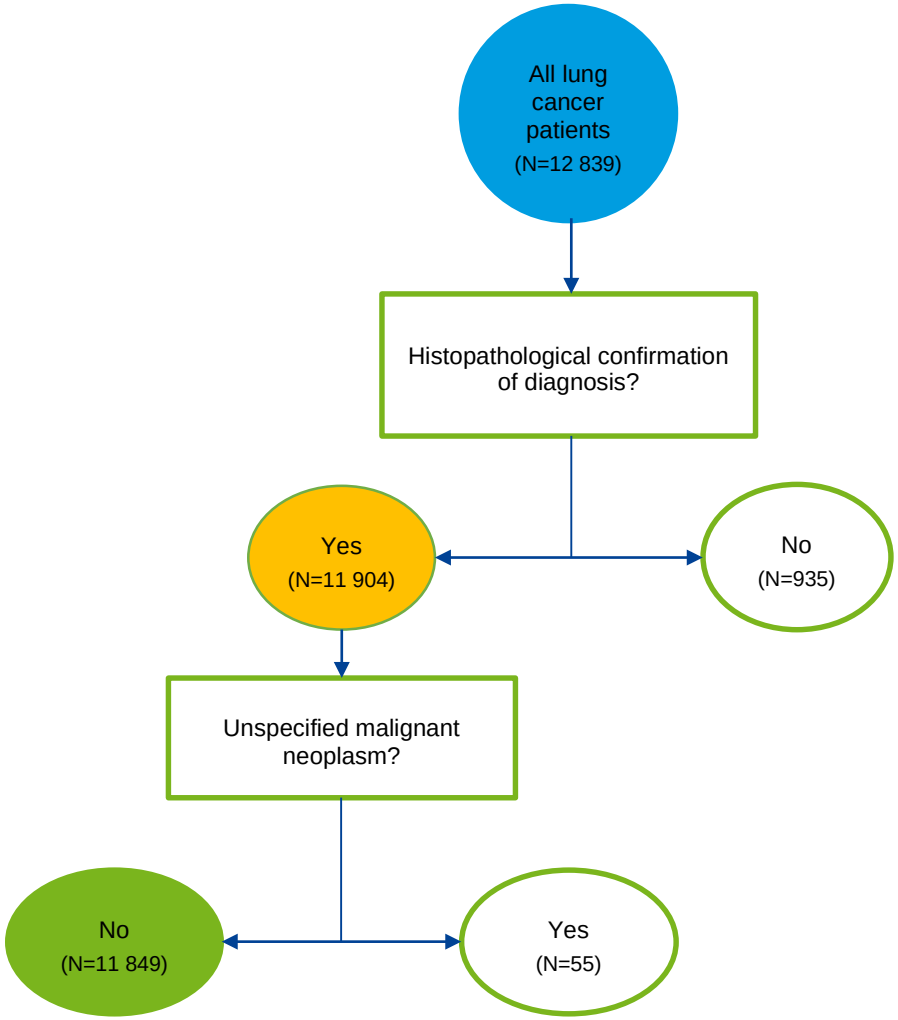
	Indicator B: Unspecified malignant neoplasm (ICD-O-3 morphology codes 8000-8005) Indicator C: Unspecified Non-Small Cell Lung Cancer (ICD-O-3 morphology code 8046))
Limitations	Reflects partly the reporting of pathological information to the BCR, not the availability of the pathology to the clinician. Target is difficult to interpret due to the fact that a variable amount of tissue is available for testing, depending on the circumstances and situation of the patient, and it is not sure what a 'reasonable' proportion of patients in whom sufficient tissue can be taken should be.
Subgroup analyses	By clinical stage, age and performance status
Sensitivity analyses	None
Benchmarking	Diagnostic centre
International indicator	National organisations: NICE (UK), SIGN (Scotland)

3.2.2 *Flowchart*

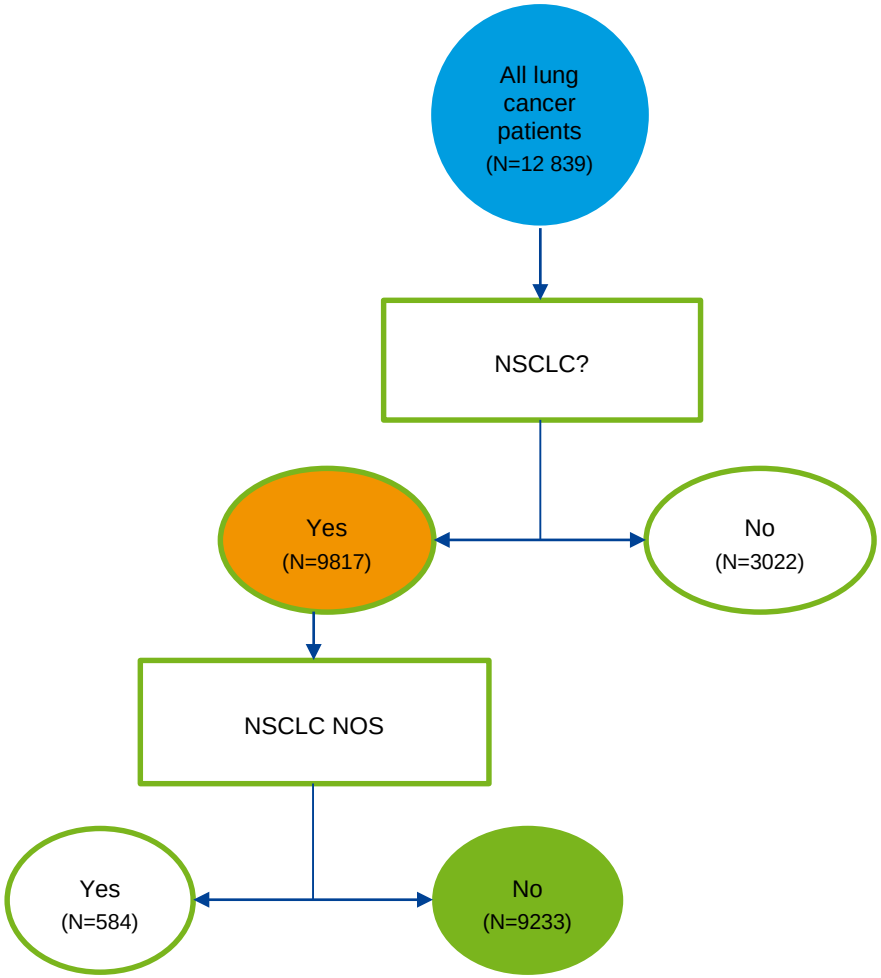
(A)



(B)


All lung cancer patients
(N=12 839)
Histopathological confirmation of diagnosis?
Yes
(N=11 904)
No
(N=935)
Unspecified malignant neoplasm?
No
(N=11 849)
Yes
(N=55)

(C)


All lung cancer patients
(N=12 839)
NSCLC?
Yes
(N=9817)
No
(N=3022)
NSCLC NOS
Yes
(N=584)
No
(N=9233)

3.2.3 Results

Table 10 – Proportion of lung cancer patients with histopathological confirmation of the diagnosis of lung cancer, by patient and tumour characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	12 839	11 904	92.7
Age group			
<50 years	643	629	97.8
50-59 years	2419	2358	97.5
60-69 years	3889	3753	96.5
70-79 years	3884	3602	92.7
80+ years	2004	1562	77.9
WHO performance status			
0 – Asymptomatic	1436	1317	91.7
1 – Symptomatic but completely ambulatory	6685	6288	94.1
2 – Symptomatic, up and about more than 50% of waking hours	1429	1271	88.9
3 – Symptomatic, confined to bed or chair more than 50% of waking hours	570	452	79.3
4 – Completely disabled; totally confined to bed or chair	194	150	77.3
Missing	2525	2426	96.1
Clinical stage			
I	1412	1165	82.5
II	748	694	92.8
III	2535	2370	93.5
IV	5142	4822	93.8
X	2974	2825	95.0

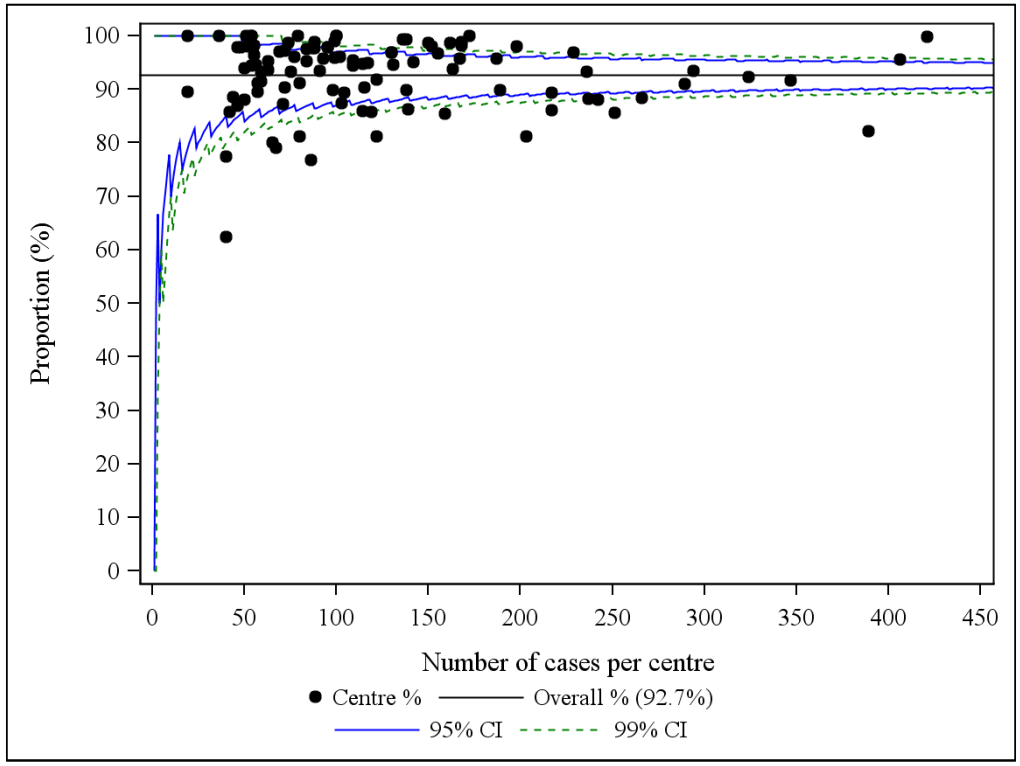
Characteristic	Denominator	Numerator	Proportion (%)
NA	28	28	100.0

Source: BCR

Table 11 – Histopathological confirmation in stage cI patients, by age group

	Histopathological Confirmation	
	No	**Yes**
Age group		
<50 years	6 (2.4%)	57 (4.9%)
50-59 years	19 (7.7%)	207 (17.8%)
60-69 years	51 (20.7%)	390 (33.5%)
70-79 years	85 (34.4%)	372 (31.9%)
80+ years	86 (34.8%)	139 (11.9%)
Total	247	1165

Figure 7 – Proportion of lung cancer patients with histopathological confirmation of the diagnosis of lung cancer by diagnostic centre



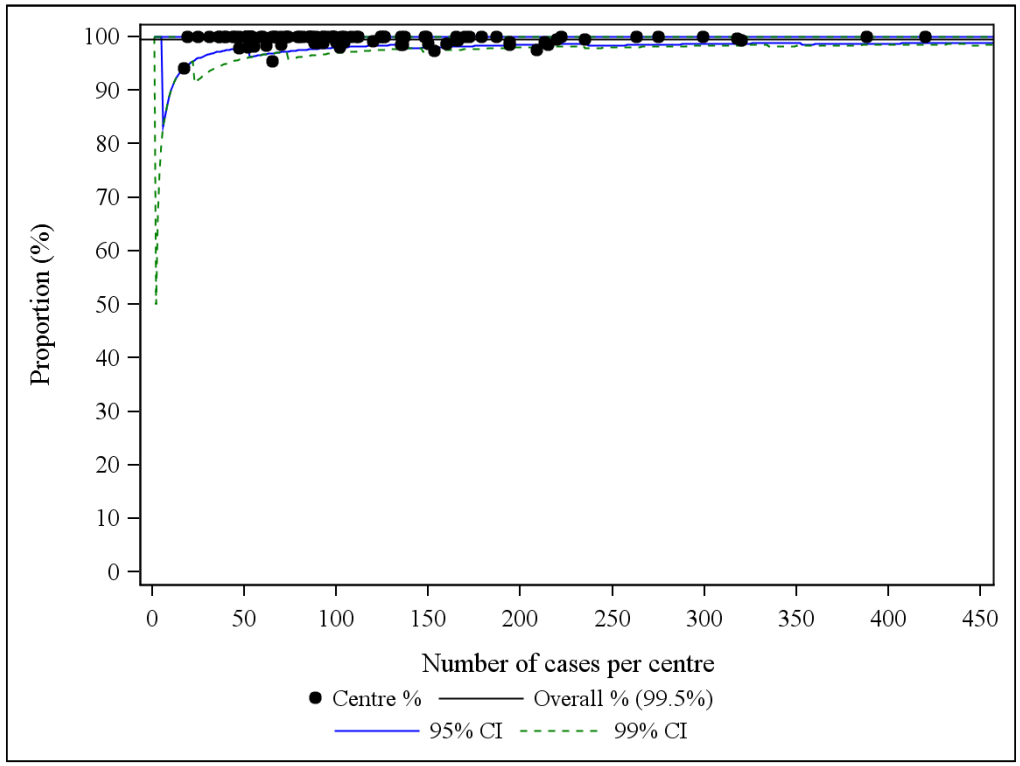
Note: 110 patients were not shown in the figure because they could not be assigned to a diagnostic centre.
Source: BCR

Table 12 – Proportion of lung cancer patients with histopathological confirmation who had the tumour type* identified, by patient and tumour characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	11 904	11 849	99.5
Age group			
<50 years	629	626	99.5
50-59 years	2358	2354	99.8
60-69 years	3753	3741	99.7
70-79 years	3602	3585	99.5
80+ years	1562	1543	98.8
WHO performance status			
0 – Asymptomatic	1317	1310	99.5
1 – Symptomatic but completely ambulatory	6288	6264	99.6
2 – Symptomatic, up and about more than 50% of waking hours	1271	1264	99.4
3 – Symptomatic, confined to bed or chair more than 50% of waking hours	452	448	99.1
4 – Completely disabled; totally confined to bed or chair	150	147	98.0
Missing	2426	2416	99.6
Clinical stage			
I	1165	1155	99.1
II	694	688	99.1
III	2370	2365	99.8
IV	4822	4801	99.6
X	2825	2812	99.5
NA	28	28	100.0

**SCLC, NSCLC or other specified lung cancer*
Source: BCR

Figure 8 – Proportion of lung cancer patients with histopathological confirmation who had the tumour type identified (SCLC, NSCLC or other specified lung cancer) by diagnostic centre



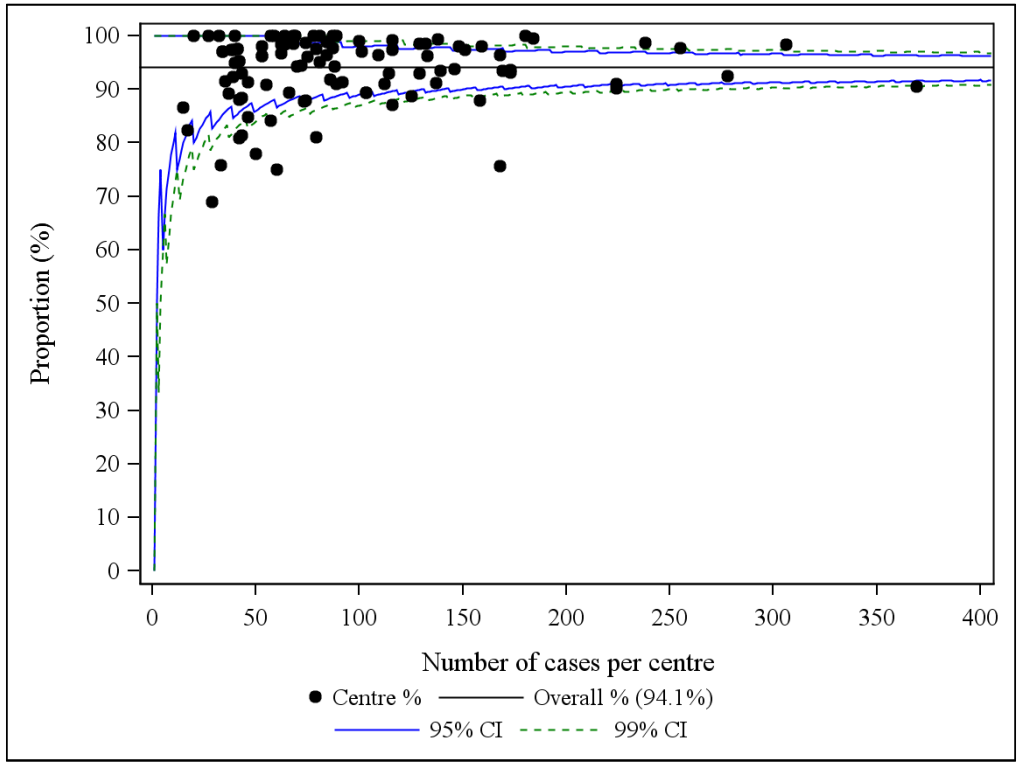
Note: 102 patients were not shown in the figure because they could not be assigned to a diagnostic centre.
Source: BCR

Table 13 – Proportion of NSCLC patients who had the tumour subtype identified, by patient and tumour characteristic

Characteristic	Denominator	Numerator	Proportion (%)
Overall	9817	9233	94.1
Age group			
<50 years	547	505	92.3
50-59 years	1931	1821	94.3
60-69 years	3058	2893	94.6
70-79 years	2981	2804	94.1
80+ years	1300	1210	93.1
WHO performance status			
0 – Asymptomatic	1163	1114	95.8
1 – Symptomatic but completely ambulatory	5232	4947	94.6
2 – Symptomatic, <50% in bed during the day	986	910	92.3
3 – Symptomatic, >50% in bed, but not bedbound	359	331	92.2
4 – Bedbound	113	104	92.0
Missing	1964	1827	93.0
Clinical stage			
I	1107	1078	97.4
II	619	593	95.8
III	1987	1862	93.7
IV	3875	3613	93.2
X	2229	2087	93.6

Source: BCR

Figure 9 – Proportion of NSCLC patients who had the tumour subtype identified by diagnostic centre



Note: 87 patients were not shown in the figure because they could not be assigned to a diagnostic centre.
Source: BCR

3.2.4 Discussion

Table 1 shows the high proportion of lung cancer patients with histopathological confirmation of the diagnosis, by clinical stage, performance status and age group. Dispersion by diagnostic centre is somewhat larger than would be expected based on chance alone. Proportion is lower for clinical stage I, the most plausible explanation is that no surgery is performed and no tumour tissue is obtained for those patients, because the general state of the patient did not allow either surgery or more invasive staging procedures needed to obtain tissue in a localised tumour. Proportion decreases with performance status and age, this is also in line with what could be expected, as it is more likely that any invasive intervention will be avoided with poorer performance status and increasing age.

If there is pathological confirmation, tumour type is nearly always determined, irrespective of age, stage and performance status. This is done nearly uniformly across centres. Also a very large proportion of NSCLC have their tumour subtype identified, irrespective of age, stage and performance status. Dispersion by diagnostic centre is somewhat larger than would be expected based on chance alone. For a minority of centres this indicator is substandard, it is unclear however if this is due to reporting or to the fact that subtype is not determined. This is better than proportions reported in the international literature, the National Lung Cancer Audit reported a confirmation rate of 75%, a rate constant in the last 5 years.[10]

Key Points

- **Proportion of lung cancer patients with histopathological confirmation of the diagnosis of lung cancer is high.**
- **This proportion is lower for clinical stage I (maybe explained because patients are treated with radiotherapy based on radiological evolution), and decreases with worsening performance status and increasing age.**
- **Nearly all patients with pathological confirmation have their tumour type determined.**
- **Most patients with NSCLC have their subtype determined, in some diagnostic centres this proportion is relatively low however.**

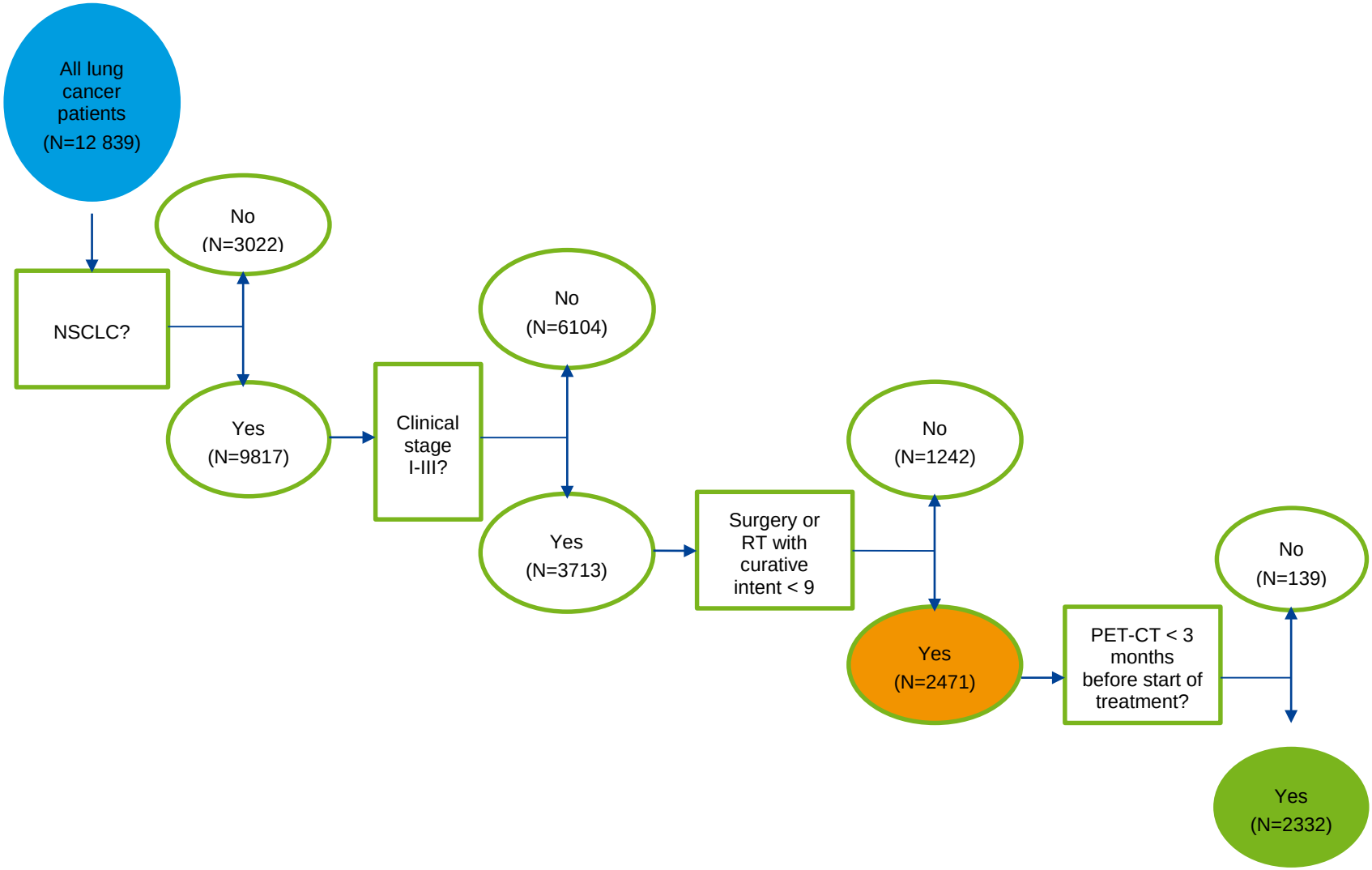
3.3 PET-CT and brain imaging before treatment with curative intent (DS-3 and DS-4)

3.3.1 Documentation sheet

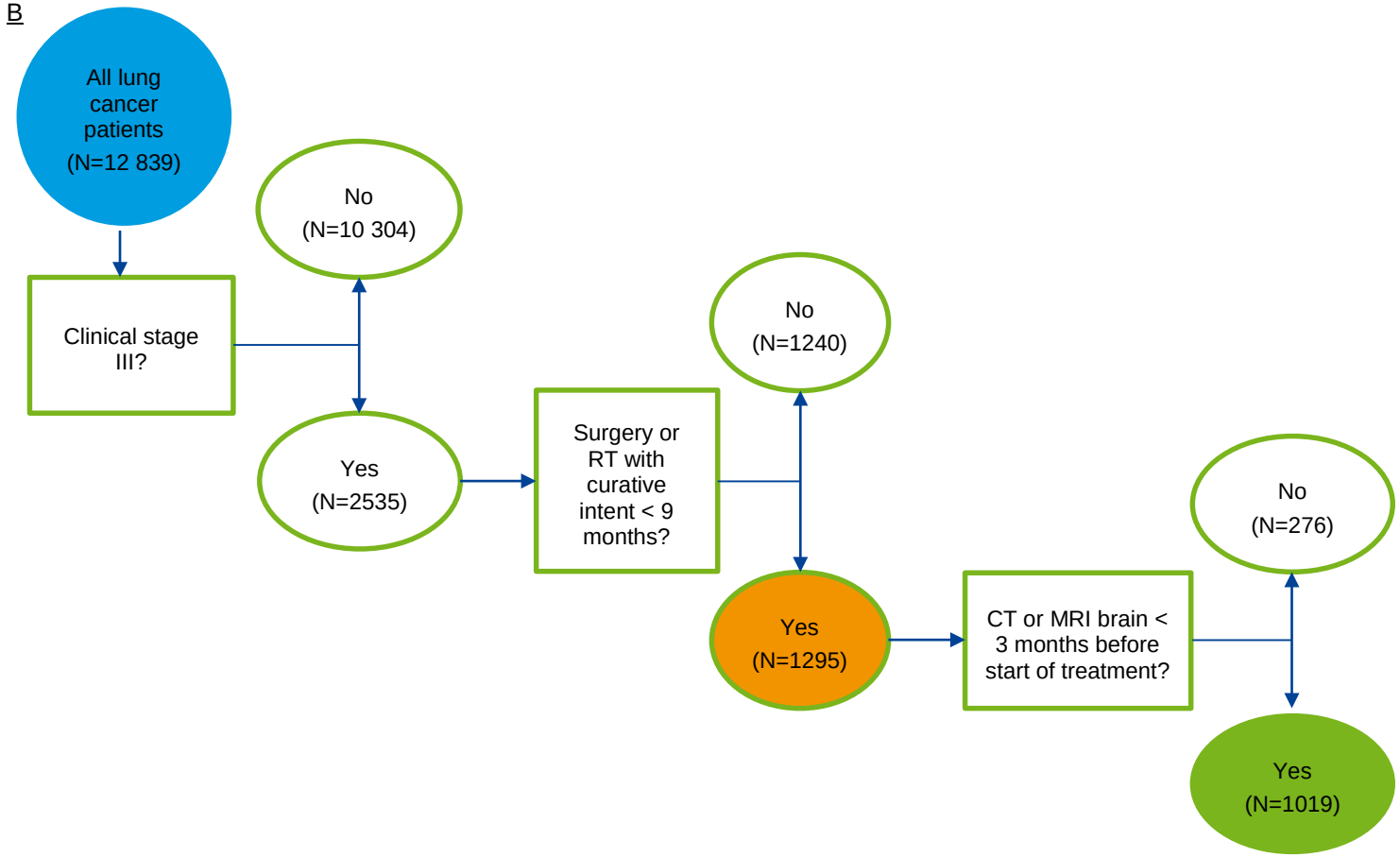
Title	**Proportion of cI-III NSCLC patients who had PET-CT prior to first treatment with curative intent (A)** **Proportion of cIII lung cancer patients who had brain imaging (CT or MRI) before first treatment with curative intent (B)**
Rationale	Recommendation from Belgian GCP: Offer PET-CT to all patients potentially suitable for treatment with curative intent in order to look for metastases. Offer CT or MRI of the brain with IV contrast to NSCLC patients selected for treatment with curative intent, especially in cIII disease.
Type of QI	Process
Calculation	Indicator A: Numerator: number of cI-III NSCLC patients in whom a PET-CT was obtained before the start of their first treatment with curative intent (<3 months before start of treatment) Denominator: all cI-III NSCLC patients who received first treatment with curative intent within 9 months after incidence date Indicator B: Numerator number of cIII lung cancer patients in whom brain imaging by CT or MRI was obtained before the start of their first treatment with curative intent (<3 months before start of treatment) Denominator: all cIII lung cancer patients who received first treatment with curative intent within 9 months after incidence date
Target	SIGN put forward a target of 95% for indicator A.[11] The tolerance level within this target accounts for the fact that some patients will refuse to undergo PET-CT, for different reasons. In addition, in patients with small peripheral tumours (T1 N0 disease) PET-CT may not always be clinically appropriate. We did not find information allowing to set a target for B. There is however no real reason why this should not be done, but some patients may refuse.
Data source	BCR + IMA
Technical definition	Diagnostic of lung cancer: ICD-10 code C34 (BCR) (Table 103 in appendix) PET-CT: billing codes (IMA) in Table 97 in appendix Brain imaging (CT or MRI): billing codes (IMA) in Table 94(CT) and Table 96 (MRI) Treatments with curative intent: surgery (IMA, Table 74), radiotherapy (IMA, Table 75) In case of neo-adjuvant treatment or sequential chemo-radiotherapy, start date is start of chemotherapy.
Subgroup analyses	By type of lung cancer (NSCLC, SCLC), per clinical stage, per treatment modality, per age at diagnosis and sex.

Sensitivity analyses	Indicator A: 3 versus 6 months before start of treatment, combined stage I-III included if clinical stage unknown Indicator B: 3 versus 6 months before start of treatment, cI-II for brain imaging
Benchmarking	Diagnostic centre
International indicator	Indicator A: used by SIGN (Scotland) and in Italy[12], US[13], Australia[14] Indicator B: used in the US[13] and in Taiwan [4]

3.3.2 *Flowchart*



B


All lung cancer patients (N=12 839)
Clinical stage III?
No (N=10 304)
Yes (N=2535)
Surgery or RT with curative intent < 9 months?
No (N=1240)
Yes (N=1295)
CT or MRI brain < 3 months before start of treatment?
No (N=276)
Yes (N=1019)

3.3.3 Results

3.3.3.1 INDICATOR A: PET-CT before start of treatment with curative intent

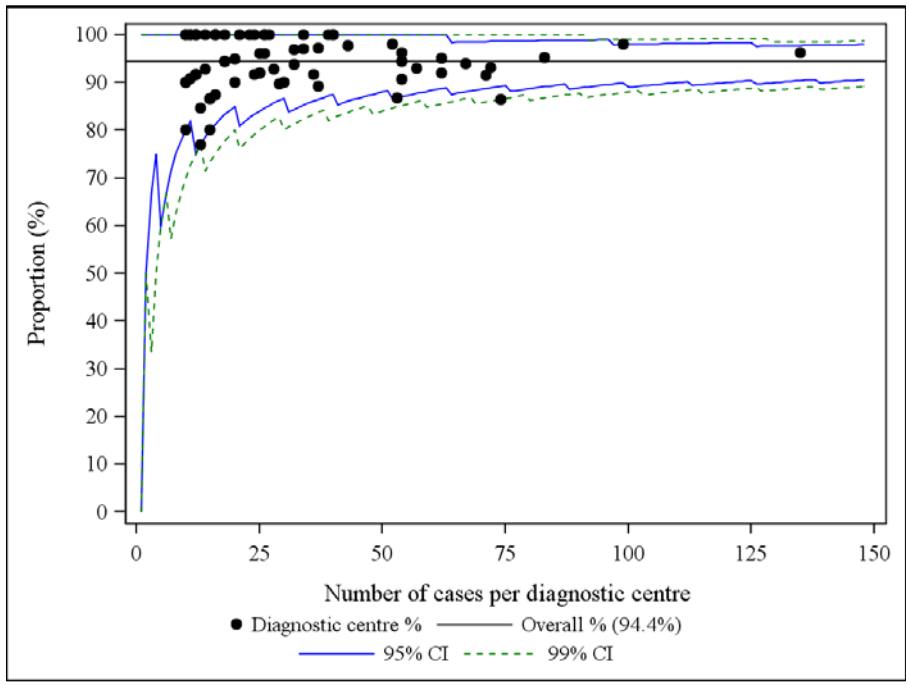
Table 14 – Proportion of cI-III NSCLC patients who had PET-CT prior to first treatment with curative intent, by patient, tumour and treatment characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	2471	2332	94.4
Sex			
Males	1762	1665	94.5
Females	709	667	94.1
Age group			
<50 years	133	115	86.5
50-59 years	500	482	96.4
60-69 years	848	811	95.6
70-79 years	749	709	94.7
80+ years	241	215	89.2
Histological Subtype			
Adenocarcinoma	1086	1028	94.7
Squamous cell carcinoma	1095	1038	94.8
Large cell carcinoma	89	83	93.3
Other	201	183	91.0
Clinical stage			
I	953	902	94.6
II	463	441	95.2
III	1055	989	93.7

Characteristic	Denominator	Numerator	Proportion (%)
Treatment modality			
(Chemo)radiotherapy	1157	1074	92.8
Surgical resection with curative intent	1314	1258	95.7

Source: BCR-IMA

Figure 10 – Proportion of cI-III NSCLC patients who had PET-CT prior to first treatment with curative intent, by diagnostic centre



Note 1: 3 patients were not shown in the figure because they could not be assigned to a diagnostic centre.
Note 2: 11 centres were not shown in the figure because they reported less than 50% of clinical stages.
Note 3: 19 centres were not shown in the figure because the denominator was smaller than 10.
Note 4: 1 centre was not shown in the figure because it had no cI-III NSCLC patients.
Source: BCR-IMA

Table 15 – Proportion of cI-III NSCLC patients who had PET-CT within 3 months before start curative treatment versus within 6 months before start curative treatment

	Denominator	Numerator	Proportion (%)
3 months before start treatment	2471	2332	94.4
6 months before start treatment	2471	2375	96.1

Source: BCR-IMA

Table 16 – Proportion of cI-III versus combined stage I-III (unknown clinical stage) NSCLC patients who had PET-CT before start of treatment with curative intent

	Denominator	Numerator	Proportion (%)
Clinical stage I-III	2471	2332	94.4
Combined stage I-III (unknown clinical stage)	3052	2874	94.2

Source: BCR-IMA

3.3.3.2 INDICATOR B: brain imaging before start of treatment for cIII lung cancer patients

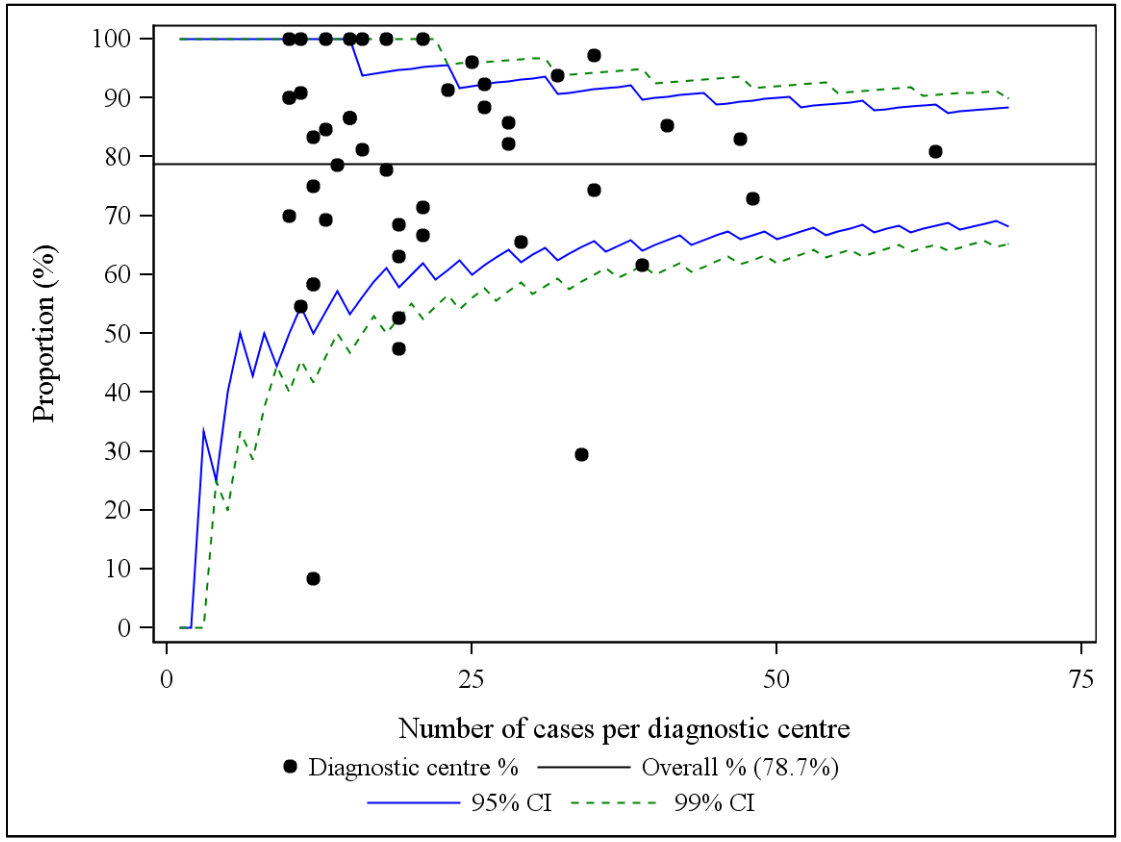
Table 17 – Proportion of cIII patients who had brain imaging (CT or MRI) before first treatment with curative intent, by patient, tumour and treatment characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	1295	1019	78.7
Sex			
Males	950	760	80.0
Females	345	259	75.1
Age group			
<50 years	68	53	77.9
50-59 years	319	259	81.2
60-69 years	463	362	78.2

Characteristic	Denominator	Numerator	Proportion (%)
70-79 years	334	267	79.9
80+ years	111	78	70.3
Histological (sub)type			
Non-small cell lung cancer	1055	821	77.8
Adenocarcinoma	422	315	74.6
Squamous cell carcinoma	504	410	81.3
Large cell carcinoma	42	34	81.0
Other	87	62	71.3
Small cell lung cancer	210	179	85.2
Other specified lung cancer	30	19	63.3
Treatment modality			
(Chemo)radiotherapy	1028	810	78.8
Surgical resection with curative intent	267	209	78.3

Source: BCR-IMA

Figure 11 – Proportion of cIII patients who had brain imaging (CT or MRI) before first treatment with curative intent, by diagnostic centre



Note 1: 1 patient was not shown in the figure because he/she could not be assigned to a diagnostic centre.
Note 2: 10 centres were not shown in the figure because they reported less than 50% of clinical stages.
Note 3: 43 centres were not shown in the figure because the denominator was smaller than 10.
Note 4: 2 centres were not shown in the figure because it had no cIII patients.
Source: BCR-IMA

Table 18 – Proportion of cIII patients who had brain imaging (CT or MRI) before start of treatment, within 3 months versus within 6 months before start treatment

	Denominator	Numerator	Proportion (%)
3 months before start curative treatment	1295	1019	78.7
6 months before start curative treatment	1295	1034	79.8

Source: BCR-IMA

Table 19 – Proportion of cIII patients who had brain imaging (CT or MRI) before treatment with curative intent, versus cI patients and cII patients

	Denominator	Numerator	Proportion (%)
Clinical stage I patients	1109	752	67.8
Clinical stage II patients	515	397	77.1
Clinical stage III patients	1295	1019	78.7

Source: BCR-IMA

3.3.4 Discussion

Indicator A

The use of PET scan in stage I to III NSCLC patients who received treatment with curative intent was uniformly high at 94%, with only limited variation accros subgroups and in the sensitivity analysis. Also variability across centres was not higher than could be explained purely by chance, with only one centre outside the 95% confidence limits and none outside the 99% limits. In Australia[14], PET was used before combined chemotherapy and radiotherapy in 100% of the cases. In Italy[12], proportion of patients receiving PET was 30.8% (28.4–33.2%) in 2004 and 23.1% (16.7–29.5%) in 2006, however this percentage was calculated over all patients, so it is not comparable to our indicator.

Indicator B

Overall proportion was 79%, with limited variation across age groups, with the exception of the age group above 80 years old, which was a bit lower, at 70.5%. There is a small difference between sexes, with a slightly lower proportion in women. Proportion is highest among patients with small cell lung cancer. There seems to be no difference between patients undergoing (chemo)radiotherapy and patients undergoing surgical resection with curative intent. There is more variation across centres than what could be expected solely based on chance, with some outliers having a low percentage, and on the other hand, a larger number of centres seem to have for 100% than can be expected due to chance. In the sensitivity analysis, no difference is seen if you look at 6 months before treatment, and a lower percentage of clinical stage I patients underwent brain imaging.

In Taiwan, proportion of patients receiving either spine or brain MRI was around 60%, with slight variations depending on region and type of health structure.[4] In 11 Oncology Practices in Florida[13], 60% of patients with chemoradiation underwent brain imaging, ranging between centres from 28% to 90%. Proportion in Belgium are thus higher than what is internationally reported, although only a limited number of publications exist.

Key Points

- **The use of PET scan in clinical stage I to III NSCLC patients was uniformly high at 94%**
- **The use of brain imaging was reported in 78.5% of stage III patients, with moderate variation across centres and somewhat lower rates in women and patients above 80 years old.**

3.4 Invasive mediastinal staging (DS-5)

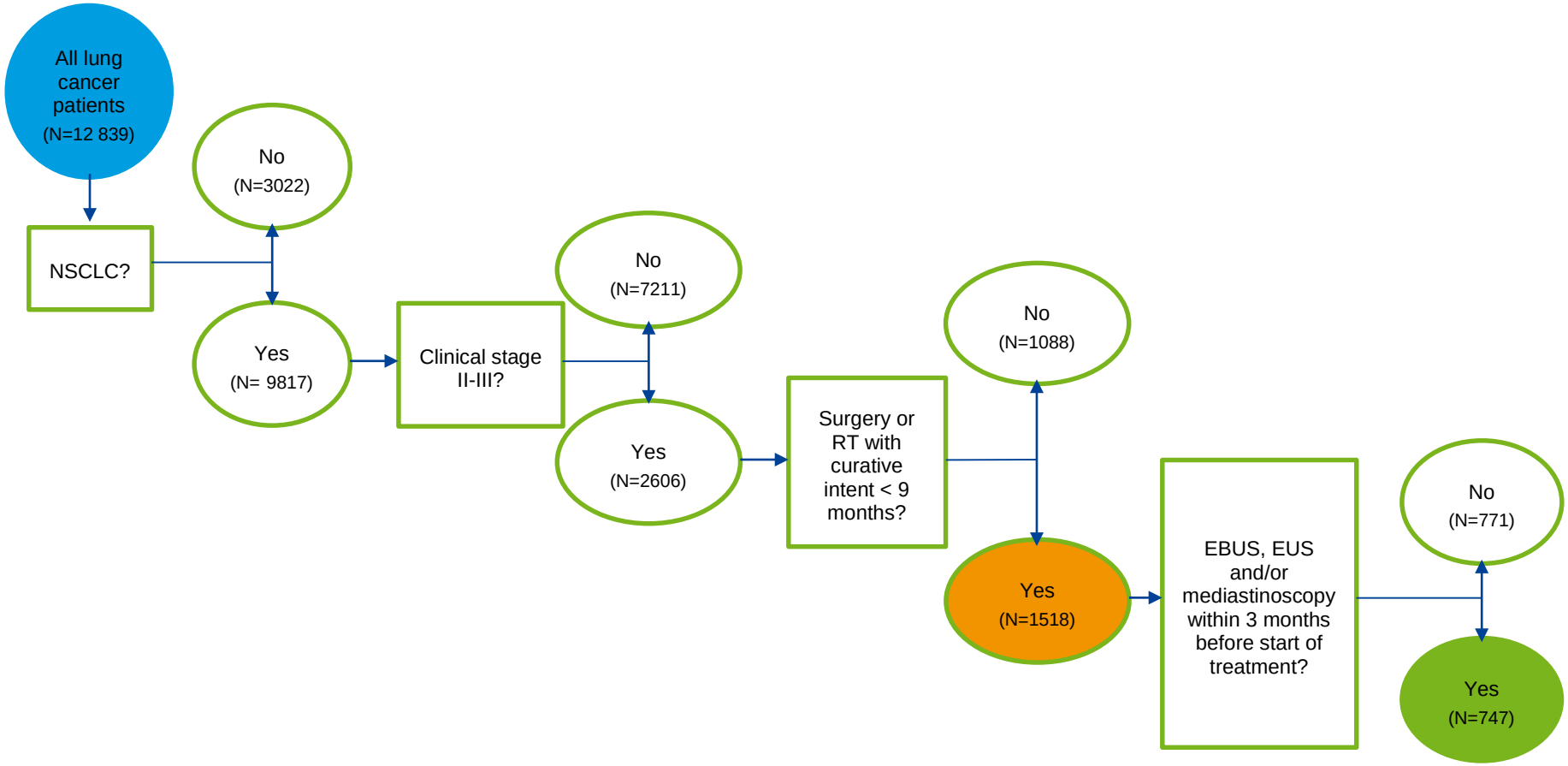
3.4.1 Documentation sheet

Title	**Indicator A:** **Proportion of cII-III NSCLC patients who had (minimally) invasive mediastinal staging before treatment with curative intent** **Indicator B:** **Proportion of cII-III NSCLC patients who had mediastinoscopy for whom the mediastinoscopy was preceded by EBUS or EUS before treatment with curative intent**
Rationale	Recommendation Belgian clinical guideline: If distant metastases are excluded, proceed to pathological confirmation of lymph node metastasis when o PET-CT of the lymph nodes is positive (in case of a PET positive primary tumour) or o if CT shows mediastinal lymph nodes of more than 1 cm or o if the primary tumour is close to the mediastinum or o when hilar adenopathies are present. Such patients should be offered invasive mediastinal staging. The preferred approach is combined EBUS and EUS (endoscopic ultrasound), followed by mediastinoscopy if no lymph node metastasis is found by EBUS or EUS. Otherwise proceed directly to thoracotomy.
Type of QI	Process
Calculation	Indicator A: Numerator: number of cII-III NSCLC patients who had EBUS, EUS or mediastinoscopy within 3 months before start of their first treatment with curative intent Denominator: all cII-III NSCLC patients who received treatment with curative intent within 9 months after incidence date Indicator B: Numerator: number of cII-III NSCLC patients for whom EBUS or EUS was performed *before* the mediastinoscopy Denominator: all cII-III NSCLC patients who had a mediastinoscopy before treatment with curative intent within 9 months after incidence date
Target	A target is difficult to determine, as it depends on the results of PET or CT. We can only see what the average practice is in Belgium. For indicator B it depends on the feasibility of EUS and EBUS.
Data source	BCR + IMA

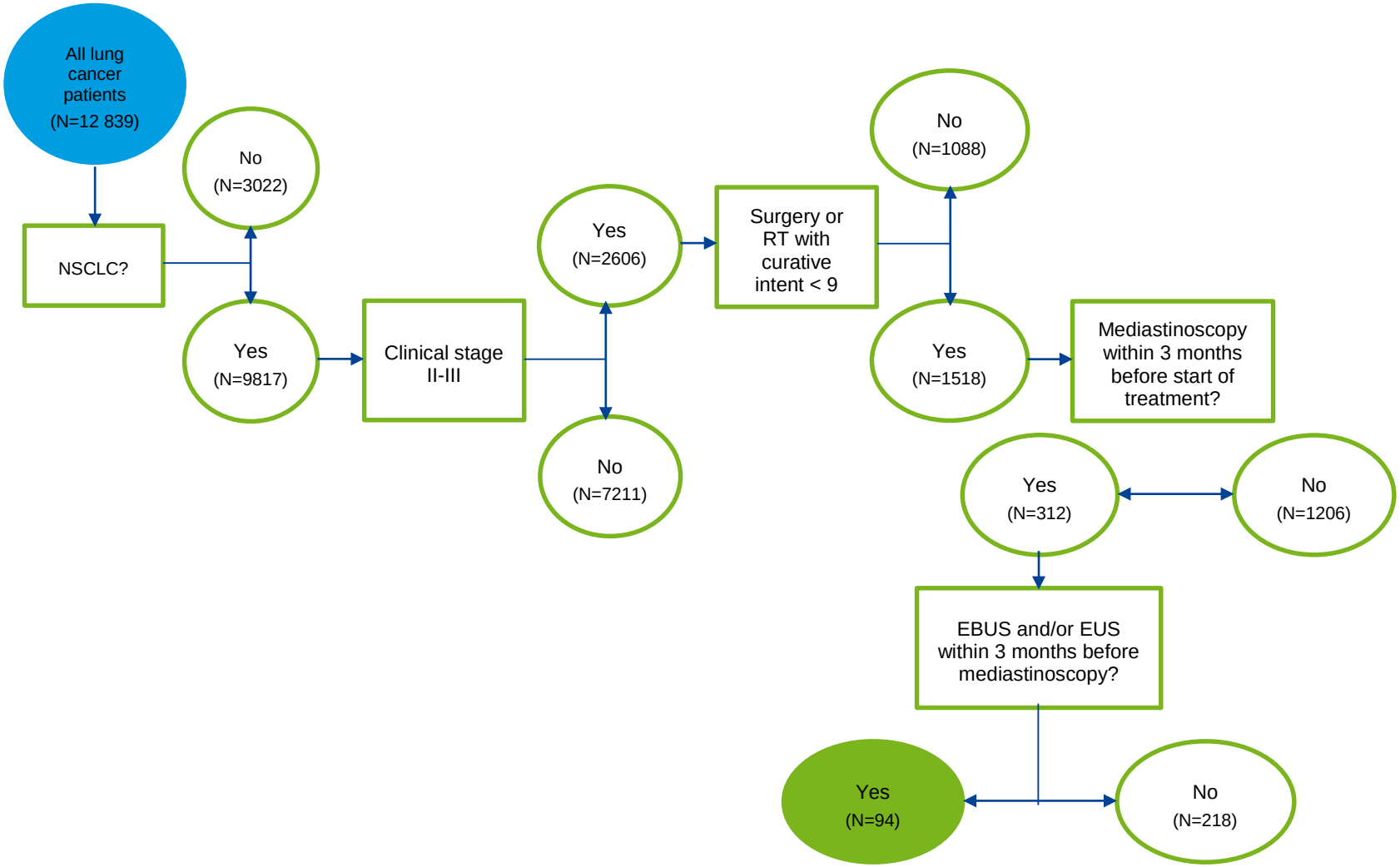
Technical definition	Diagnosis of lung cancer: ICD-10 code C34 (BCR) Surgery with curative intent: billing codes (IMA) in Table 74 (appendix) Radiotherapy with curative intent: billing codes (IMA) in Table 75 (appendix). In case of neo-adjuvant chemotherapy or sequential chemoradiation: start of treatment = start of chemotherapy
Limitations	Mediastinal staging according to the Belgian guidelines is recommended depending on the results of PET or CT. As results of PET-CT are not available, it is not easy to interpret the proportions measured.
Subgroup analyses	Per clinical stage, treatment modality
Sensitivity analyses	Proportion of patients who underwent surgery with pN2/3 despite preoperative mediastinal staging, by staging procedure Proportion of patients who had PET-CT only and have pN0 stage Clinical stage or pathological stage (when clinical stage is missing)
Benchmarking	For indicator A: diagnostic centre For indicator B: no analysis per centre
International indicator	National organisations: SIGN (Scotland), NICE (UK) Results published in US[15] [16] [17] [3] and Italy[12]

3.4.2 *Flowchart*

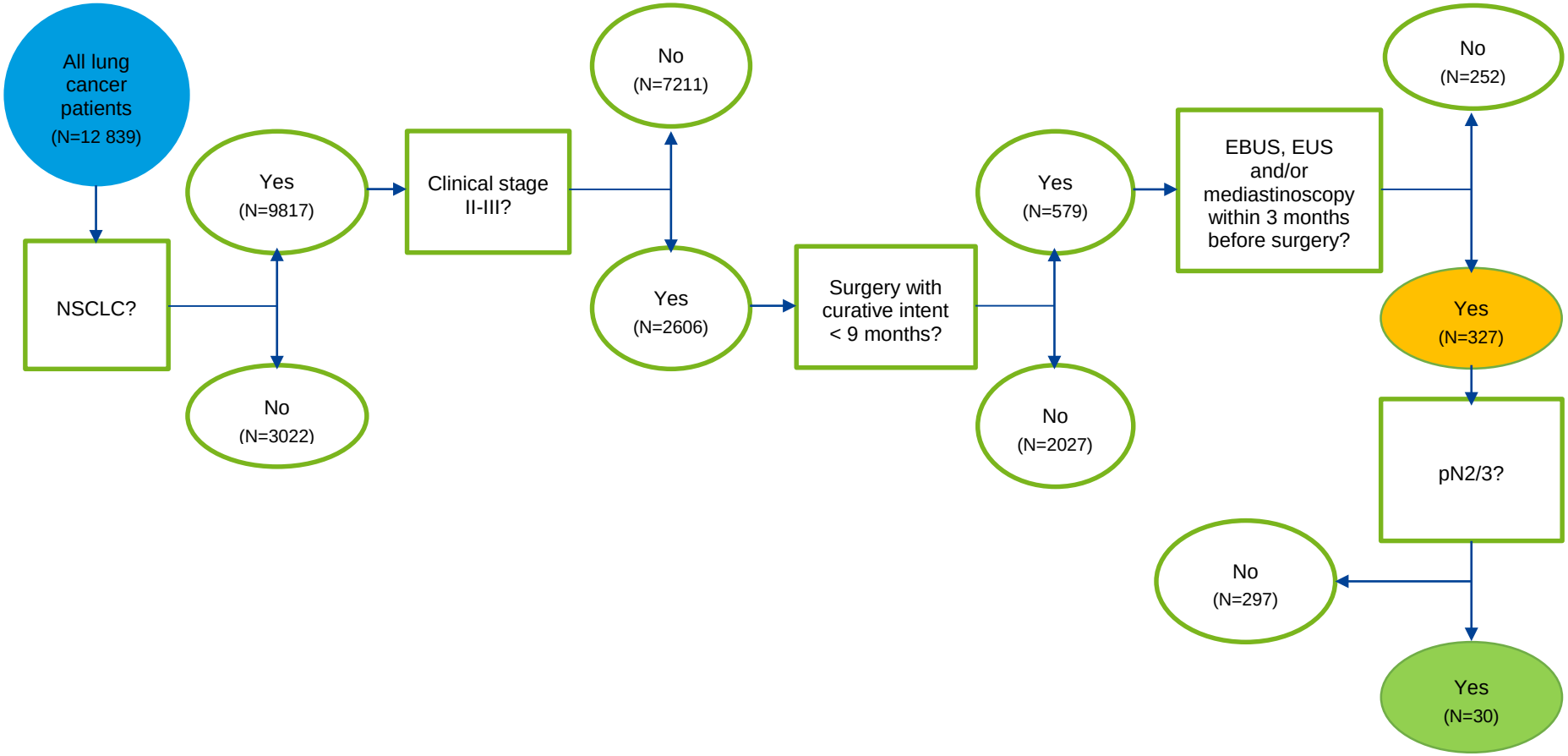
A)

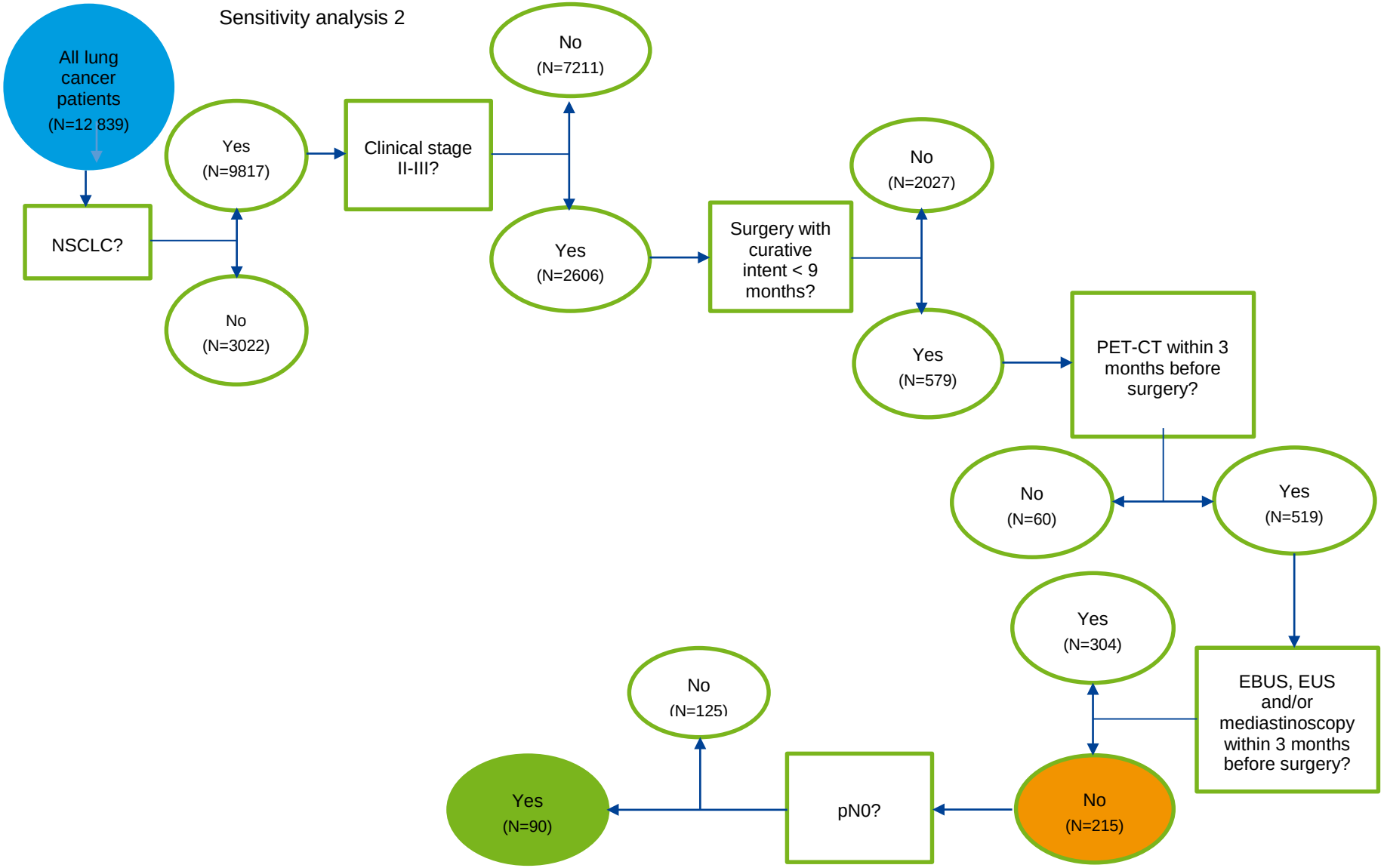


B)


All lung cancer patients (N=12 839)
NSCLC?
No (N=3022)
Yes (N=9817)
Clinical stage II-III
Yes (N=2606)
No (N=7211)
Surgery or RT with curative intent < 9
No (N=1088)
Yes (N=1518)
Mediastinoscopy within 3 months before start of treatment?
Yes (N=312)
No (N=1206)
EBUS and/or EUS within 3 months before mediastinoscopy?
Yes (N=94)
No (N=218)

Sensitivity analysis 1




Sensitivity analysis 2
All lung cancer patients (N=12 839)
NSCLC?
Yes (N=9817)
No (N=3022)
Clinical stage II-III?
No (N=7211)
Yes (N=2606)
Surgery with curative intent < 9 months?
No (N=2027)
Yes (N=579)
PET-CT within 3 months before surgery?
No (N=60)
Yes (N=519)
EBUS, EUS and/or mediastinoscopy within 3 months before surgery?
Yes (N=304)
No (N=215)
pN0?
No (N=125)
Yes (N=90)

3.4.3 Results

Table 20 – Proportion of cII-III NSCLC patients who had (minimally) invasive mediastinal staging before treatment with curative intent, by clinical stage and treatment

Characteristic	Denominator	Numerator	Proportion (%)
Overall	1518	747	49.2
Clinical stage			
II	463	223	48.2
III	1055	524	49.7
Treatment modality			
(Chemo)radiotherapy	939	393	41.9
Surgical resection with curative intent	579	354	61.1

Source: BCR-IMA

Table 21 – Proportion of patients with pN2/3 despite preoperative mediastinal staging

	Denominator	Numerator	Proportion (%)
Overall	327	30	9.2

Source: BCR-IMA

Table 22 – Pathological N stage for patients who had PET-CT only

	Denominator	Numerator	Proportion (%)
pN0	215	90	41.9
pN1	215	42	19.5
pN2/3	215	21	9.8
pN unknown	215	62	28.8

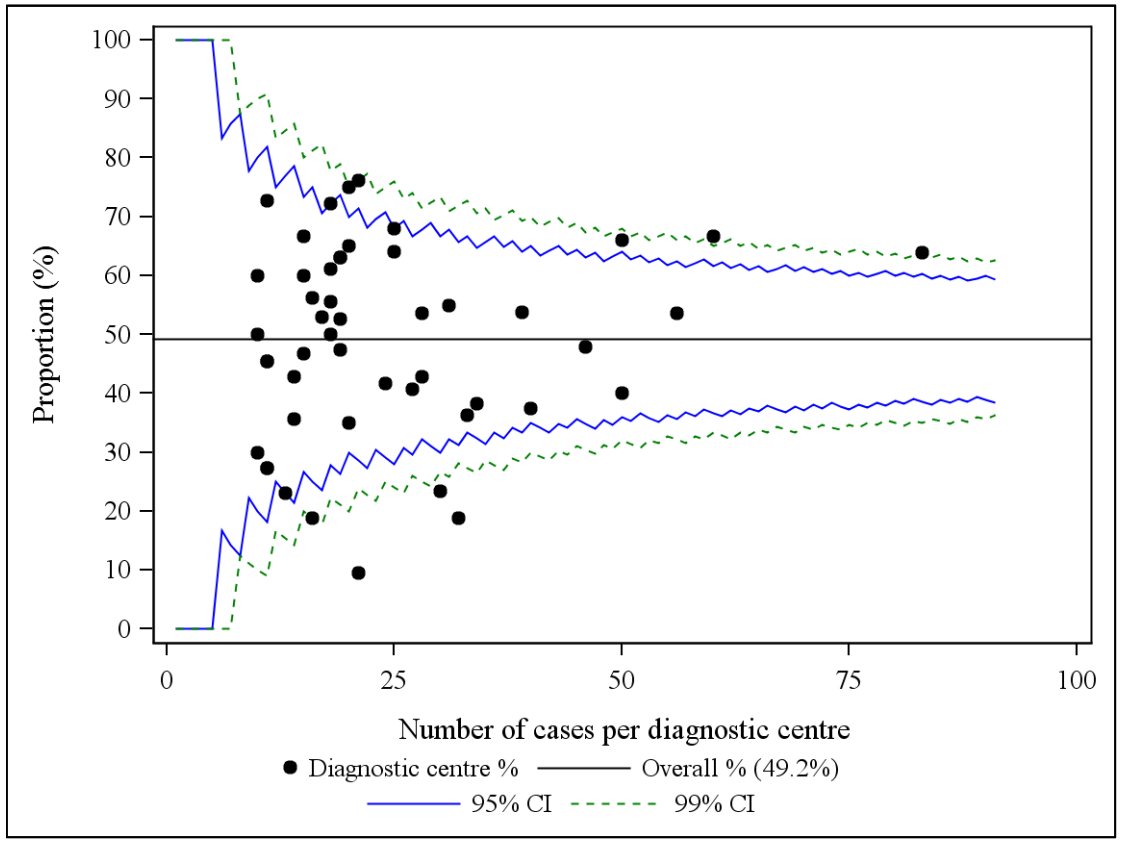
Source: BCR-IMA

Table 23 – Stage distribution of operated patients, clinical stage if available, otherwise pathological stage

	Numerator	Proportion (%)
Overall	2084	100.0
I	1084	52.0
II	464	22.3
III	332	15.9
IV	100	4.8
X	104	5.0

Source: BCR-IMA

Figure 12 – Proportion of cII-III NSCLC patients who had (minimally) invasive mediastinal staging before treatment with curative intent, by diagnostic centre

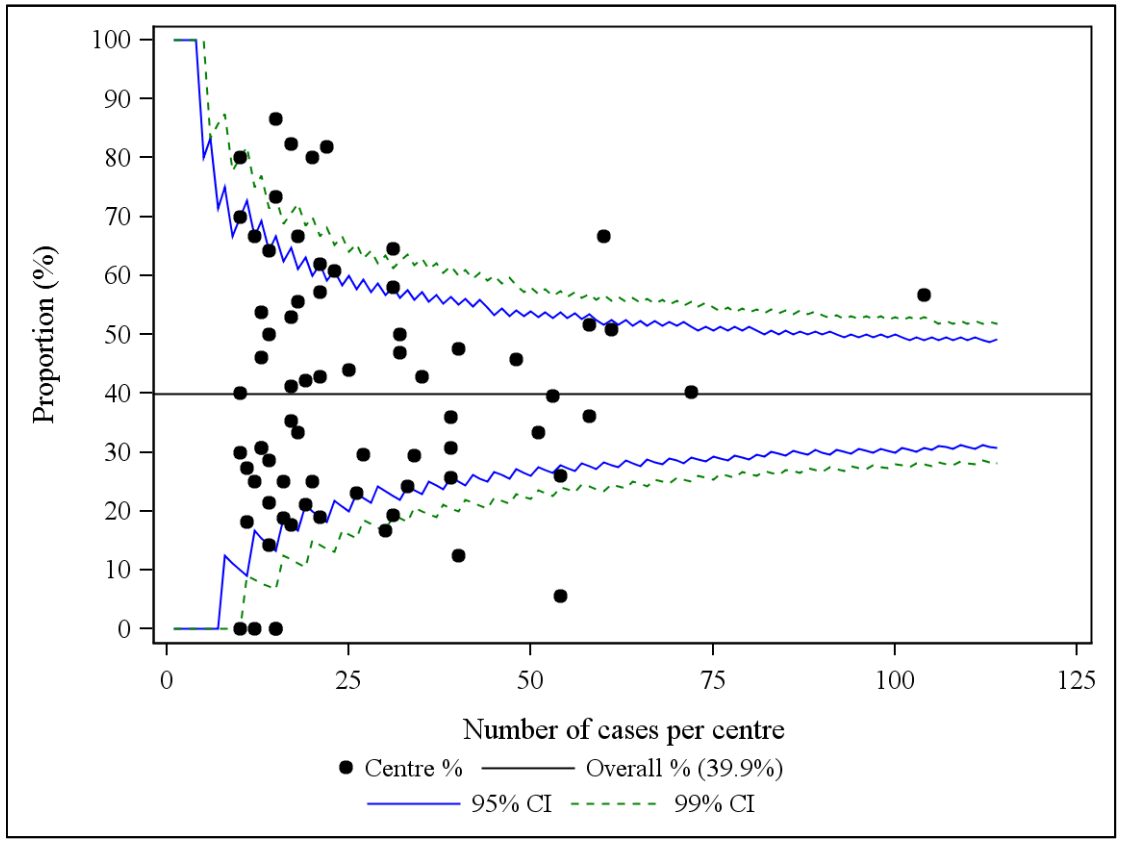


Note 1: 1 patient was not shown in the figure because he/she could not be assigned to a diagnostic centre.
Note 2: 10centres were not shown in the figure because they reported less than 50% of clinical stages.
Note 3: 41 centres were not shown in the figure because the denominator was smaller than 10.
Note 4: 2 centre were not shown in the figure because they had no cI-III NSCLC patients.
Source: BCR-IMA

Table 24 – Proportion of surgically treated NSCLC patients who had (minimally) invasive mediastinal staging before treatment with curative intent, by clinical stage

Characteristic	Denominator	Numerator	Proportion (%)
Overall	2084	832	39.9
Clinical stage			
I	735	220	29.9
II	321	184	57.3
III	258	170	65.9
IV	89	32	36.0
X	681	226	33.2

Figure 13 – Proportion of surgically treated NSCLC patients who had (minimally) invasive mediastinal staging before treatment with curative intent, by diagnostic centre



Note 1: 1 patient was not shown in the figure because he/she could not be assigned to a diagnostic centre.
Note 2: 31 centres were not shown in the figure because the denominator was smaller than 10.
Source: BCR-IMA

Table 25 – Proportion of cII-III NSCLC patients who had mediastinoscopy preceded by EBUS or EUS before treatment with curative intent, by tumour and treatment characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	312	94	30.1
Clinical stage			
II	122	43	35.2
III	190	51	26.8
Treatment modality			
(Chemo)radiotherapy	116	31	26.7
Surgical resection with curative intent	196	63	32.1

Source: BCR-IMA

3.4.4 Discussion

Forty-nine percent of cII-III NSCLC patients had (minimally) invasive mediastinal staging before treatment with curative intent. This proportion was somewhat higher in cIII patients compared to cII patients and considerably higher in patients with surgical resection with curative intent compared to (chemo)radiotherapy. Variability of this parameter is only marginally larger than what could be expected based on random error alone, with a few outliers recording a low rate.

Recommended mediastinal staging according to the Belgian guidelines depends on the results of PET and CT, which we do not have, so it is not easy to interpret the proportions measured, as this may also depend on the number of patients that actually are suspected to have pathological lymph nodes based on imaging. In order to understand this better we did some sensitivity analyses, or rather some additional analyses that could provide some help in interpreting the indicator.

- 90 out of 215 (42%) of patients that underwent PET before surgery but no invasive mediastinal staging were pN0, these patients would clearly not have benefitted from invasive staging.
- 9% of patients who underwent surgery had pN2/3 despite preoperative mediastinal staging, indicating that staging has a fair negative predictive value and seems effective. We do not have data to compare this internationally.

Of the patients that do undergo mediastinoscopy, less than a third underwent first either EBUS or EUS. This proportion is relatively low, as EBUS or EUS, less invasive techniques, may spare unnecessary mediastinoscopies that are more invasive.

Results for similar indicators are reported in the international literature for the US[15] [16] [17] [3] and Italy[12], but the way the indicators are operationalised differs too much to use them as a base for comparison, often because results of the imaging were available and can be informative when measuring the indicator.

In Italy[12], 2% of all lung cancer patients underwent mediastinoscopy. In the US, 93% “Pathologic staging of mediastinum in stage I, II, or III NSCLC” was reported (adherence was defined as receiving it, refusing it or documented clinical contra-indication) but close to one fifth of facilities with at least six eligible cases had adherence rates as low as 40% to 80%.[3] In another

setting in the US, if tumour >4 cm, central, and/or has a max SUV of 9 or greater, mediastinal staging procedures such as EUS–FNA and/or EBUS performed with rapid on site cytology and/or mediastinoscopy were realized in 100% of cases. In another setting in the US it was reported that 44% never had mediastinal sampling before start of therapy (patients with nodal spread but without distant metastases).[16] In a fourth setting in the US, of 333 patients undergoing pulmonary resection for primary lung cancer, mediastinal staging was accomplished by at least one of the three criteria processes in 313 cases (94%). Cervical mediastinoscopy with lymph node biopsy was done in 90 patients (27%), positron emission tomography in 199 (59.8%), mediastinal lymphadenectomy in 283 (85%), and all three modalities in 60 (18%).[15]

Key Points

- **Fourty-nine percent of clinical stage II-III NSCLC patients had (minimally) invasive mediastinal staging before treatment with curative intent.**
- **Interpretation is hampered because we do not have the results of the PET scan or CT, to evaluate if invasive mediastinal staging was justified/needed (Belgian guidelines). However, centres that have a lower proportion of patients who underwent mediastinal staging should be encouraged to review their practice.**
- **Of the patients who underwent mediastinoscopy, less than a third was preceded by either EBUS or EUS.**

3.5 Pulmonary function tests before surgery (DS-6)

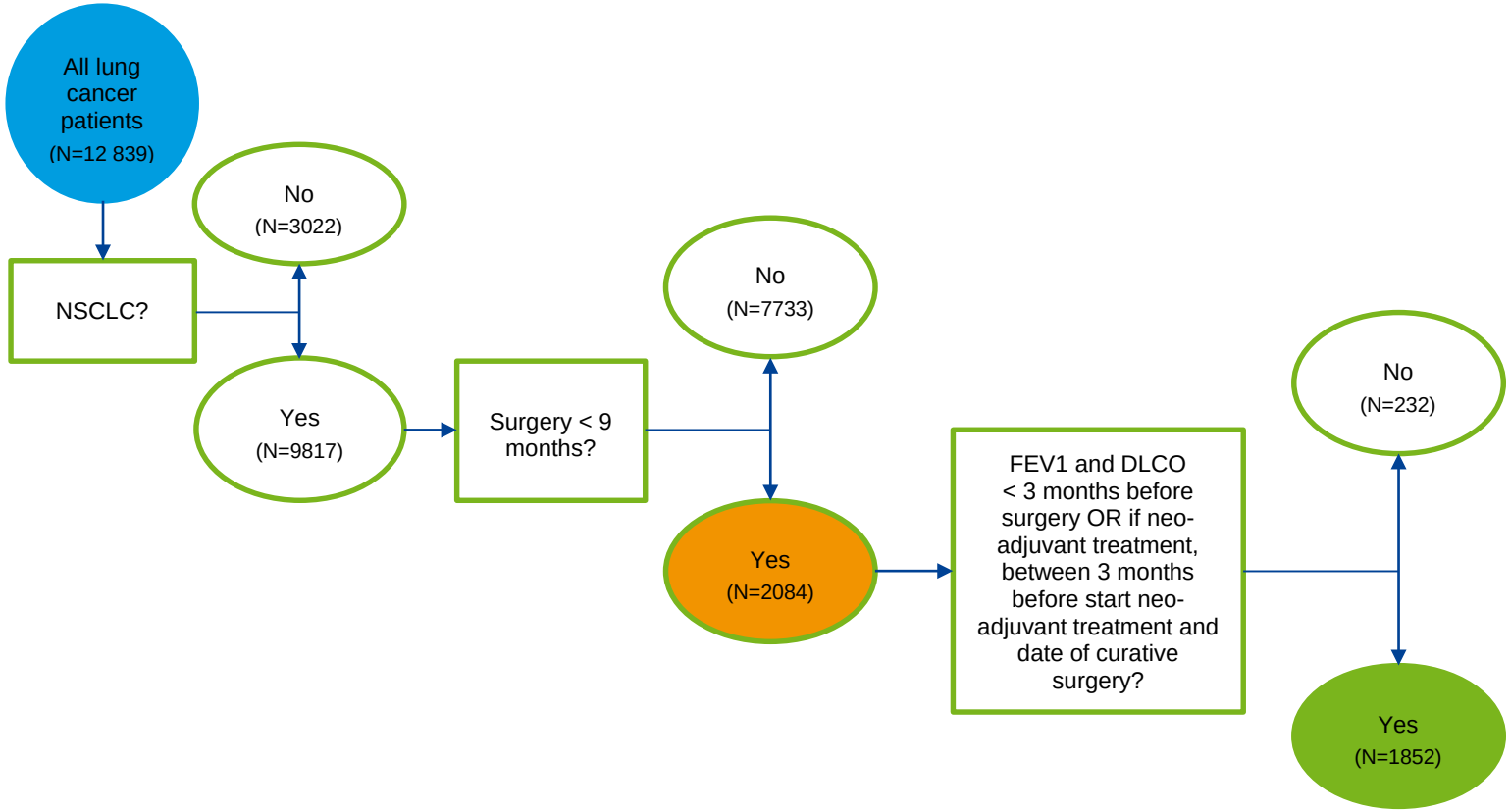
3.5.1 Documentation sheet

Title	Proportion of NSCLC patients who have FEV1 and DLCO performed before surgery
Rationale	Preoperative lung function is an important factor to evaluate the expected benefits and risks of operative treatment of lung cancer, both in the short term (perioperative complications) and long term (postoperative quality of life, survival). Lung tests are thus important for selecting patients who are eligible for surgery with curative intent. Furthermore, early detection of reduced lung function provides the opportunity to optimise respiratory function preoperatively.[15] Both the American college of chest physicians and the Belgian clinical guideline recommends to perform both FEV1 and DLCO preoperatively.[18, 19]
Type of QI	Process
Calculation	Numerator: number of NSCLC patients who had FEV1 and DLCO performed within 3 months before curative surgery (with or without neoadjuvant chemotherapy) Denominator: all NSCLC patients who had surgery with curative intent within 9 months after incidence date
Target	95%
Data source	BCR + IMA
Technical definition	Diagnostic of lung cancer: ICD-10 code C34 with ICD-O-3 morphology codes 8010-8040, 8046-8245, 8247-8576 (BCR) (Table 103) Surgery with curative intent: billing codes (IMA) in Table 74 FEV1 codes: billing codes 471251-471262 en 471273-471284 (Table 82) DLCO codes: billing codes 471354-471365 (Table 82) In case of neo-adjuvant treatment, use 3 months before start of chemotherapy or radiotherapy until date of surgery
Limitations	
Subgroup analyses	Per patient age at diagnosis, sex Per clinical stage
Sensitivity analyses	Per type of lung test performed
Benchmarking	Diagnostic centre

Table 26 – Pulmonary function before surgery: International results

Author	Period covered	Country	Results
National Lung Cancer Audit Report 2014	2013	United Kingdom	The overall proportion having the percentage predicted FEV1 (result) recorded in the audit database is 67.1% for patients with good performance status and earlier stage cancer.
Cassivi 2008	2005	Single institution, USA	74.2% had pulmonary function testing, defined as FEV1 and DLCO obtained within 365 days before lung resection
Cerfolio 2011	2007-2009	Single institution, USA	89% of operated patients had pre-operatively a full set of pulmonary function tests defined as FEV1%, DLCO% and DLCO/VA% obtained ≤30 days before surgery.
Brunelli 2009	2001-2003	Europe	The average rate of DLCO measurement (in patients with ppoFEV1 <40%) was 16.3% (SD 31.6)

3.5.2 Flowchart



3.5.3 Results

Table 27 – Proportion of NSCLC patients who had FEV1 and/or DLCO performed before surgery

	Denominator	Numerator	Proportion (%)
Both tests (FEV1 + DLCO)	2084	1852	88.9
FEV1 (with or without DLCO)	2084	1936	92.9
DLCO (with or without FEV1)	2084	1866	89.5
No test performed	2084	134	6.4

Source: BCR-IMA

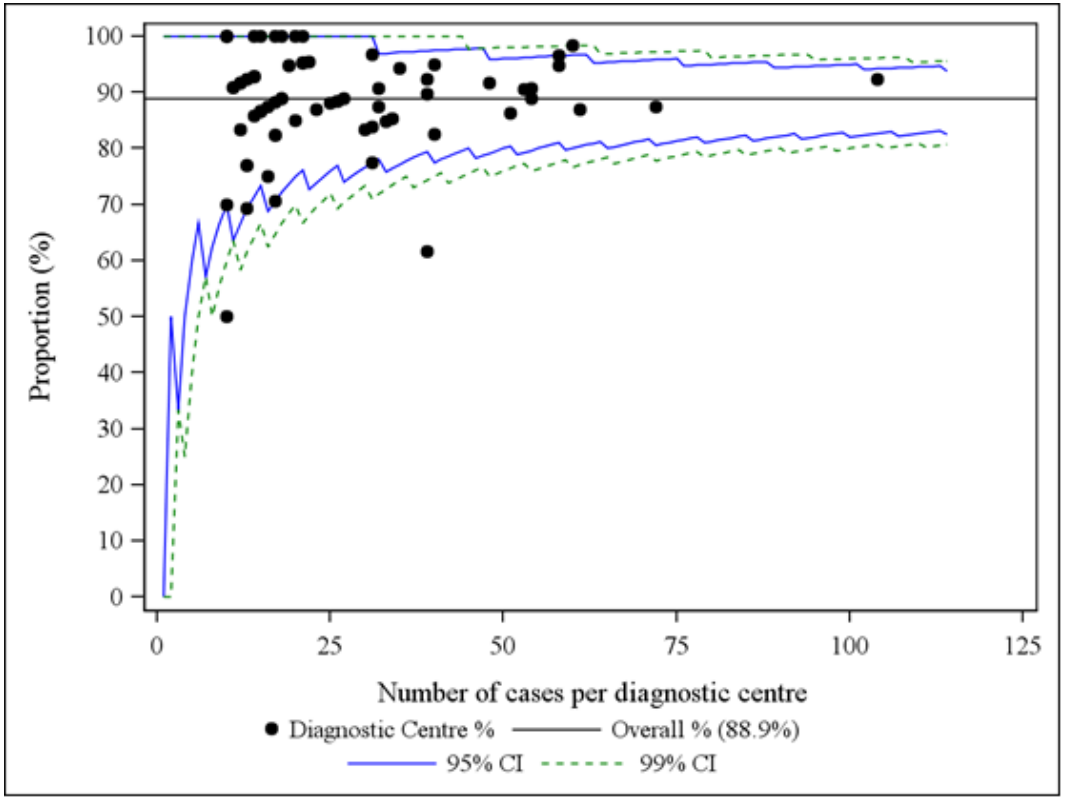
Table 28 – Proportion of NSCLC patients who have FEV1 and DLCO performed before surgery, by patient and tumour characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	2084	1852	88.9
Sex			
Male	1404	1255	89.4
Female	680	597	87.8
Age group			
<50 years	135	115	85.2
50-59 years	489	440	90.0
60-69 years	783	691	88.3
70-79 years	596	534	89.6
80+ years	81	72	88.9
Clinical stage			
I	735	653	88.8
II	321	297	92.5
III	258	242	93.8

Characteristic	Denominator	Numerator	Proportion (%)
IV	89	71	79.8
X	681*	589	86.5

Source: BCR-IMA
** pathological stage: pI: N=349; pII N=143, pIII N=74, pIV N=11, pX N=104*

Figure 14 – Proportion of NSCLC patients who have FEV1 and DLCO performed before surgery, by diagnostic centre



Note 1: 1 patient was not shown in the figure because he/she could not be assigned to a diagnostic centre.
Note 2: 31 centres were not shown in the figure because the denominator was smaller than 10.
Source: BCR-IMA

3.5.4 Discussion

Overall, the proportion of patients who underwent both recommended lung function tests is high (89%), also compared with results from other countries. Slightly more patients underwent FEV1 or DLCO only.

Variability between centres appears acceptable with only few outliers and test performance is not related to age, stage, or sex.

Possible reasons why the two pulmonary function tests may not be obtained in all patients include:

Test was performed in reality but did not appear in reimbursement data of IMA. A more in depth evaluation with two outlying hospitals revealed that this was the case for all patients who scored negatively for this indicator.

Test was performed slightly out of the timeframe or date of reimbursement may be different

Performing both tests may be perceived as unnecessary. The NICE guideline on lung cancer for example, recommends to perform a DLCO test only if breathlessness is disproportionate or if there is other lung pathology (for example, lung fibrosis).[20]

Finally, (one of the) tests may not be performed due to failure of local processes.

Proposed actions for improvement

Theoretically, both tests can be performed preoperatively in all patients as contra-indications are extremely rare. Centres, and especially centres that performed both tests in less than 90% of patients, are encouraged to verify and optimise their local protocols and clinical care pathways so that appropriate lung function testing occurs in nearly 100% of the patients.

Key Points

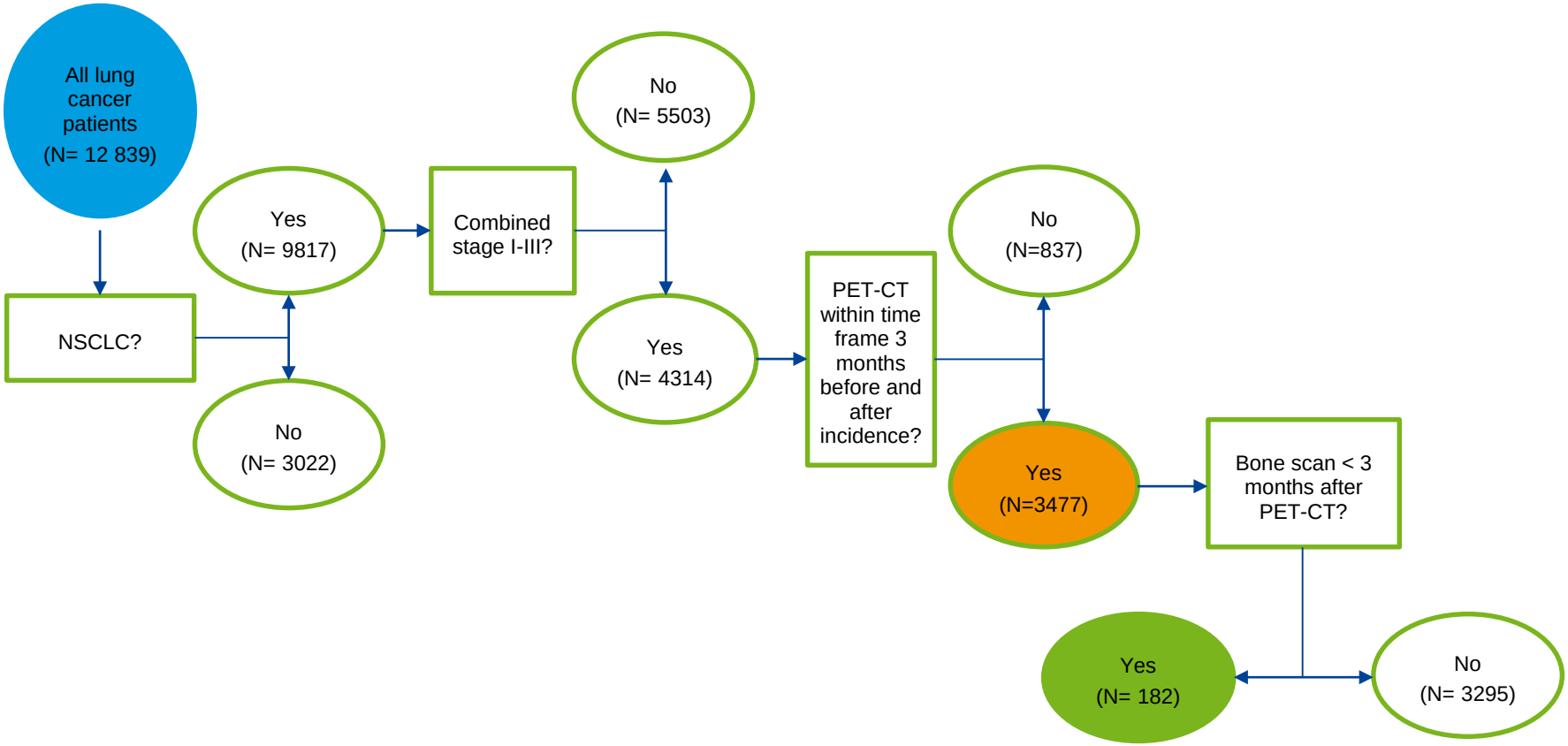
- **Ninety percent of patients who underwent surgical treatment for lung cancer had both recommended pulmonary function tests (FEV1, DLCO) performed before surgery.**
- **Variability between centres appears acceptable and test performance is not related to age, stage or sex.**

3.6 No bone scintigraphy performed after a PET-CT (DS-7)

3.6.1 Documentation sheet

Title	Proportion of early stage NSCLC patients who had a bone scintigraphy performed after a PET-CT
Rationale	In the Belgian guideline the following recommendation is formulated: “Do not offer bone scintigraphy to NSCLC patients if a PET-scan has been performed and all relevant body parts are included.”
Type of QI	Process
Calculation	Numerator: number of early stage NSCLC patients who had a bone scintigraphy performed within 3 months after a PET-CT Denominator: number of early stage NSCLC patients who had a PET-CT performed within 3 months before or after incidence date
Target	No target
Data source	BCR + IMA
Technical definition	Diagnostic of NSCLC: ICD-10 code C34 with ICD-O-3 morphology codes 8010-8040, 8046-8245, 8247-8576 (BCR) (Table 103 in appendix) PET-CT: billing codes (IMA) in Table 97 (appendix) Bone scan: billing codes in Table 98 (appendix)
Limitations	Some patients may have symptoms that lead to suspicion of bone metastases but were not covered by the PET scan, in particular if distal parts of the skeleton are involved.
Subgroup analyses	None
Sensitivity analyses	Early stage patients who received bone scan before PET-CT, early stage patients who received bone scan around incidence date
Benchmarking	Diagnostic centre
International indicator	We did not find reports on the exact indicator, only on the total number of patients undergoing bone scan.

3.6.2 *Flowchart*



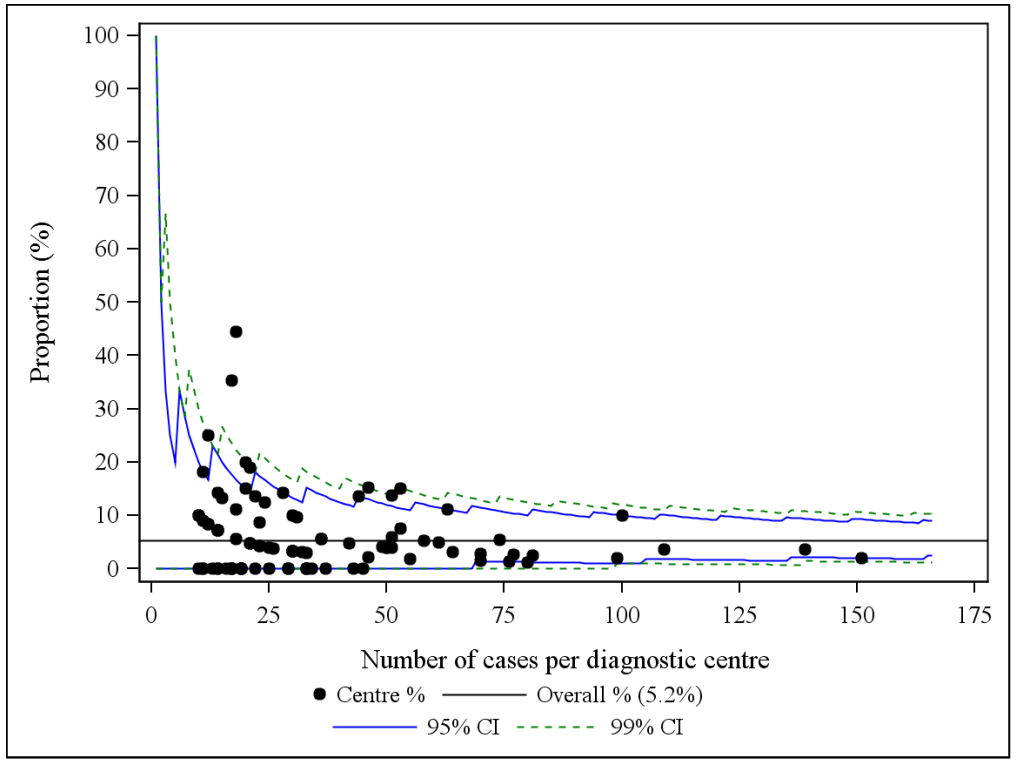
3.6.3 Results

Table 29 – Proportion of early stage NSCLC patients who had a bone scintigraphy performed after a PET-CT

	Denominator	Numerator	Proportion (%)
Overall	3477	182	5.2

Source: BCR-IMA

Figure 15 – Proportion of early-stage NSCLC patients who had a bone scintigraphy performed after a PET-CT, by diagnostic centre



Note: 9 centres were not shown in the figure because the denominator was smaller than 10.
Source: BCR-IMA

Table 30 – Sensitivity analyses on the timing of bone scan versus PET-CT and incidence date

	Denominator (early stage)	Numerator	Proportion (%)
Bone scan within 3m after PET-CT (-3m < inc <+3m)	3 477	182	5.2
Bone scan within 3m before PET-CT (-3m < inc < +3m)	3 477	693	19.9
Bone scan around incidence date (-3m < inc <+3 m)	4 314	1 270	29.4

Source: BCR-IMA

3.6.4 Discussion

The percentage of bone scans performed after a PET-CT is low, the funnel plot shows that this percentage is fairly uniform, with a couple of real outliers and a number of centres falling in the zone between the 95% and 99% confidence intervals. The sensitivity analysis shows that the percentage of patients receiving both PET-CT and bone scan (around 20%) as well as the total percentage of patients receiving bone scans is much higher. This can be explained by the limited access to PET-scan at the time of diagnosis.

In Taiwan, between 37 and 60% of patients received a bone scan, but this indicator is for all stages and difficult to interpret in our context.[4]

Key Points

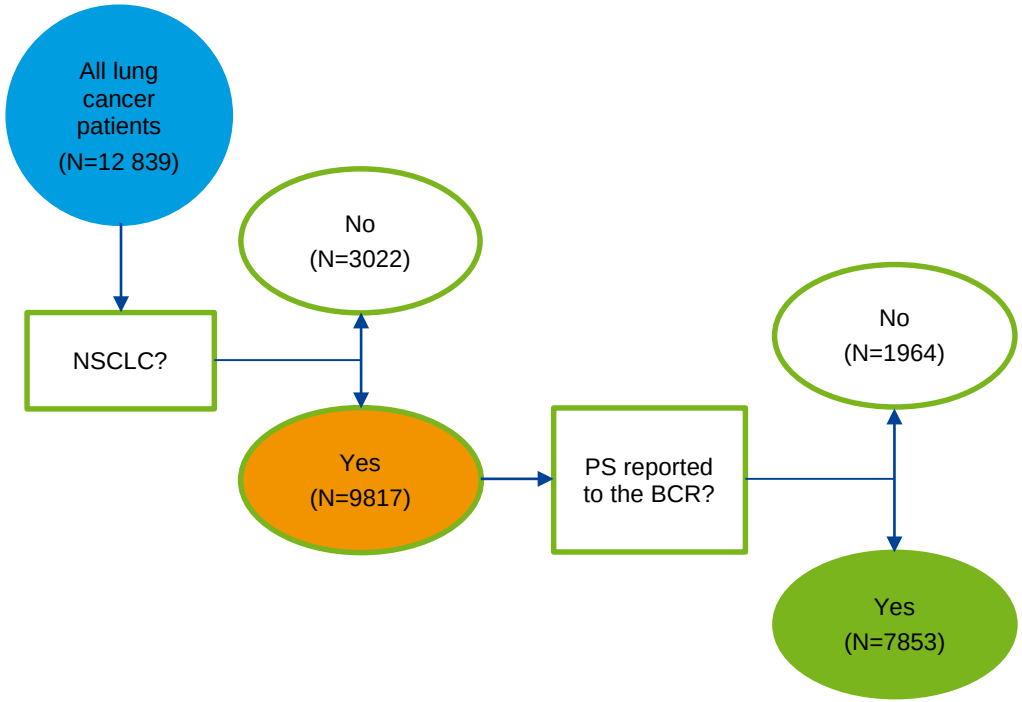
- **Around 5% of early stage patients received a bone scan after a PET scan.**

3.7 Performance status reported to the BCR (DS-8)

3.7.1 Documentation sheet

Title	Proportion of NSCLC patients for whom WHO performance status was assessed at presentation
Rationale	Performance status (PS) is an important prognostic factor for clinical outcomes after lung cancer care. Judging performance status is key to determine the optimal treatment for each individual patient. Furthermore, complete data on performance status can be used to investigate the effect of treatment in a population not included in clinical trials and for case-mix correction purposes.
Type of QI	Process
Calculation	Numerator: number of NSCLC patients for whom performance status (WHO) at presentation was reported to the BCR Denominator: all NSCLC patients
Data source	BCR
Technical definition	Diagnosis of NSCLC: ICD-10 code C34 with ICD-O-3 morphology codes 8010-8040, 8046-8245, 8247-8576 (Table 103 in appendix)
Limitations	Performance status may be assessed but not reported in the medical file and/or not reported to the Belgian Cancer Registry.
Subgroup analyses	By age at diagnosis, sex, treatment modality, by stage
Sensitivity analyses	Include also SCLC
Benchmarking	By diagnostic centre
International indicator	Tanvetyanon et al. noted that PS was assessed in 75% of stage III-IV NSCLC patients.[13] The National Lung Cancer Report from the UK had PS information available for 92.9% of 2013 cases.[10]

3.7.2 *Flowchart*



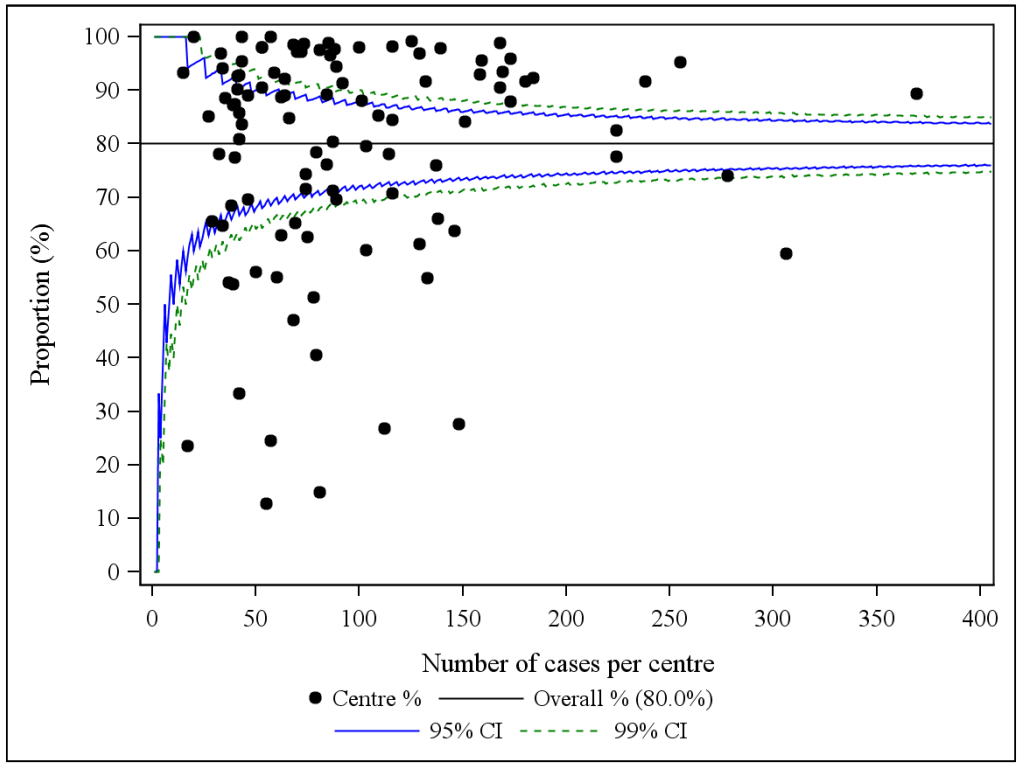
3.7.3 Results

Table 31 – Proportion of NSCLC patients for whom WHO performance status at presentation was reported to the Belgian Cancer Registry, by patient, tumour and treatment characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	9817	7853	80.0
Sex			
Males	6904	5541	80.3
Females	2913	2312	79.4
Age group			
<50 years	547	464	84.8
50-59 years	1931	1564	81.0
60-69 years	3058	2462	80.5
70-79 years	2981	2373	79.6
80+ years	1300	990	76.2
Clinical stage			
I	1107	1006	90.9
II	619	581	93.9
III	1987	1835	92.4
IV	3875	3569	92.1
X	2229	862	38.7
Treatment modality			
(Chemo)radiotherapy	2001	1713	85.6
Chemotherapy including targeted treatment	3692	2991	81.0
Surgical resection with curative intent	2084	1657	79.5
No treatment	2040	1492	73.1

Source: BCR

Figure 16 – Proportion of NSCLC patients for whom WHO performance status at presentation was reported to the Belgian Cancer Registry, by diagnostic centre



Note: 87 patients were not shown in the figure because they could not be assigned to a diagnostic centre.
Source: BCR

Table 32 – Proportion of lung cancer patients for whom WHO performance status at presentation was reported to the Belgian Cancer Registry, by histological type

Characteristic	Denominator	Numerator	Proportion (%)
Non-small cell lung cancer	9817	7853	80.0
Small cell lung cancer	2004	1558	77.7
Other specified lung cancer	1018	903	88.7

Source: BCR

3.7.4 Discussion

Overall, 80% of patients have their performance status reported to the BCR with not much variability according to age, sex or treatment received. There is considerable variability between centres however, and patients for whom no clinical stage was recorded were clearly less likely to have the PS at diagnosis reported to the BCR.

Theoretically, failure to report performance status to the BCR can be due to absence of formal assessment and recording of the PS in the medical file or due to errors in the transfer of data from the medical file to the BCR. Therefore, results cannot be interpreted as an unambiguous reflection of the quality of care delivered. However, correct and complete data collection is an essential part of an integrative quality system that assures continuous quality improvement and delivery of high quality care to all oncological patients.

Centres are thus encouraged to verify if WHO performance status is systematically assessed and reported at diagnosis and if all data are correctly transferred to the BCR so that possible flaws can be corrected.

Key Points

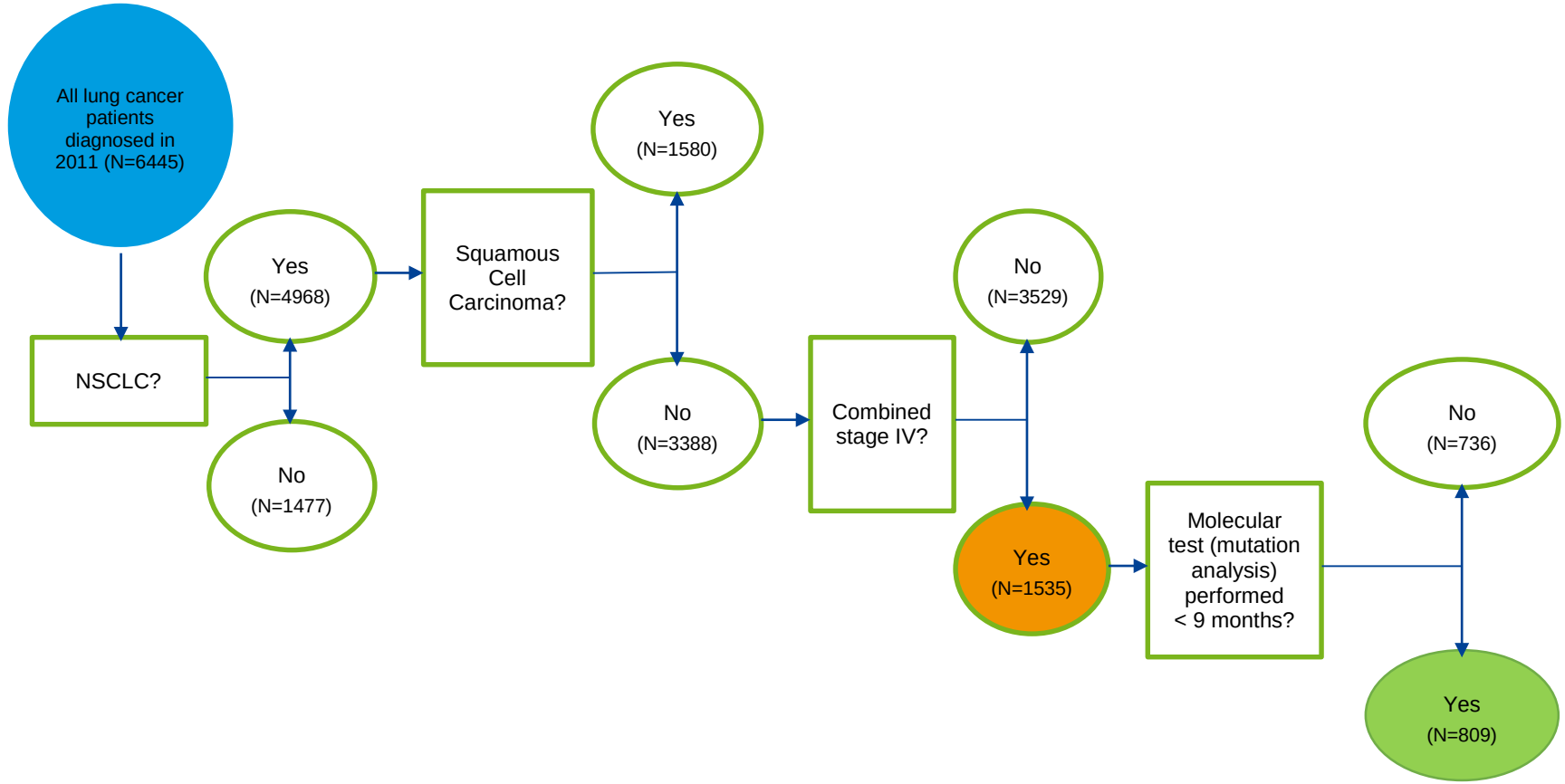
- **Performance status at presentation is not reported to the BCR for 20% of patients, especially for patients for whom clinical stage is also not reported, with considerable variability between centres.**
- **Underreporting of PS has important consequences for the measurement of other quality indicators, because TNM stage is a crucial parameter for the evaluation of quality (patient selection, definition of indicators, case mix adjustment for outcomes,...)**
- **Centres are encouraged to verify if data are lacking in the medical files or if transfer of data to the BCR can improve.**

3.8 EGFR Mutation analysis in stage IV non-squamous NSCLC patients (DS-9)

3.8.1 Documentation sheet

Title	Proportion of stage IV non-squamous NSCLC patients in whom (EGFR) mutation analysis was performed
Rationale	KCE guideline recommended EGFR testing. As response to EGFR targeted therapy depends on the presence of activating EGFR mutations, tests for these mutations should be offered to patients with non-squamous NSCLC or never/light smokers with mixed squamous/non-squamous cell carcinoma, potentially eligible for EGFR targeted therapy.
Type of QI	Process
Calculation	Numerator: number of patients from the denominator in whom (any) mutation analysis was performed within 9 months after incidence date Denominator: all combined stage IV non-squamous cell NSCLC patients diagnosed during 2011
Target	Two reasons for not testing: no treatment planned due to comorbidity and no enough tissue to perform the test.
Data source	BCR + IMA
Technical definition	Diagnosis of stage IV NSCLC: ICD-10 code C34 (BCR) (squamous excluded) (Table 103) Mutation analyses: billing codes in IMA (Table 86, article 33, 33bis)
Limitations	At the moment the data were collected EGFR mutation analysis was not yet recommended
Subgroup analyses	
Sensitivity analyses	Include also results for squamous cell, patients who received no active treatment within 9 months after incidence date excluded
Benchmarking	Diagnostic centre
International indicator	Similar indicators are used in UK and the Netherlands

3.8.2 Flowchart



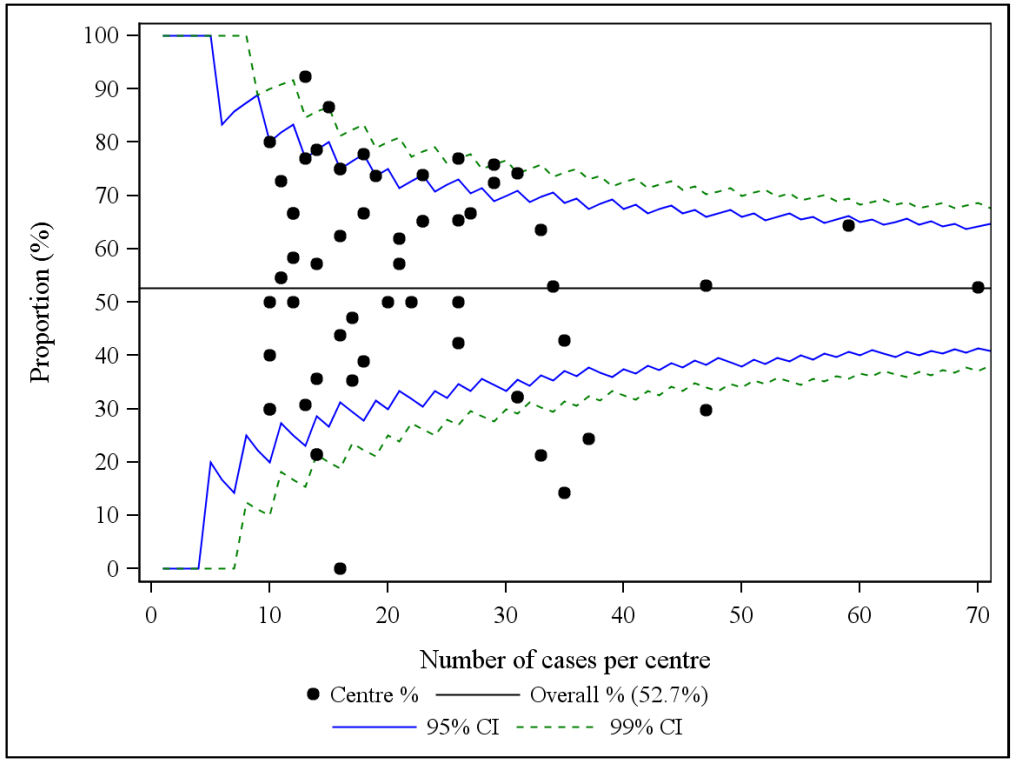
3.8.3 Results

Table 33 – Proportion of stage IV non-squamous NSCLC patients in whom (EGFR) mutation analysis was performed (2011)

Characteristic	Denominator	Numerator	Proportion (%)
Overall	1535	809	52.7

Source: BCR-IMA

Figure 17 – Proportion of stage IV non-squamous NSCLC patients for whom (EGFR) mutation analysis was performed (2011), by diagnostic centre



Note 1: 11 patients were not shown in the figure because they could not be assigned to a diagnostic centre.
Note 2: 41 centres were not shown in the figure because the denominator was smaller than 10.
Source: BCR-IMA

Table 34 – Proportion of stage IV NSCLC patients for whom (EGFR) mutation analysis was performed, by histopathological subtype (2011)

Characteristic	Denominator	Numerator	Proportion (%)
Non-squamous cell NSCLC	1535	809	52.7
Adenocarcinoma	1268	731	57.6
Other non-squamous cell	267	78	29.2
All NSCLC	1961	866	44.2

Source: BCR-IMA

Table 35 – Proportion of stage IV non-squamous NSCLC patients who received active treatment in whom (EGFR) mutation analysis was performed (2011), treatment received versus no treatment received

Characteristic	Denominator	Numerator	Proportion (%)
All stage IV non-squamous cell NSCLC (with EGFR)	1535	809	52.7
Stage IV non-squamous cell NSCLC who received active treatment (with EGFR)	1260	726	57.6

Source: BCR-IMA

3.8.4 Discussion

A bit more than half of the patients with stage IV non-squamous NSCLC received EGFR mutation analysis. Variability is somewhat larger than what could be expected purely by chance, with a few centres having very low testing rates. To correctly interpret this indicator, it is important to take into account that, at the moment the data were collected, there was no recommendation to ask for EGFR mutation testing as its role was still under debate. It will be important to see how this indicator will evolve in the future.

We did a sensitivity analysis and found that the proportion is somewhat higher in patients who received active treatment, as clinicians may choose not to test if no treatment is planned. Note that this sensitivity analysis of the indicator may be over-optimistic: it remains possible that patients that could have been treated with TKI inhibitors did not receive treatment due to lack of testing. Proportion dropped to 44% if all NSCLC were used as denominator, as could be expected, as testing is only indicated in non-squamous NSCLC.

NICE calculates the proportion of people with lung cancer who have an analysis of predictive markers, without specifying tumour type or cancer stage. This indicator was measured by the LungPath project in 22 centres. EGFR mutations were in some centres tested only in the adenocarcinomas and other non-squamous cell carcinomas while in other centres all non-small cell carcinomas were tested. The cases which had had an EGFR mutation test were taken as a percentage of the cases with adenocarcinomas and the non-small cell carcinomas and varied from 12.0% to 91.7%. The majority of EGFR tests were returned as “wild type” where no mutation was detected. The percentage of cases returned as “mutant” varied between centres from 4.8% to 50.0%.[21]

The Scottish Cancer Taskforce adopted a very similar indicator, with the difference that they used as denominator all NSCLC patients that underwent

pathological testing. As the proportion undergoing pathology testing in Belgium is high this should not make a big difference. The Taskforce put forward a target of 75%, leaving a tolerance margin accounting for the fact that part of the biopsies do not contain enough tissue to perform the testing. It is not clear why this tolerance margin is as high as 25%. [11]

IKNL reported that in 2011, 48% of the stage IV non-squamous NSCLC cases were tested for EGFR mutations, a figure similar to ours. Authors considered that the proportion of EGFR testing was too low and that there was a need to identify bottlenecks and barriers to testing. [22]

Key Points

- **In 2011, 53% of patients with non-squamous NSCLC underwent EGFR mutation analysis.**
- **At that time, guidelines on the importance of EGFR mutation analysis were not yet available. Therefore, the data analysis for 2011 can not yet be used as an indicator to evaluate the quality of care for that time period. However, this indicator must be followed-up in the future.**

3.9 EGFR mutation analysis before anti-EGFR treatment (DS-10)

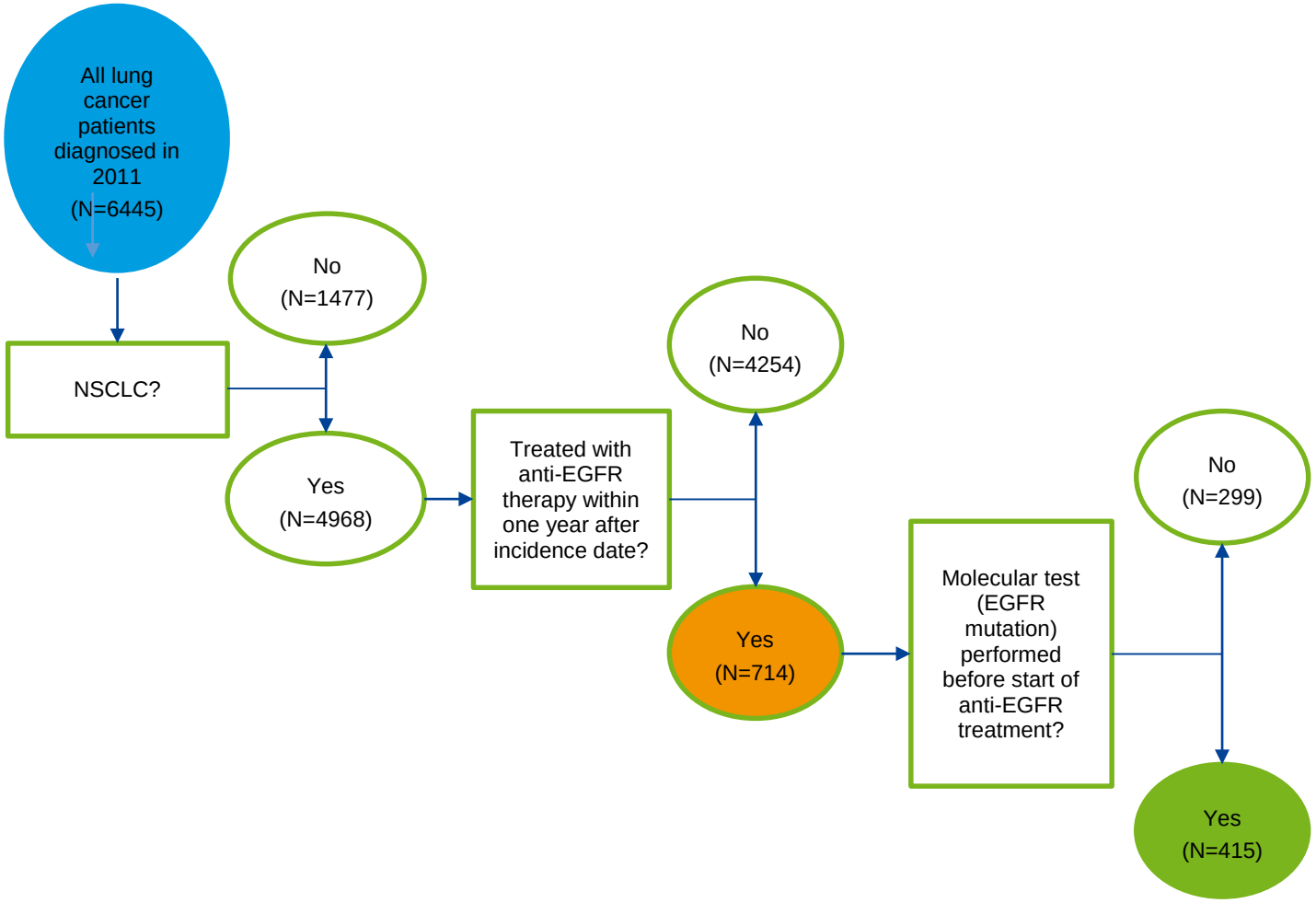
3.9.1 Documentation sheet

Title	Proportion of NSCLC patients receiving anti EGFR treatment who were tested for EGFR-mutation prior to treatment
Rationale	The clinical effectiveness of anti-EGFR treatment in lung cancer has been shown in several RCTs. Post-hoc meta-analysis has shown that the effect may be limited to tumours that harbour an activating EGFR mutation. Most recent data suggest very limited effect in wild type tumours. To avoid treatment when benefit is unlikely (and thus causing unnecessary toxicity and costs), anti-EGFR treatment should be preserved for patients with a mutation-positive tumour revealed by molecular tests.
Type of QI	Process
Calculation	Numerator: number of NSCLC patients who receive anti-EGFR treatment for whom a molecular test (EGFR mutation analysis) on the tumour was performed before the start of anti-EGFR treatment Denominator: all NSCLC patients diagnosed in 2011 who receive anti-EGFR treatment within one year after incidence date
Target	90% The tolerance within this guidance is designed to account for patients with insufficient tissue available to perform mutation analysis.
Data source	BCR + IMA
Technical definition	Diagnostic of NSCLC: ICD-10 code C34 with ICD-O-3 morphology codes 8010-8040, 8046-8245, 8247-8576 (BCR) Anti EGFR targeted treatment: gefitinib (L01XE02), erlotinib (L01XE03), afatinib (L01XE13) Mutation analysis: billing codes in Table 86 (article 33, 33 bis) Test using immunohistochemistry (IHC): billing codes in Table 85 (article 32)
Limitations	Reimbursement criteria for erlotinib as second (or further) line therapy do not require EGFR mutation analysis, immunohistochemistry (IHC) is sufficient. Results of the mutation tests are not known, patients can thus be treated with anti-EGFR therapy in spite of a negative mutation test, following the reimbursement criteria based on immunohistochemistry.
Subgroup analyses	
Sensitivity analyses	Numerator: IHC only, no mutation analysis Denominator: all NSCLC patients diagnosed in 2011 who receive anti-EGFR treatment within one year after incidence date
Benchmarking	No benchmarking analysis
International indicator	See Table 36

Table 36 – EGFR mutation analysis before treatment: International results

Author	Period covered	country	Results
IKNL Longkanker – kankerzorg in beeld	2011	The Netherlands	In 2011, an EGFR analysis was performed for half of the patients with an adenocarcinoma. For large cell carcinoma and squamous cell carcinoma, the mutation analysis was performed in 25% and 4% respectively.

3.9.2 Flowchart



3.9.3 Results

Table 37 – Proportion of NSCLC patients receiving anti EGFR treatment who were tested for EGFR-mutation

	Denominator	Numerator	Proportion (%)
Overall	714	415	58.1

Source: BCR-IMA

Table 38 – Proportion of NSCLC patients receiving anti EGFR treatment who were tested for EGFR-mutation compared with NSCLC patients receiving anti EGFR treatment who were only tested with IHC

	Denominator	Numerator	Proportion (%)
EGFR mutation analysis performed	714	415	58.1
EGFR mutation analysis and IHC performed	714	275	38.5
Only IHC performed	714	187	26.2
No test	714	112	15.7

Source: BCR-IMA

3.9.4 Discussion

Currently, three anti-EGFR tyrosine kinase inhibitors are reimbursed in Belgium. For erlotinib as maintenance therapy or in second-line (or more), at least 10% of the cells should be positive for EGFR on IHC. For other indications and molecules, mutation analysis should show an activating mutation in the EGFR region. These reimbursement criteria are based on the eligibility criteria of the clinical trials performed for each indication. However, also for erlotinib, more recent subgroup analyses for mutation carrying versus wild-type tumours suggest that the efficacy of anti-EGFR treatment is restricted to mutation carrying tumours and the effect in EGFR wild-type tumours remain very uncertain and may be very limited.[19]

As the recommendations to limit anti-EGFR therapy to patients with a mutation carrying tumour came out only after the period analysed (2011), the results cannot be interpreted as an indication of the quality of care delivered at that time. Nevertheless, insight in the testing and prescribing pattern of 2011 may be helpful to draw attention to current knowledge and discrepancies between reimbursement criteria and optimal patient selection criteria.

More than half of the patients receiving anti-EGFR treatment had a mutation analysis performed before start of treatment. As 66% also had IHC testing, it is possible that patients with a wild-type tumour also started treatment based on the IHC results (results of tests not known for this study). Of the 299 patients without mutation analysis, 112 had no IHC test performed either. It must be noted however that only specific reimbursement codes were taken into account, possibly performed tests may be reimbursed using other codes or within the setting of a clinical trial.

To implement current recommendations, centres are encouraged to review their prescribing patterns of 2011, evaluate possible changes in their processes during recent years and further adapt if necessary.

Key Points

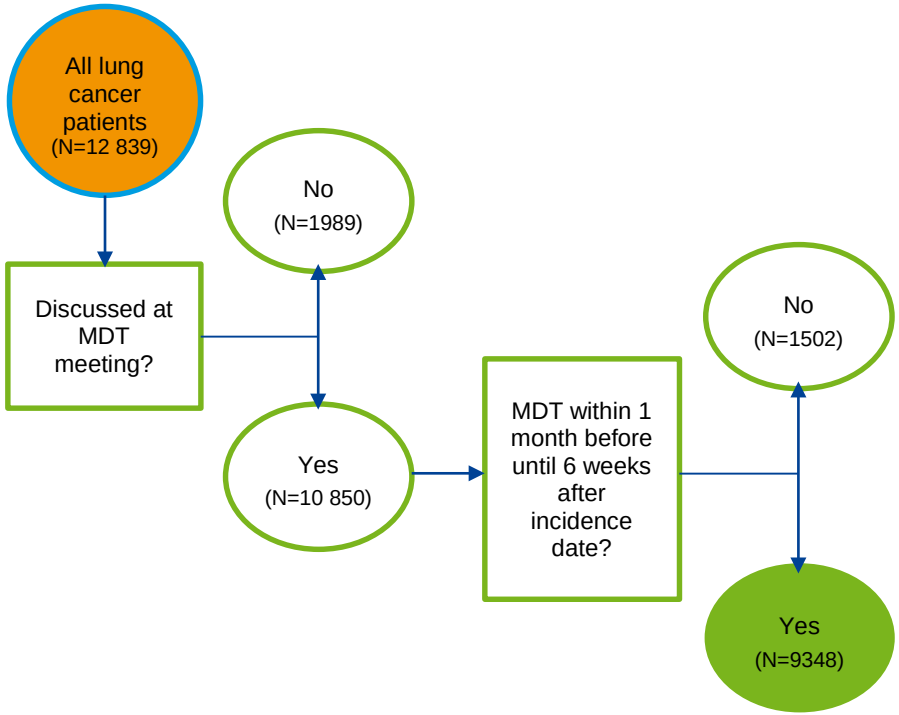
- **In 2011, 58% of patients receiving anti-EGFR treatment during the first year after diagnosis had a mutation analysis performed before the start of treatment. In 2011, guidelines on the importance of EGFR mutation analysis were not yet available. Therefore, the data for 2011 can not yet be considered as an indicator of quality of care for that time period.**
- **The interpretation of the data is limited as the results of the performed tests are not available. It can thus not be assessed if anti-EGFR treatment was preserved for tumours carrying a mutation.**
- **As current guidelines recommend anti-EGFR only for tumours carrying an activating mutation, the proportion of patients who have the tumour tested for mutations should increase in a near future (target 90%).**

3.10 Multidisciplinary team (MDT) meeting (DS-11)

3.10.1 Documentation sheet

Title	Proportion of lung cancer patients who was discussed during a multidisciplinary team (MDT) meeting
Rationale	MDT meetings were identified as the best approach to organize cancer care in a way that consistently brings together all healthcare professionals involved in cancer diagnosis and treatment. In 2014, the European Partnership Action Against Cancer (EPAAC) published a policy statement on multidisciplinary cancer care which was endorsed by the majority of European scientific societies, patient organizations and stakeholders.[23]
Type of QI	Process
Calculation	Numerator: number of patients diagnosed with lung cancer who were discussed during the multidisciplinary team meeting between 1 month before incidence date and 6 weeks after incidence date Denominator: all patients diagnosed with lung cancer
Target	SIGN put forward a target of 95%.[11] The tolerance with this target is designed to account for situations where the medical team decided that there was no added value to discuss the patient in MDT meeting, or that the patient refused to be discussed multidisciplinary, or that the patient died before the meeting could take place.
Data source	BCR + IMA
Technical definition	BCR data: selection of patients with diagnosis of lung cancer: ICD-10 code C34 (Table 103 in appendix). IMA data: billing codes for “first” MDT (MOC-COM) meeting are presented in Table 78 (appendix).
Limitations	Main limitation is that we measure the indicator as the number of MDT meetings charged, that is only a proxy of the number of MDT meetings effectively held. Billing rules of MDT meetings imply that only one MDT meeting can be billed per patient for the first diagnosis. A validation study in oesophageal cancer revealed that some centres discussing patients pre-op and post op did only bill the last meeting[23], and MDT meeting was consequently not taken into account using the defined (limited) timeframe. This discussion should take place *before* any definitive treatment is given. Due to limitation of billing data mentioned above, a time window of 6 weeks has been chosen as a proxy. Another limitation is that we have no information on the quality of the multidisciplinary meeting itself, only that it was held.
Subgroup analyses	Per lung cancer type (NSCLC vs SCLC), clinical stage, main treatment modality. Per age at diagnosis and sex
Sensitivity analyses	MDT meeting within 1, 2, 3 and 6 months after incidence date
Benchmarking	Diagnostic centre
International indicator	Indicator was used in Scotland, the Netherlands and Italy.

3.10.2 Flowchart



3.10.3 Results

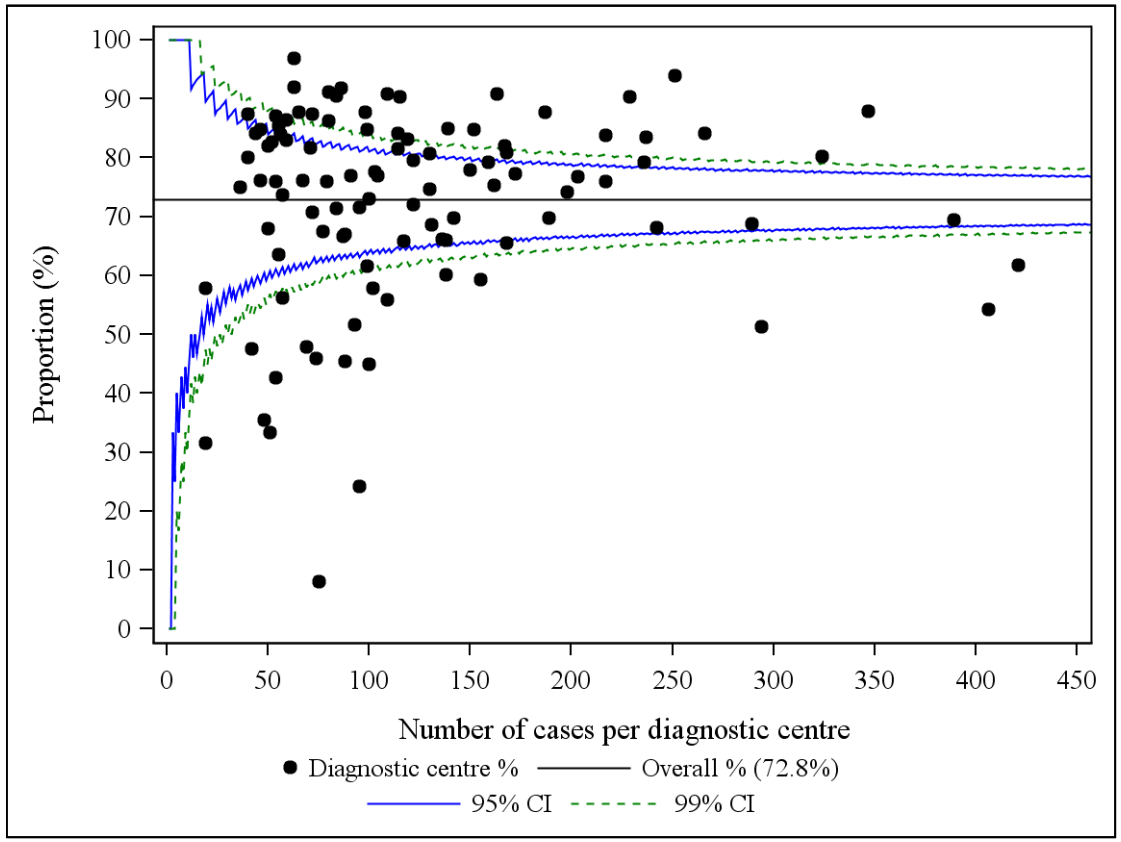
Table 39 – Proportion of lung cancer patients for whom a multidisciplinary team (MDT) meeting was charged within 6 weeks after incidence date, by patient, tumour and treatment characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	12 839	9348	72.8
Sex			
Males	9053	6629	73.2
Females	3786	2719	71.8
Age group			
<50 years	643	482	75.0
50-59 years	2419	1800	74.4
60-69 years	3889	2856	73.4
70-79 years	3884	2813	72.4
80+ years	2004	1397	69.7
Clinical stage			
I	1412	1080	76.5
II	748	609	81.4
III	2535	2069	81.6
IV	5142	4208	81.8
X	2974	1361	45.8
Histological type			
Non-small cell lung cancer	9817	7153	72.9
Small cell lung cancer	2004	1474	73.6
Other specified lung cancer	1018	721	70.8

Characteristic	Denominator	Numerator	Proportion (%)
Treatment modality			
(chemo)radiotherapy	2634	2092	79.4
chemotherapy including targeted treatment	4919	3730	75.8
surgical resection with curative intent	2172	1551	71.4
no treatment	3114	1975	63.4

Source: BCR-IMA

Figure 18 – Proportion of lung cancer patients for whom a multidisciplinary team (MDT) meeting was charged within 6 weeks after incidence date, by diagnostic centre



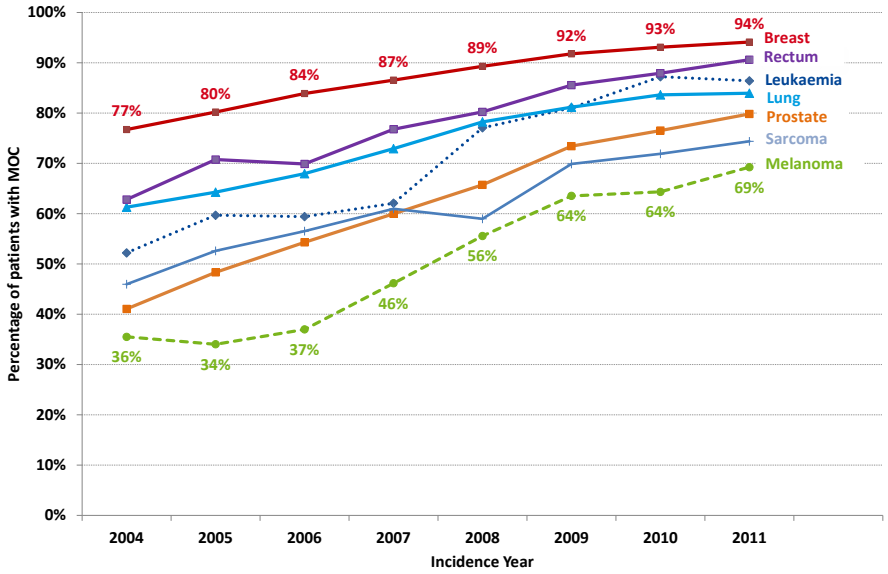
Note: 110 patients were not shown in the figure because they could not be assigned to a diagnostic centre.
Source: BCR-IMA

Table 40 – Proportion of lung cancer patients for whom a multidisciplinary team (MDT) meeting was charged within the timeframe of 1 month, 2 months, 3 months and 6 months after incidence date

	Denominator	Numerator	Proportion (%)
1 month	12 839	8523	66.4
2 months	12 839	9864	76.8
3 months	12 839	10 217	79.6
6 months	12 839	10 513	81.9

Source: BCR-IMA

Figure 19 – Comparison with other cancer types: Percentage of patients for whom a multidisciplinary team (MDT) meeting was charged between 3 months before and 3 years after incidence date



Source: BCR-IMA data, KCE report MOC-COM[23]

3.10.4 Discussion

Overall proportion is 72% for this indicator. The funnel plot shows that there is a large variability across centres, much larger than could be expected purely on the base of random variation. Proportion is somewhat lower in older age groups, but the difference between the oldest and the youngest age-group is only 5%. There is some variation according to treatment. The proportion of MDT discussions in patients who received (chemo)radiotherapy is higher than in patients who were surgically treated. Percentage among patients who received no therapy is even lower.

The percentage of patients discussed in a MDT meeting does not vary with clinical stage, except for patients with early disease (stage I) who were 76.5% to benefit from multidisciplinary discussion (vs. 81.5% for higher stages). Forty-five percent of patients with unereported clinical stages were discussed during an MDT meeting.

A quality program in Italy reported an overall proportion of 50%.[6] The target however was only 55%, a puzzling low figure. In a quality project implicating six hospitals in the Netherlands a proportion of 57% was reported, with a large variation between centres, ranging from 26% to 91%.[24, 25] The Dutch Institute for clinical auditing reported that 97% of patients who underwent elective surgery for NSCLC got a pre-operative multidisciplinary consult and 89% a post-operative consult. The target was 90%.

The large variability across centres and the link with unknown clinical stage indicate that there is, at the country level, large room for improvement.[26]

Comparison with other cancer types

Overall, for all cancers diagnosed during the year 2011, the coverage rate of cancers by a MDT meeting is above 70%. Even for cancer types that were less systematically discussed during a MDT meeting in 2004, the observed increases in coverage between 2004 and 2011 were noticeable (for rectum (+28%), soft tissue sarcoma (+28%), malignant melanoma (+34%) and prostate (+39%).

Key Points

- **Since 2004, proportion of patients discussed in MDT meetings is continuously increasing, for all cancer types.**
- **In 2011, 73% of the lung cancer patients were discussed in a MDT meeting within 6 weeks after the incidence date. Taking into account a 3 months delay to account for possible problems with delays in billing the MDT meeting, the proportion raises to 79.5%. This indicates that there is still room for improvement at the country level.**
- **There is also a large variability across centres, but this may be due to variability in MDT billing process.**

3.11 MDT meeting before surgery for cIII patients (DS-12)

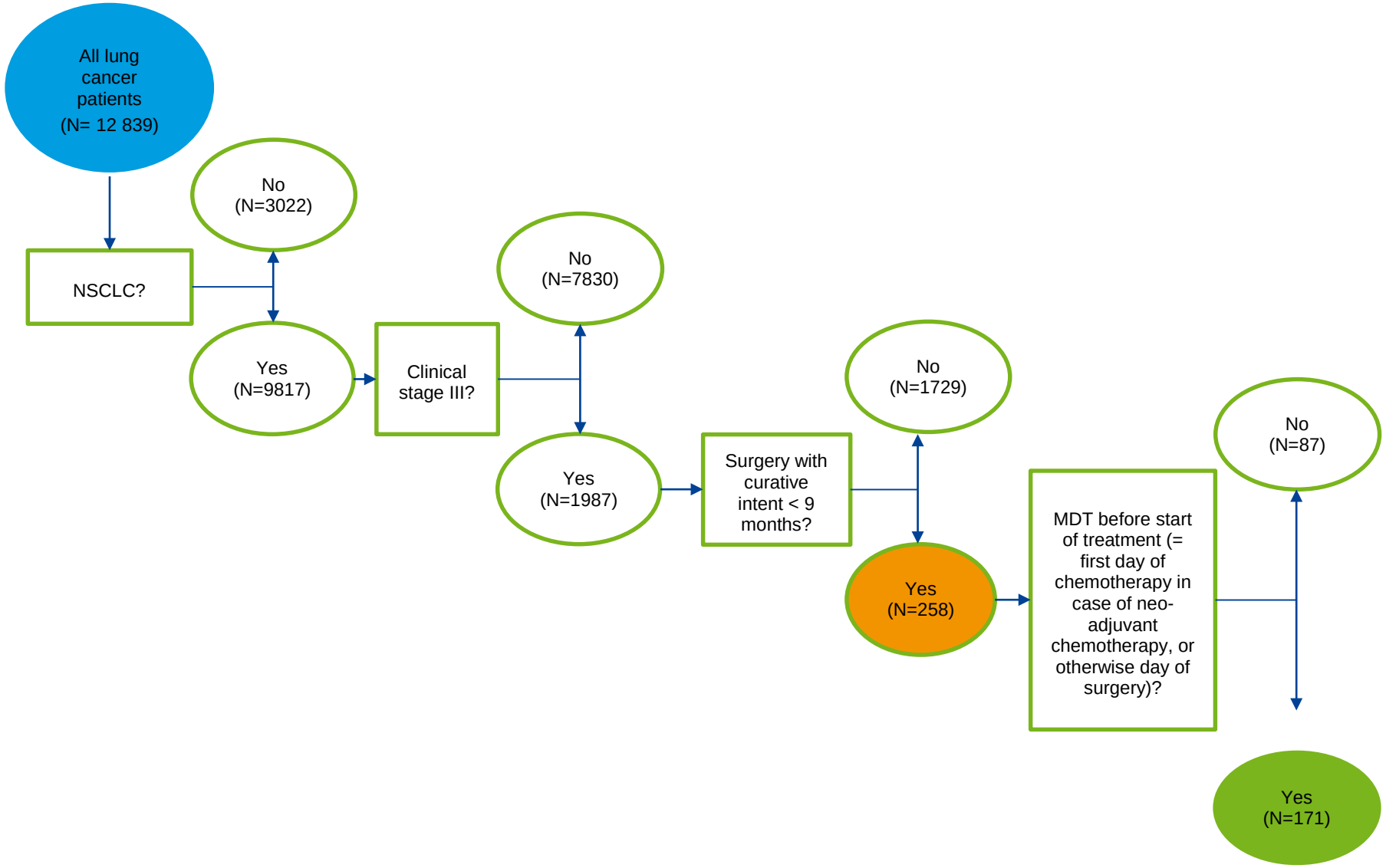
3.11.1 Documentation sheet

Title	Proportion of cIII NSCLC operated patients who were discussed in MDT meeting before start of treatment
Rationale	For the majority of cIII NSCLC patients, chemoradiation is the recommended treatment, considering the patient is sufficiently fit. However, for some clinical stage IIIA patients with resectable disease at diagnosis, neo-adjuvant chemotherapy followed by surgery can be a (less toxic) alternative. Careful patient selection taking into account patient and tumour related factors and local expertise are very important for this patient group. Therefore, multidisciplinary discussion before the start of treatment is paramount.[19]
Type of QI	Process
Calculation	Numerator: number of patients who were discussed in MDT meeting before the start of treatment Denominator: all cIII NSCLC patients who had surgery with curative intent within 9 months after incidence date Start of treatment defined as: First day of chemotherapy in case of neo-adjuvant chemotherapy. Day of surgery in case no neo-adjuvant chemotherapy is given
Target	95%[11]
Data source	BCR + IMA
Technical definition	Diagnostic of NSCLC: ICD-10 code C34 with ICD-O-3 morphology codes 8010-8040, 8046-8245, 8247-8576 (BCR) (Table 103) Surgery with curative intent: billing codes (IMA) in Table 74 Chemotherapy: billing codes (IMA) in Table 76 MDT meeting: billing code (IMA) in Table 78
Limitations	Due to reimbursement rules for MDT (MOC/COM) meetings, date of MDT meeting available in the IMA database may not correctly reflect whether or not a MDT discussion was held before the start of treatment (see fiche DS-11).
Subgroup analyses	Clinical stage IIIA with cN2 versus others
Sensitivity analyses	None
Benchmarking	Analysis by centre of diagnosis: not performed (only 3 centres have more than 10 patients included in the denominator).
International indicator	See Table 41

Table 41 – Clinical stage III NSCLC patients who underwent surgery discussed in MDT before start of treatment: international results

Author	Period covered	country	Results
DICA-DLSA jaarrapportage[26]	2012-2014	The Netherlands	Proportion of operated NSCLC patients who were discussed at an MDT meeting pre-operatively was 95.8% in 2012, 98.1% in 2013 and 98.7% in 2014.

3.11.2 Flowchart



3.11.3 Results

Table 42 – Proportion of cIII NSCLC operated patients for whom a multidisciplinary team (MDT) meeting was charged before start of treatment, by clinical stage

Characteristic	Denominator	Numerator	Proportion (%)
Overall	258	171	66.3
Clinical stage IIIA with cN2	143	90	62.9
Other	115	81	70.4

Source: BCR-IMA

3.11.4 Discussion

Clinical trials looking at the role of surgery in clinical stage IIIA disease could not show a benefit in overall survival after neoadjuvant therapy and surgery compared to chemoradiation. The included population differed between trials. Only one trial, that included patients with limited N2 disease considered possibly resectable by clinicians, showed an advantageous progression-free survival (PFS) after surgery compared to chemoradiation. As correct staging and patient selection is paramount, it is recommended that all cIII patients considered for surgery are discussed by a multidisciplinary team before the start of treatment.[19]

Although a target of 95% was put forward, the recommendation was followed in only 66%. Variability between centres could not be assessed as the total number of patients per centre was too small.

An important reason for non-compliance may be of administrative nature however, as it has been shown that billing date does not refer to the first MDT discussion that took place.[23] The same reason may explain why results are much lower than reported in the Netherlands.[26]

Nevertheless, centres are encouraged to verify the reasons why patients do not have a MDT meeting billed before the start of treatment and improve processes if applicable.

Key Points

- **A MDT meeting was pre-operatively charged for 66% of the clinical stage III NSCLC patients who were operated.**
- **Variability between centres could not be assessed as the total number of patients per centre was too small.**

4 QUALITY OF TREATMENT

4.1 Guideline-concordant treatment for patients with NSCLC (TRT-1)

4.1.1 Documentation sheet

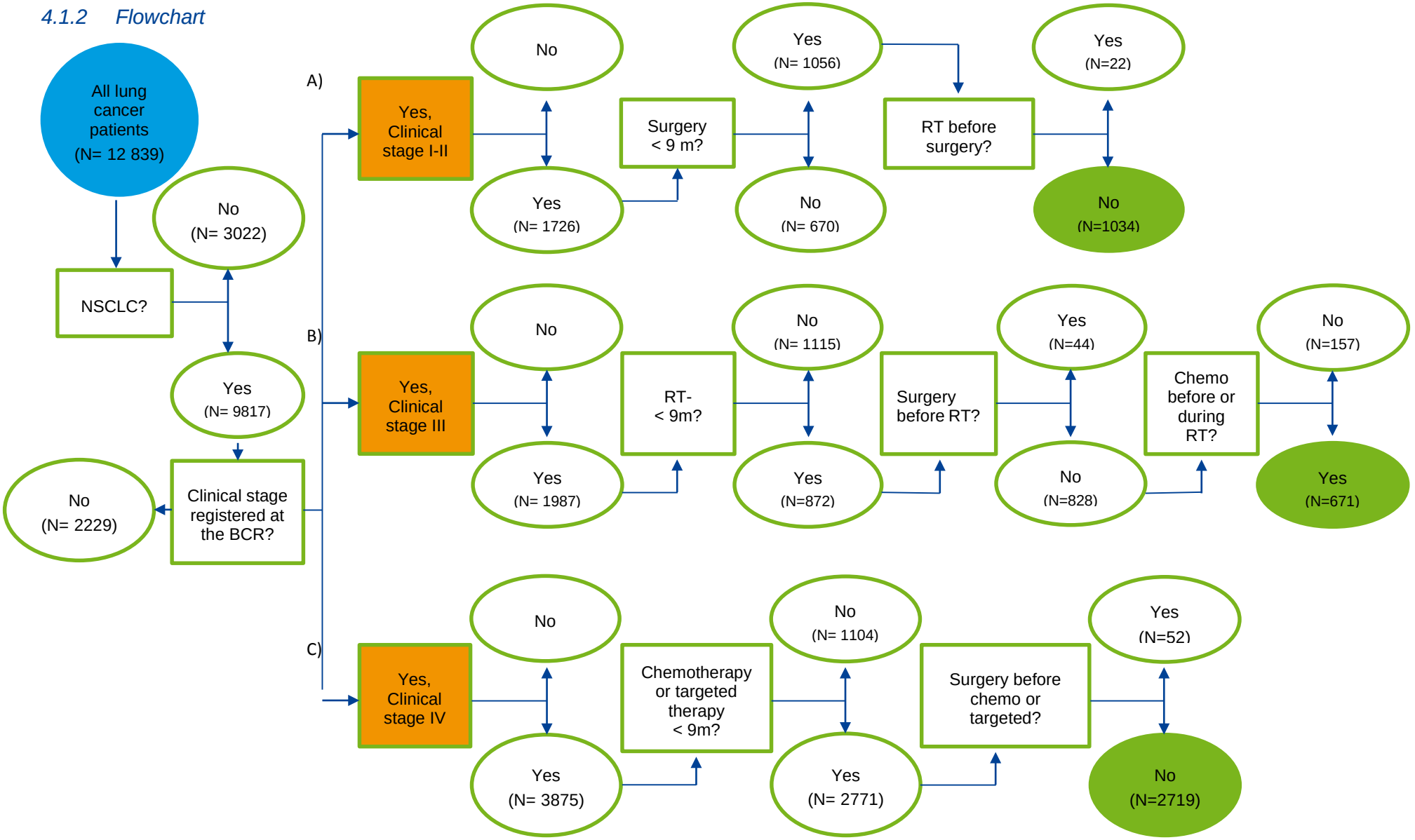
Title	Proportion of patients with NSCLC who received surgical resection for stage cI-II, chemoradiation for stage cIII and chemotherapy or targeted therapy for stage cIV
Rationale	Based on best available evidence, the Belgian guideline on the treatment of lung cancer formulates recommendations for each clinical stage to optimise patients' chances for survival. For cI or II NSCLC patients, surgical resection is the recommended treatment. For cIII, (concurrent) chemoradiation is advised. Chemotherapy or targeted treatment (anti-EGFR) are the recommended strategies for cIV patients at diagnosis.[19]
Type of QI	Process
Calculation	Numerator: number of cI-II NSCLC patients with surgery with curative intent + number of cIII NSCLC patients with (concurrent or sequential) chemoradiation (followed or not by surgery) + number of cIV NSCLC patients with chemotherapy or targeted therapy (all within 9 months of incidence date) Denominator: all patients with NSCLC and clinical stage reported to BCR (results will also presented by stage group)
Target	No target (see rationale)
Data source	BCR + IMA
Technical definition	Diagnostic of NSCLC lung cancer: ICD -10 code C34 with ICD-O-3 morphology codes 8010-8040, 8046-8245, 8247-8576 (BCR) (Table 103) Surgery with curative intent: billing codes (IMA) in Table 74 Radiotherapy with curative intent: billing codes (IMA) in Table 75 Chemotherapy: billing codes (IMA) in Table 76 Targeted therapy: billing codes in Table 77
Limitations	
Subgroup analyses	By age at diagnosis (<60, 60-74, ≥75), sex, performance status By stage (including stage IIIA and IIIB separately)

	Other primary treatment modality, especially stereotactic radiotherapy for stage cI-II and neo-adjuvant chemotherapy followed by surgery for stage cIIIAN2 By hospital diagnostic volume By presence of radiotherapy centre in the diagnostic hospital (same versus different location) for stage cIII
Sensitivity analyses	None
Benchmarking	Diagnostic centre
International indicator	See Table 43

Table 43 – Treatment of NSCLC patients: international results

Author	Period covered	Country	Results
Wouters 2010[27]	2001-2006	The Netherlands	Resection rates for stage I-II varied from 54% to 97% per hospital. Predictive factors: age, size of the tumour, teaching hospital for thoracic surgeons, diagnostic volume of the hospital Stage III: 24% received combined modality treatment (18% in 2001; 29% in 2006). Related factors: age, tumour size, academic centre (NOT volume). Surgery for stage IIIa varied between 9 and 25%. Stage IV: +/- 40% no active treatment
Nadpara 2015[28]	2002-2007	USA	Overall 44.7% of Medicare patients ≥ 65 years old received guideline-concordant care. Stage I: 55.7% Stage II: 49.1% Stage III: 35.3%
Santeon 2014[29]	2013	The Netherlands	Stage IV: varied between 36% and 59% per hospital
National Lung Cancer Audit Report 2014[10]	2013	UK	% of NSCLC stage IA, IB, IIA or IIB having surgery: England: 51.8% Wales: 36.5% Scotland: 45.5% % PS 0-1 stage IIIB or IV NSCLC having chemotherapy England: 57.5% Wales: 56.4% Scotland: 50.2%

4.1.2 Flowchart



4.1.3 Results

4.1.3.1 All patients

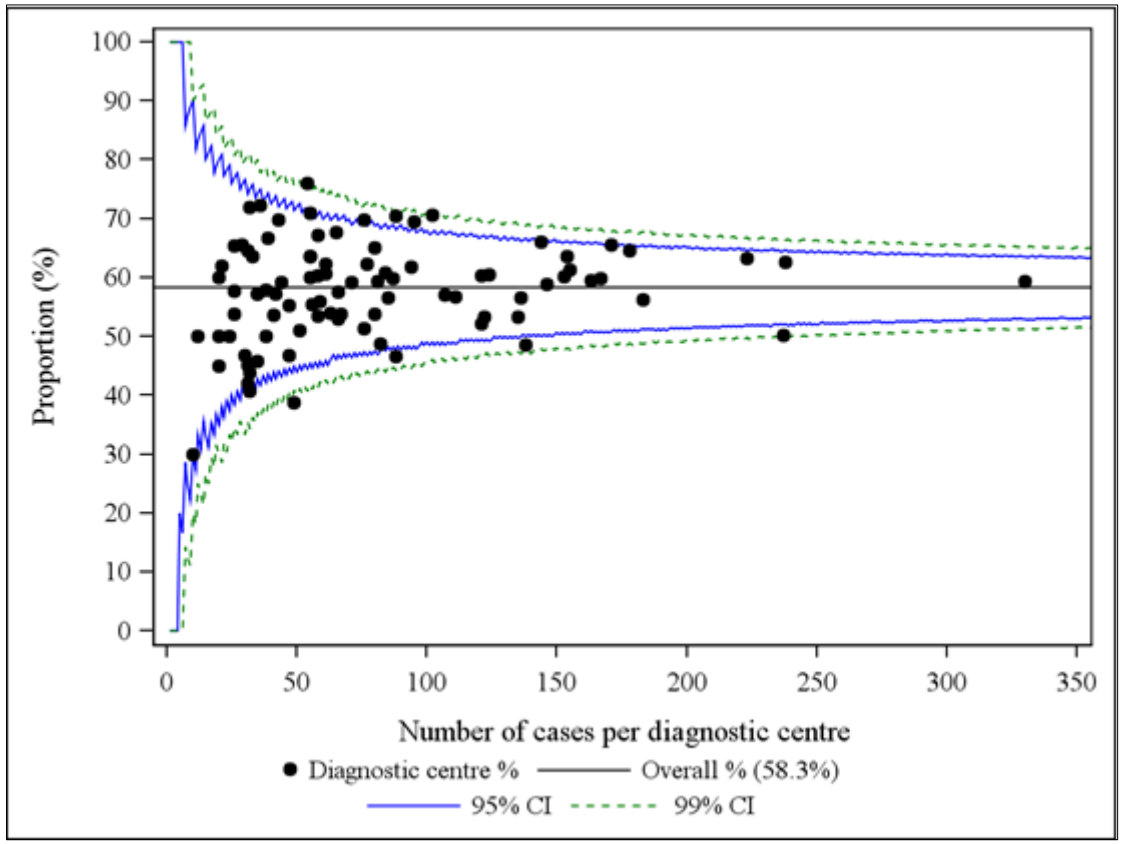
Table 44 – Proportion of NSCLC patients who received surgical resection for stage cI-II, chemoradiation for stage cIII, chemotherapy for stage cIV, by patient and tumour characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	7588	4424	58.3
Sex			
Males	5369	3042	56.7
Females	2219	1382	62.3
Age group			
<60 years	1943	1395	71.8
60-74 years	3571	2256	63.2
75+ years	2074	773	37.3
WHO performance status			
0 – Asymptomatic	969	651	67.2
1 – Symptomatic but completely ambulatory	4689	2881	61.4
2 – Symptomatic, up and about more than 50% of waking hours	903	418	46.3
3 – Symptomatic, confined to bed or chair more than 50% of waking hours	326	95	29.1
4 – Completely disabled; totally confined to bed or chair	104	28	26.9
Missing	597	351	58.8
Chronic respiratory disease			
No	5496	3372	61.4
Yes	2092	1052	50.3
Cardiovascular disease			

Characteristic	Denominator	Numerator	Proportion (%)
No	3419	2177	63.7
Yes	4169	2247	53.9
Diabetes mellitus			
No	6605	3890	58.9
Yes	983	534	54.3
Days of hospitalisation one year before incidence date lung cancer			
1-5 days	1110	686	61.8
6-15 days	470	241	51.3
More than 15 days	325	122	37.5
None	5683	3375	59.4
Clinical stage			
I	1107	731	66.0
II	619	303	48.9
IIIA	1197	393	32.8
IIIB	790	278	35.2
IV	3875	2719	70.2

Source: BCR-IMA

Figure 20 – Proportion of NSCLC patients who received surgical resection for stage cI-II, chemoradiation for stage cIII, chemotherapy for stage cIV, by diagnostic centre



Note 1: 57 patients were not shown in the figure because they could not be assigned to a diagnostic centre.

Note 2: 12 centres were not shown in the figure because they reported less than 50% of clinical stages.

Source: BCR-IMA

Table 45 – NSCLC patients: treatment received by clinical stage

	Primary surgery +/- (neo)adjuvant chemotherapy	Primary chemo-radiation (sequential or concomitant)	Primary radiotherapy (without chemotherapy)	Primary chemotherapy or targeted therapy*	No therapy (or radiotherapy type I only)	Total
Stage cI-II	1034 (59.9%)	119 (6.9%)	263 (15.2%)	139 (8.1%)	171 (9.9%)	1726
Stage cIII	227 (11.4%)	671 (33.8%)	132 (6.6%)	651 (32.8%)	306 (15.4%)	1987
Stage cIIIA	203 (17.0%)	393 (32.8%)	97 (8.1%)	324 (27.1%)	180 (15.0%)	1197
Stage cIIIB	24 (3.0%)	278 (35.2%)	35 (4.4%)	327 (41.4%)	126 (15.9%)	790
Stage cIV	52 (1.3%)	0 (0.0%)	146 (3.8%)	2719 (70.2%)	958 (24.7%)	3875

**For stage IV, radiotherapy before chemotherapy or targeted therapy was not an exclusion criterion, as probably palliative radiotherapy for symptomatic metastases.*

4.1.3.2 Clinical stage I-II NSCLC: surgery

Table 46 – Proportion of cI-II NSCLC patients who were operated, by patient and tumour characteristics

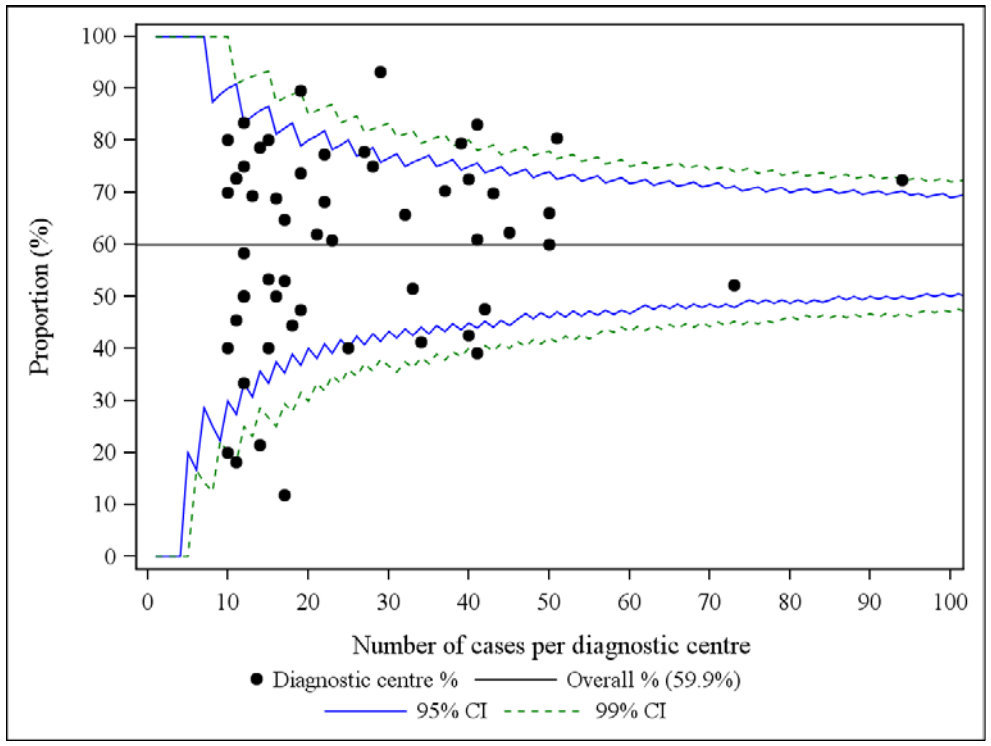
Characteristic	Denominator	Numerator	Proportion (%)
Overall	1726	1034	59.9
Sex			
Males	1191	685	57.5
Females	535	349	65.2
Age group			
<60 years	383	289	75.5
60-74 years	846	561	66.3
75+ years	497	184	37.0

Characteristic	Denominator	Numerator	Proportion (%)
WHO performance status			
0 – Asymptomatic	409	307	75.1
1 – Symptomatic but completely ambulatory	1027	609	59.3
2 – Symptomatic, <50% in bed during the day	103	23	22.3
3 – Symptomatic, >50% in bed, but not bedbound	33	3	9.1
4 – Completely disabled; totally confined to bed or chair	15	4	26.7
Missing	139	88	63.3
Chronic respiratory disease			
No	1 00	722	65.6
Yes	626	312	49.8
Cardiovascular disease			
No	680	439	64.6
Yes	1046	595	56.9
Diabetes mellitus			
No	1487	901	60.6
Yes	239	133	55.6
Days of hospitalisation one year before incidence date lung cancer			
1-5 days	312	210	67.3
6-15 days	135	73	54.1
More than 15 days	112	47	42.0
None	1167	704	60.3
Clinical stage			

Characteristic	Denominator	Numerator	Proportion (%)
I	1107	731	66.0
II	619	303	48.9

Source: BCR-IMA

Figure 21 – Proportion of cI-II NSCLC patients who were operated, by diagnostic centre



Note 1: 10 patients were not shown in the figure because they could not be assigned to a diagnostic centre.
Note 2: 10 centres were not shown in the figure because they reported less than 50% of clinical stages.
Note 3: 34 centres were not shown in the figure because the denominator was smaller than 10.
Note 4: 2 centres were not shown in the figure because they had no cI-II patients.
Source: BCR-IMA

4.1.3.3 *Clinical stage III NSCLC patients: chemoradiation*

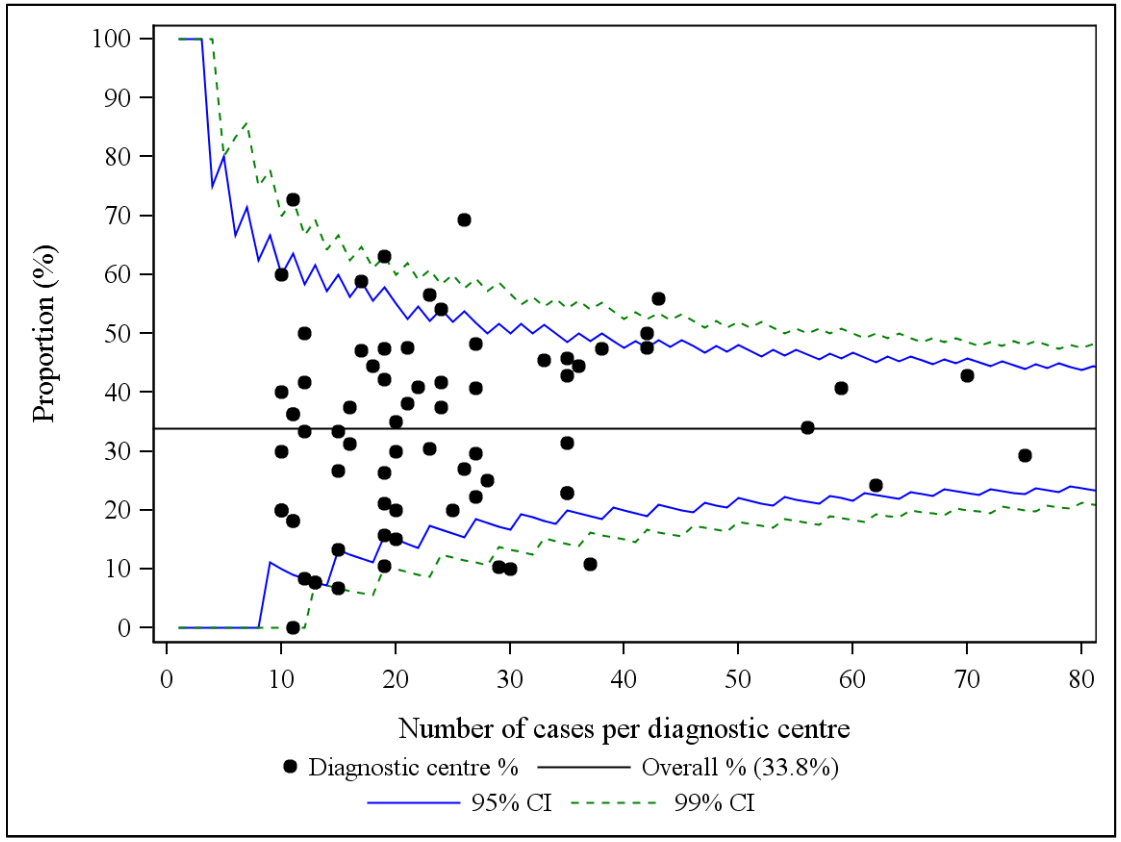
Table 47 – Proportion of cIII NSCLC patients who received chemoradiation, by patient, tumour and hospital characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	1987	671	33.8
Sex			
Males	1474	493	33.4
Females	513	178	34.7
Age group			
<60 years	475	219	46.1
60-74 years	935	357	38.2
75+ years	577	95	16.5
WHO performance status			
0 – Asymptomatic	244	101	41.4
1 – Symptomatic but completely ambulatory	1311	481	36.7
2 – Symptomatic, up and about more than 50% of waking hours	197	38	19.3
3 – Symptomatic, confined to bed or chair more than 50% of waking hours	64	4	6.3
4 – Completely disabled; totally confined to bed or chair	19	1	5.3
Missing	152	46	30.3
Chronic respiratory disease			
No	1409	504	35.8
Yes	578	167	28.9
Cardiovascular disease			
No	865	335	38.7

Characteristic	Denominator	Numerator	Proportion (%)
Yes	1122	336	29.9
Diabetes mellitus			
No	1722	587	34.1
Yes	265	84	31.7
Days of hospitalisation one year before incidence date lung cancer			
None	1515	532	35.1
1-5 days	281	93	33.1
6-15 days	123	33	26.8
More than 15 days	68	13	19.1
Clinical stage			
IIIA	1197	393	32.8
IIIB	790	278	35.2
Location of RT centre			
RT at different location	1161	371	32.0
RT at same location	826	300	36.3

Source: BCR-IMA

Figure 22 – Proportion of cIII NSCLC patients who received chemoradiation, by diagnostic centre



Note 1: 17 patients were not shown in the figure because they could not be assigned to a diagnostic centre.

Note 2: 11 centres were not shown in the figure because they reported less than 50% of clinical stages.

Note 3: 17 centres were not shown in the figure because the denominator was smaller than 10.

Note 4: 1 centre was not shown in the figure because it had no cIII patients.

Source: BCR-IMA

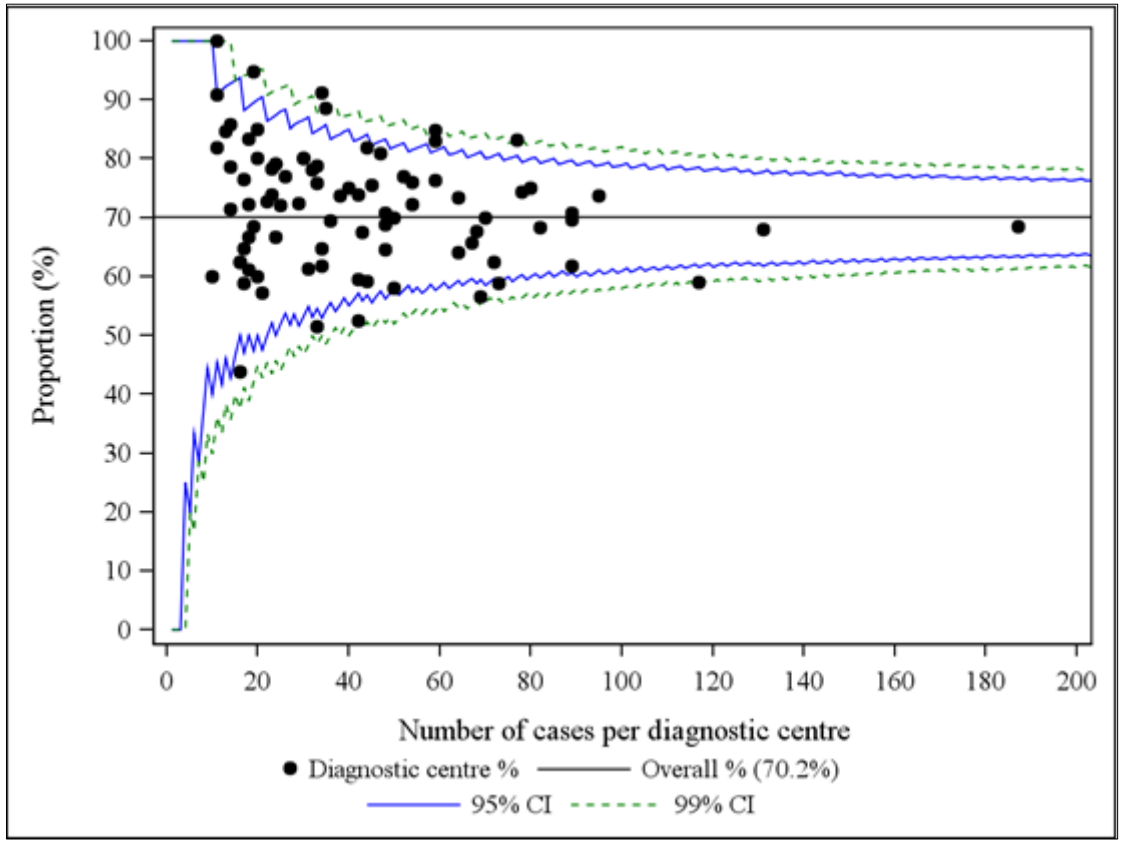
Table 48 – Proportion of cIV NSCLC patients who received chemotherapy, by patient characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	3875	2719	70.2
Sex			
Males	2704	1864	68.9
Females	1171	855	73.0
Age group			
<60 years	1085	887	81.8
60-74 years	1790	1338	74.7
75+ years	1000	494	49.4
WHO performance status			
0 – Asymptomatic	316	243	76.9
1 – Symptomatic but completely ambulatory	2351	1791	76.2
2 – Symptomatic, up and about more than 50% of waking hours	603	357	59.2
3 – Symptomatic, confined to bed or chair more than 50% of waking hours	229	88	38.4
4 – Completely disabled; totally confined to bed or chair	70	23	32.9
Missing	306	217	70.9
Chronic respiratory disease			
No	2987	2146	71.8
Yes	888	573	64.5
Cardiovascular disease			
No	1874	1403	74.9
Yes	2001	1316	65.8
Diabetes mellitus			

Characteristic	Denominator	Numerator	Proportion (%)
No	3396	2402	70.7
Yes	479	317	66.2
Days of hospitalisation one year before incidence date lung cancer			
1-5 days	517	383	74.1
6-15 days	212	135	63.7
More than 15 days	145	62	42.8
None	3001	2139	71.3

Source: BCR-IMA

Figure 23 – Proportion of cIV NSCLC patients who received chemotherapy or targeted therapy, by diagnostic centre



Note 1: 30 patients were not shown in the figure because they could not be assigned to a diagnostic centre.
Note 2: 12 centres were not shown in the figure because they reported less than 50% of clinical stages.
Note 3: 5 centres were not shown in the figure because the denominator was smaller than 10.
Source: BCR-IMA

4.1.4 Discussion

Clinical stage I-II

Compared to international results, overall a rather high proportion of cI-II NSCLC patients were operated, with or without (neo)adjuvant chemotherapy (see Table 44). Proportion was lower for cII (49% vs. 66%), older patients (particularly ≥75 years old, 37%) and patients with poor performance status or comorbidity.

Overall, another 22% was treated with (chemo)radiation, a proportion that also may differ by centre. It is not known which proportion of these patients received stereotactic radiotherapy, as specific nomenclature codes were not available during the studied time period (2010-2011).

The funnel plot shows a moderate variability beyond random-error, with both high and low outliers. Differences between centres may be explained by several factors, such as case-mix, patient preferences, availability of surgical expertise, availability of (stereotactic) radiotherapy modalities and also physician related factors. As surgical treatment for stage cI-II is potentially curative, careful selection of patients is paramount. As stated by the NICE guideline, all patients who are eligible for potentially curative treatment, should be assessed by a thoracic surgeon and a radiation oncologist experienced in lung cancer treatment.[20] Referral for second opinion may be appropriate for less experienced centres with lower proportions of patients treated with curative intent.

Clinical stage III

Proportion of cIII NSCLC patients who received combined chemoradiation is slightly higher than reported in the Netherlands in 2006 (34% vs. 24%) (see Table 44). Centres with on-site radiotherapy facilities had a slightly higher proportion of patients treated with chemoradiation than centres that needed to refer patients for radiotherapy (36% versus 32%).

Also for stage cIII, there was moderate variability between centres beyond random error, with both high and low outliers.

Eleven percent of cIII NSCLC patients were treated with surgery (and (neo)adjuvant chemotherapy) and more than six percent was treated by radiotherapy alone. Hence, in total 52% of cIII patients received treatment that was potentially curative. Alternative treatments may partially explain differences in chemoradiation rates between centres.

Clinical stage IV

Seventy percent of cIV NSCLC patients at diagnosis received primary treatment with chemotherapy or targeted treatment, which is a higher proportion than reported in other countries (see Table 44). There is moderate variability between centres beyond what can be expected due to random error.

Differences between hospitals were also noted in the Dutch Santeon project. The seven participating hospitals noted survival differences between hospitals for cIV patients, even after case-mix correction. The differences appear partly explained by differences in the proportion of patients that received chemotherapy.[29]

Key Points

- **Proportion of NSCLC patients receiving guideline-concordant therapy is similar or slightly higher than reported in other countries.**
- **For clinical stage I-II and III patients, there was moderate variability between centres.**

4.2 Chemoradiation for cIII NSCLC patients (TRT-2)

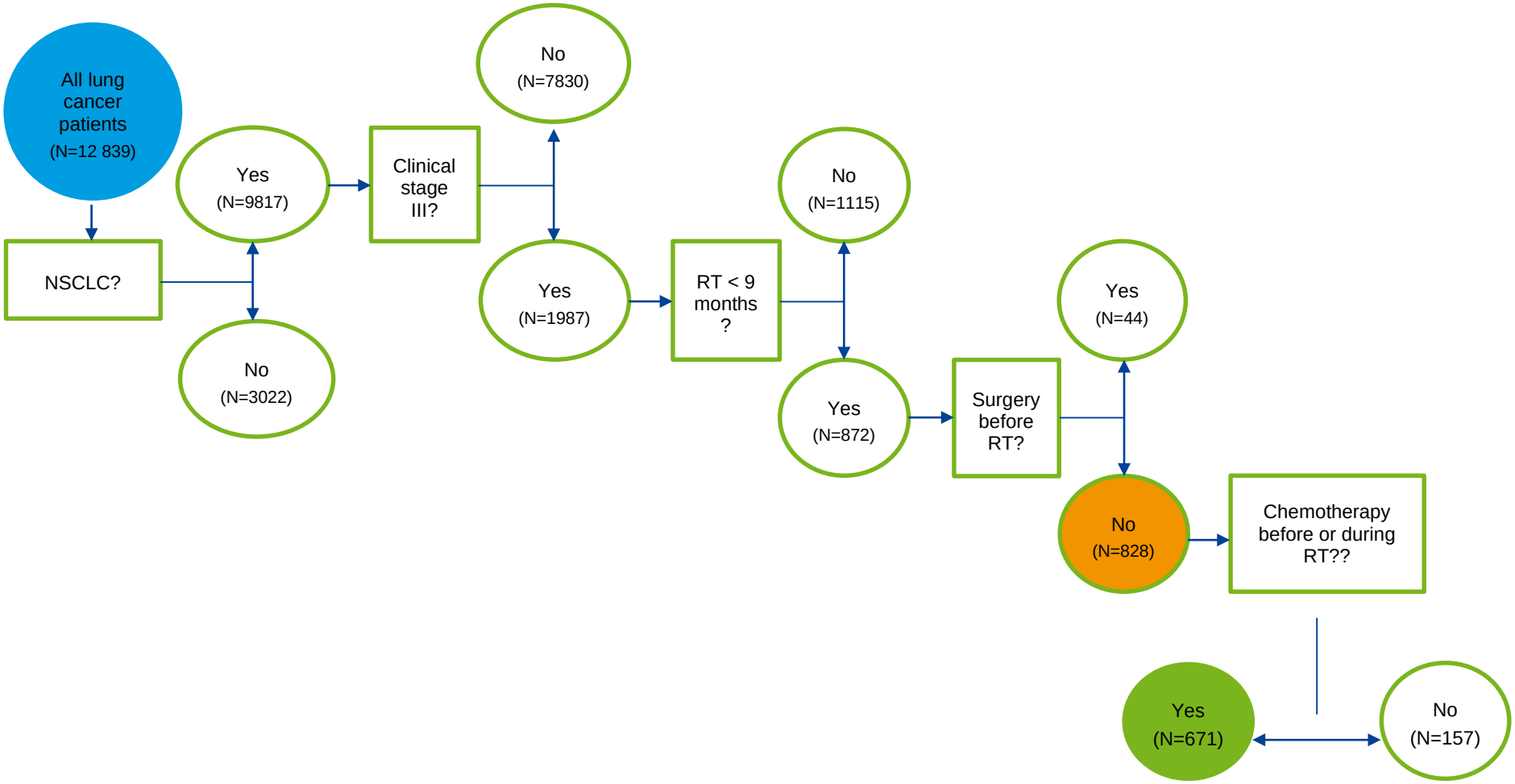
4.2.1 Documentation sheet

Title	**Proportion of cIII NSCLC patients receiving concurrent or sequential chemoradiotherapy, based on all patients who received radiotherapy**
Rationale	Randomized controlled trials have shown a benefit in progression-free and overall survival with combined chemoradiation compared to radiotherapy alone in fit patients, at the cost of increased, but manageable, toxicity.[19]
Type of QI	Process
Calculation	Numerator: number of cIII NSCLC patients who received concurrent or sequential chemoradiation Denominator: all cIII NSCLC patients who received (at least) radiotherapy with curative intent within 9 months of incidence date Exclusion: patients with adjuvant radiotherapy (surgery before radiotherapy)
Target	No target
Data source	BCR + IMA
Technical definition	Diagnosis of NSCLC: ICD -10 code C34 with ICD-O-3 morphology codes 8010-8040, 8046-8245, 8247-8576 (BCR) (Table 103) Surgery with curative intent: billing codes (IMA) in Table 74 Radiotherapy with curative intent: billing codes (IMA) in Table 75 Chemotherapy: billing codes (IMA) in Table 76 Sequential or concurrent chemotherapy = chemotherapy between incidence date and end date of radiotherapy Sequential chemoradiation = start date of chemo and start date of RT lie within 120 days around each other Concurrent chemoradiation = start date of chemo and start date of RT lie within 30 days around each other
Limitations	Population in daily practice may differ from the population included in the clinical trials in terms of age, performance status and comorbidity, concomitant chemoradiation may thus not be appropriate for all patients. Concurrent versus sequential chemotherapy needs to be determined based on time data available and may be incomplete or incorrect (billing date versus actual date).
Subgroup analyses	By patient age at diagnosis, sex Separate results by radiotherapy scheme: sequential or concurrent radiotherapy
Sensitivity analyses	NA
Benchmarking	Diagnostic centre
International indicator	See Table 49

Table 49 – Chemoradiation for cIII NSCLC patients: international results

Author	Period covered	country	Results
IKNL- Longkanker in beeld[30]	2011	The Netherlands	Concurrent chemoradiation in 68% of stage III NSCLC patients, decreasing by age to 45% in patients of 80 years old or older.
Wouters 2010[27]	2001-2006	The Netherlands	During the study period, 24% of patients received combined modality treatment, 30% of the younger patients (<75 years) and 9% of the older patients. The percentage of patients receiving chemoradiation rose from 18% in 2001 to 29% in 2006.
DLRA[26]	2014	The Netherlands	Combined chemoradiation is given concurrently in 58% of cases and sequentially in 42%, with a range of 8 to 92%.
Komaki 2013[31]	2006-2007	USA	77% of locally advanced NSCLC patients treated with EBRT received concurrent chemotherapy (45% in 1998-1999).

4.2.2 Flowchart



4.2.3 Results

Table 50 – Proportion of cIII NSCLC patients treated with radiotherapy who received concurrent or sequential chemotherapy, by patient characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	828	671	81.0
Sex			
Male	622	493	79.3
Female	206	178	86.4
Age group			
<50 years	49	48	98.0
50-59 years	174	171	98.3
60-69 years	283	262	92.6
70-79 years	229	171	74.7
80+ years	93	19	20.4
WHO performance status			
0 – Asymptomatic	112	101	90.2
1 – Symptomatic but completely ambulatory	587	481	81.9
2 – Symptomatic, <50% confined to bed/chair during the day	60	38	63.3
3 – Symptomatic, >50% in bed, but not bedbound	7	4	57.1
4 – Bedbound	2	1	50.0
Missing	60	46	76.7
Chronic respiratory disease			
No	609	504	82.8
Yes	219	167	76.3

Characteristic	Denominator	Numerator	Proportion (%)
Cardiovascular disease			
No	381	335	87.9
Yes	447	336	75.2
Diabetes mellitus			
No	715	587	82.1
Yes	113	84	74.3
Days of hospitalisation one year before incidence date lung cancer			
None	647	532	82.2
1-5 days	114	93	81.6
6-15 days	47	33	70.2
More than 15 days	20	13	65.0

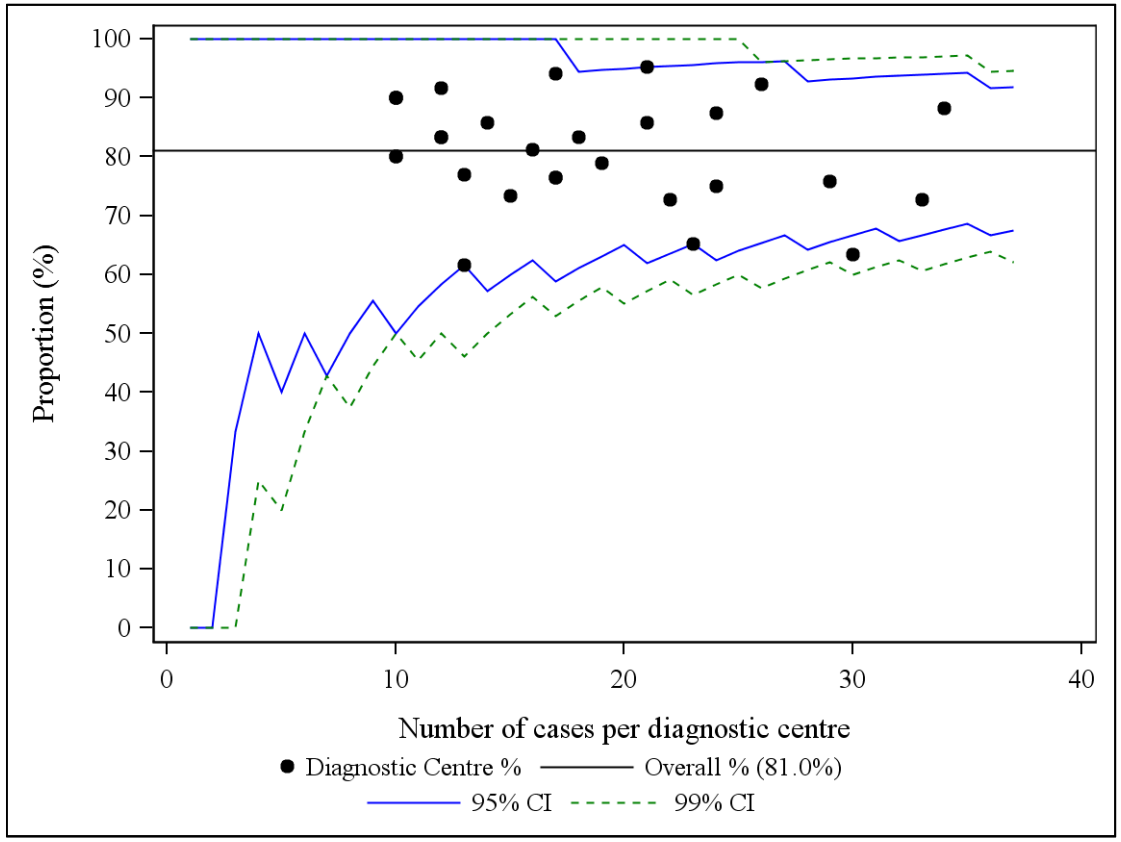
Source: BCR-IMA

Table 51 – Proportion of cIII NSCLC patients treated with radiotherapy who received concurrent, sequential or no chemotherapy

Characteristic	Denominator	Numerator	Proportion (%)
Concurrent chemotherapy	828	243	29.3
Sequential chemotherapy	828	428	51.7
No chemotherapy	828	157	18.9

Source: BCR-IMA

Figure 24 – Proportion of cIII NSCLC patients treated with radiotherapy who received concurrent or sequential chemotherapy, by diagnostic centre



Note 1: 1 patient was not shown in the figure because they could not be assigned to a diagnostic centre.
Note 2: 9 centres were not shown in the figure because they reported less than 50% of clinical stages.
Note 3: 60 centres were not shown in the figure because the denominator was smaller than 10.
Note 4: 4 centres were not shown in the figure because they had no cIII NSCLC patients who underwent primary RT within 9 months.
Source: BCR-IMA

4.2.4 Discussion

Overall, the proportion of patients receiving multimodality treatment is high. As expected, this proportion is lower in elderly patients (especially ≥80 years old, patients with poorer performance status and in patients with comorbidity).

Thirty-five percent of the patients receiving multimodality treatment received concurrent chemoradiation, which is lower than reported in the Netherlands and the United states (see table). Comparison is difficult, however, as we do not know the proportion of cIII patients who received radiotherapy with or without chemotherapy in these other countries.

Variability between centres is difficult to judge as the majority of centres is not represented in the analysis because of insufficient reporting of clinical stages or too small sample size. From available data, no obvious variability is apparent.

The ideal proportion of patients undergoing radiotherapy for stage cIII NSCLC is difficult to define. Patients should receive treatment with curative intent as much possible, but with consideration of their general fitness, comorbidities and their personal preferences. Factors to be taken into account when interpreting the results thus include case-mix variables and overall proportion of cIII NSCLC patients that had treatment with curative intent (surgery or radiotherapy with or without chemotherapy). Furthermore, overall treatment choices should be related to outcomes such as adverse events, quality of life and survival.

Centres are encouraged to review their results and compare them with the national results. If the proportion of patients receiving concurrent chemoradiation is rather low, a concomitant schedule can be considered more often. A second opinion may be helpful in cases of borderline fitness or comorbidity. A very high proportion of patients with concomitant chemoradiation may indicate an underuse of radiotherapy in monotherapy in more frail patients.

Key Points

- **Overall, the proportion of patients receiving multimodality treatment is high. As expected, this proportion is lower in elderly patients (especially ≥80 years old, patients with poorer performance status and in patients with comorbidity).**
- **Of the patients receiving chemoradiation, the proportion of patients receiving concurrent chemotherapy is lower than in other countries, but results need to be interpreted with caution.**

4.3 Adjuvant chemotherapy for pT1-3 pN1-2-M0 NSCLC patients (TRT-3)

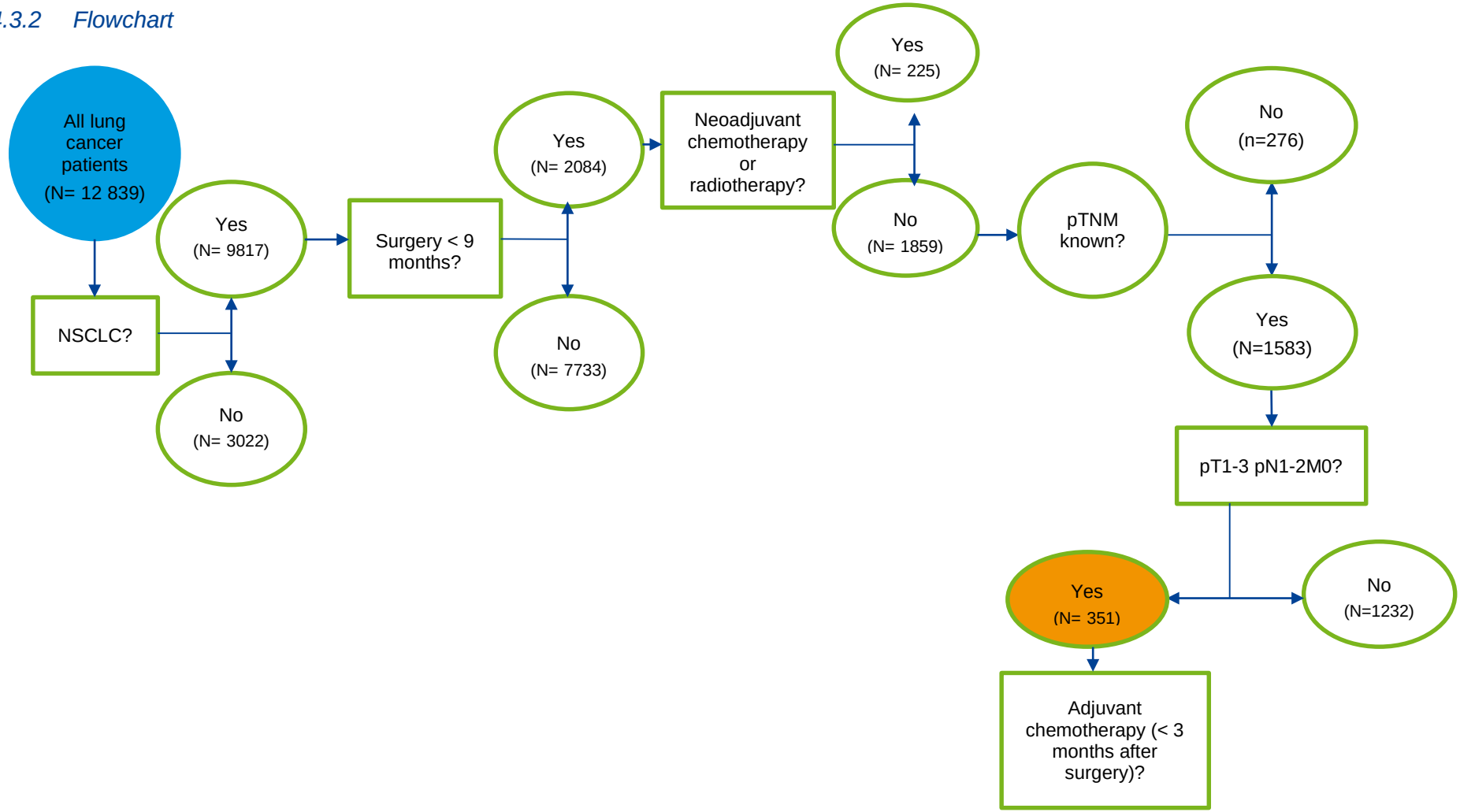
4.3.1 Documentation sheet

Title	Proportion of pT1-3 pN1-2 M0 NSCLC patients who are treated with adjuvant chemotherapy after resection
Rationale	Several RCTs (moderate level of evidence) have shown that adjuvant chemotherapy improves overall survival in completely resected early-stage lung cancer (T1-3 pN1-2 M0 NSCLC).[19]
Type of QI	Process
Calculation	Numerator: number of pT1-3 pN1-2 M0 NSCLC patients who received chemotherapy within 3 months after surgery Denominator: number of pT1-3 pN1-2 M0 NSCLC patients who had surgery with curative intent within 9 months of incidence date and no neoadjuvant chemotherapy and/or radiotherapy
Target	70% The tolerance within this target is designed to account for patients who are in poor general health, refuse to receive adjuvant chemotherapy or suffer from surgical complications.
Data source	BCR + IMA
Technical definition	Diagnosis of NSCLC: ICD -10 code C34 with ICD-O-3 morphology codes 8010-8040, 8046-8245, 8247-8576 (BCR) (Table 103) Surgery with curative intent: billing codes (IMA) in Table 74 (neoadjuvant) Radiotherapy: billing codes (IMA) in Table 75 Chemotherapy: billing codes (IMA) in Table 76 Adjuvant chemotherapy: within 3 months after date of surgery
Limitations	Reasons for not having received chemotherapy cannot be extracted from the data. No adjuvant chemotherapy due to patient refusal or comorbidity would reflect good quality care, surgical complications or non-compliant care would not. A further limitation is that pathological TNM stage is not available for a considerable number of patients treated with surgery.
Subgroup analyses	By patient age at diagnosis, by sex By performance status
Sensitivity analyses	None
Benchmarking	No results reported per centre because sample size per centre is too low (less than 10 patients for the majority of centres).
International indicator	See Table 52.

Table 52 – Adjuvant chemotherapy for pT1-3 pN1-2-M0 NSCLC: international results

Author	Period covered	country	Results			
IKNL 2014[30]	2010-2011	The Netherlands	T1N1: 51% T2aN1: 55%	T2bN1: 58% T3N0: 35%	T1/2N2: 66% T3N1/2: 61%	T4N0/1: 36%
			Factors: postoperative complications, age, comorbidity			
Ryoo 2014[3]	2007	USA	80% of resected stage II-IIIA NSCLC received adjuvant chemotherapy			

4.3.2 Flowchart



4.3.3 Results

Table 53 – Proportion of pT1-3 pN1-2 M0 NSCLC patients who are treated with adjuvant chemotherapy, by patient characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	351	231	65.8
Sex			
Male	251	161	64.1
Female	100	70	70.0
Age group			
<50 years	21	17	81.0
50-59 years	86	68	79.1
60-69 years	122	87	71.3
70-79 years	108	56	51.9
80+ years	14	3	21.4
WHO performance status			
0 – Asymptomatic	86	56	65.1
1 – Symptomatic but completely ambulatory	194	127	65.5
2 – Symptomatic, up and about more than 50% of waking hours	9	7	77.8
4 – Completely disabled; totally confined to bed or chair	1	1	100.0
Missing	61	40	65.6

Source: BCR-IMA

Table 54 – Overview of products used as adjuvant chemotherapy in pT1-3 pN1-2 M0 NSCLC patients

product ATC-code	product name	Number of patients
L01BA04	Pemetrexed	14
L01BC02	Fluorouracil	1
L01BC05	Gemcitabine	45
L01CA04	Vinorelbine	170
L01CB01	Etoposide	3
L01CD02	Docetaxel	4
L01XA01	Cisplatin	202
L01XA02	Carboplatin	40
L01XE03	Erlotinib	3
Total		321

Table 55 – Proportion of pT3 pN0 M0 NSCLC patients who are treated with adjuvant chemotherapy, by patient characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	110	58	52.7
Sex			
Male	76	39	51.3
Female	34	19	55.9
Age group			
<50 years	9	6	66.7
50-59 years	24	12	50.0
60-69 years	43	24	55.8
70-79 years	32	16	50.0
80+ years	2	0	0.0
WHO performance status			
0 – Asymptomatic	17	7	41.2
1 – Symptomatic but completely ambulatory	64	32	50.0
2 – Symptomatic, <50% in bed during the day	4	2	50.0
Missing	25	17	68.0

Source: BCR-IMA

Table 56 – Proportion of pathological stage IB NSCLC patients who are treated with adjuvant chemotherapy

Characteristic	Denominator	Numerator	Proportion (%)
Overall	317	59	18.6

Source: BCR-IMA

4.3.4 Discussion

Almost 66% of patients with a pT1-3 pN1-2 M0 NSCLC tumour received adjuvant chemotherapy, which is a higher proportion than reported in the Netherlands[22] but lower than reported for the Veteran Affairs Central Cancer Registry in the USA.[3] Overall, the pre-set target of 70% was almost met. In patients younger than 60 years old however, more than 70% received adjuvant chemotherapy. Patients over 60 years old, representing 70% of all pT1-3 pN1-2 M0 NSCLC patients, are less likely to be treated with adjuvant chemotherapy.

Individual results for the centres are not reported, as results per centre may not be representative due to small numbers.

Both patient and tumour related factors play a role in clinical decisions regarding adjuvant chemotherapy, as demonstrated in the low rates of chemotherapy in older patients, patients with comorbidity or poor performance status and with stage pIB or pT3 N0 M0.

For further appropriate implementation of the guideline, centres are encouraged to:

- Correctly report pathological TNM stage and propose adjuvant chemotherapy to fit patients with pT1-3 pN1-2 M0 NSCLC tumours. Discuss benefits and harms with all patients to promote shared decision making.

Key Points

- **The proportion of patients with pT1-3 pN1-2 M0 NSCLC who are treated with adjuvant chemotherapy is 66%, which is slightly below the pre-set target of 70%.**
- **Patients over 60 years old represent 70% of all pT1-3 pN1-2 M0 NSCLC patients. This large group is less likely to be treated with adjuvant chemotherapy.**
- **Results for individual centres are not reported due to the small number of patients per centre.**

4.4 Adjuvant chemotherapy for pIA NSCLC patients (TRT-4)

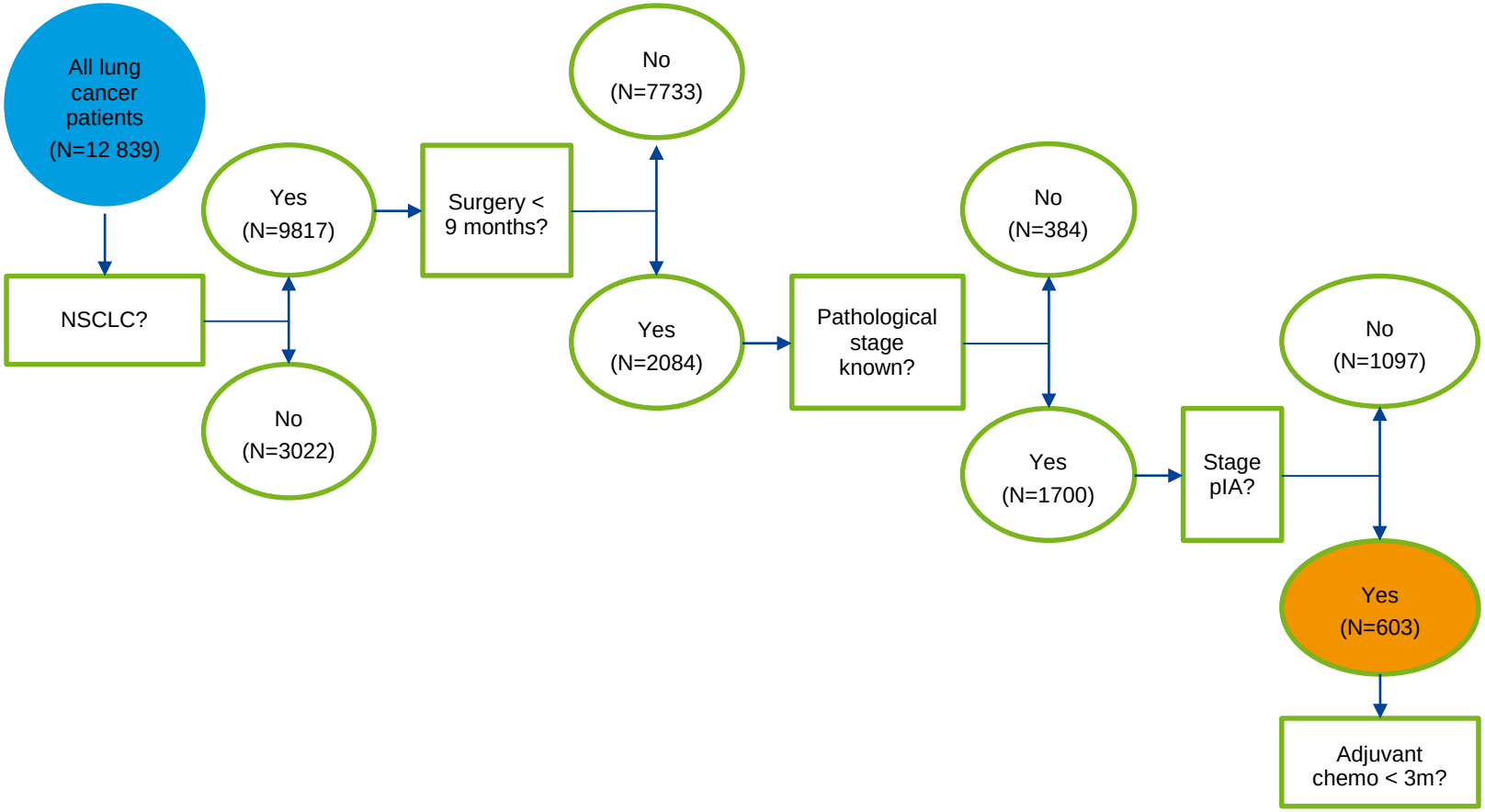
4.4.1 Documentation sheet

Title	Proportion of pIA NSCLC patients who received adjuvant chemotherapy
Rationale	There is no proof of clinical benefit of adjuvant chemotherapy for tumours smaller than 4 cm and no lymph node involvement.[19]
Type of QI	Process
Calculation	Numerator: number of stage pIA NSCLC patients who received adjuvant chemotherapy within 3 months after surgery Denominator: number of stage pIA NSCLC patients who underwent surgery within 9 months after incidence date and received no neoadjuvant chemotherapy or radiotherapy
Target	<1 % (Ryoo, 2014) [3]
Data source	BCR + IMA
Technical definition	Diagnostic of NSCLC: ICD-10 code C34 with ICD-O-3 morphology codes 8010-8040, 8046-8245, 8247-8576 (BCR) (Table 103) Pathological stage IA includes T1a,b N0 M0 tumours Surgery with curative intent: billing codes (IMA) in Table 74 Chemotherapy: billing codes (IMA) in Table 76
Limitations	Pathological stage is not reported for all surgical patients.
Subgroup analyses	
Sensitivity analyses	Exclusion of patients with clinical metastases (combined stage IV)
Benchmarking	Diagnostic centre and surgery centre: not performed Because of the small numbers, a lot of centres had a denominator smaller than 10 (the predefined limit to present a centre in the funnel plot). For the benchmark analyses by diagnostic centre, 79% of centres had a denominator smaller than 10, while this number was 75% for the analyses by surgery centre. Therefore, we did not present these analyses.
International indicator	See Table 57

Table 57 – Adjuvant chemotherapy for pIA NSCLC patients: international results

Author	Period covered	Country	Results
Ryoo 2014[3]	2007	USA	99% of stage IA patients received no adjuvant chemotherapy.
IKNL – Longkanker in beeld[30]	2010-2011	The Netherlands	1% of stage IA patients received adjuvant chemotherapy.

4.4.2 Flowchart



4.4.3 Results

Table 58 – Proportion of pIA NSCLC patients who received adjuvant chemotherapy

	Denominator	Numerator	Proportion (%)
Adjuvant Chemotherapy	603	7	1.2

Source: BCR-IMA

Table 59 – Proportion of pIA NSCLC patients who received adjuvant chemotherapy, excluding patients with clinical metastases

	Denominator	Numerator	Proportion (%)
All patients with pathological stage IA	603	7	1.2
Patients with pathological stage IA, excluding patients with clinically confirmed metastases	591	7	1.2

Source: BCR-IMA

4.4.4 Discussion

In Belgium, 1.2% of patients with pathological stage IA receive adjuvant chemotherapy. That proportion approximates the proposed target of one percent, as was seen in the Netherlands and the USA.[3, 30]

Results for individual centres are not reported as the small numbers per centre make results difficult to interpret.

Centres are encouraged to review their own results and indications for adjuvant chemotherapy and further avoid its use in patients with pathological stage IA.

Key Points

- **In Belgium, 1.2% of pathological stage IA NSCLC patients (and no clinical distant metastases) received adjuvant chemotherapy, which is similar to the proportion reported in other countries (1%).**
- **Centres are encouraged to review their practice and avoid overuse of adjuvant chemotherapy in pathological stage IA NSCLC patients.**

4.5 Guideline-concordant treatment for patients with SCLC (TRT-5)

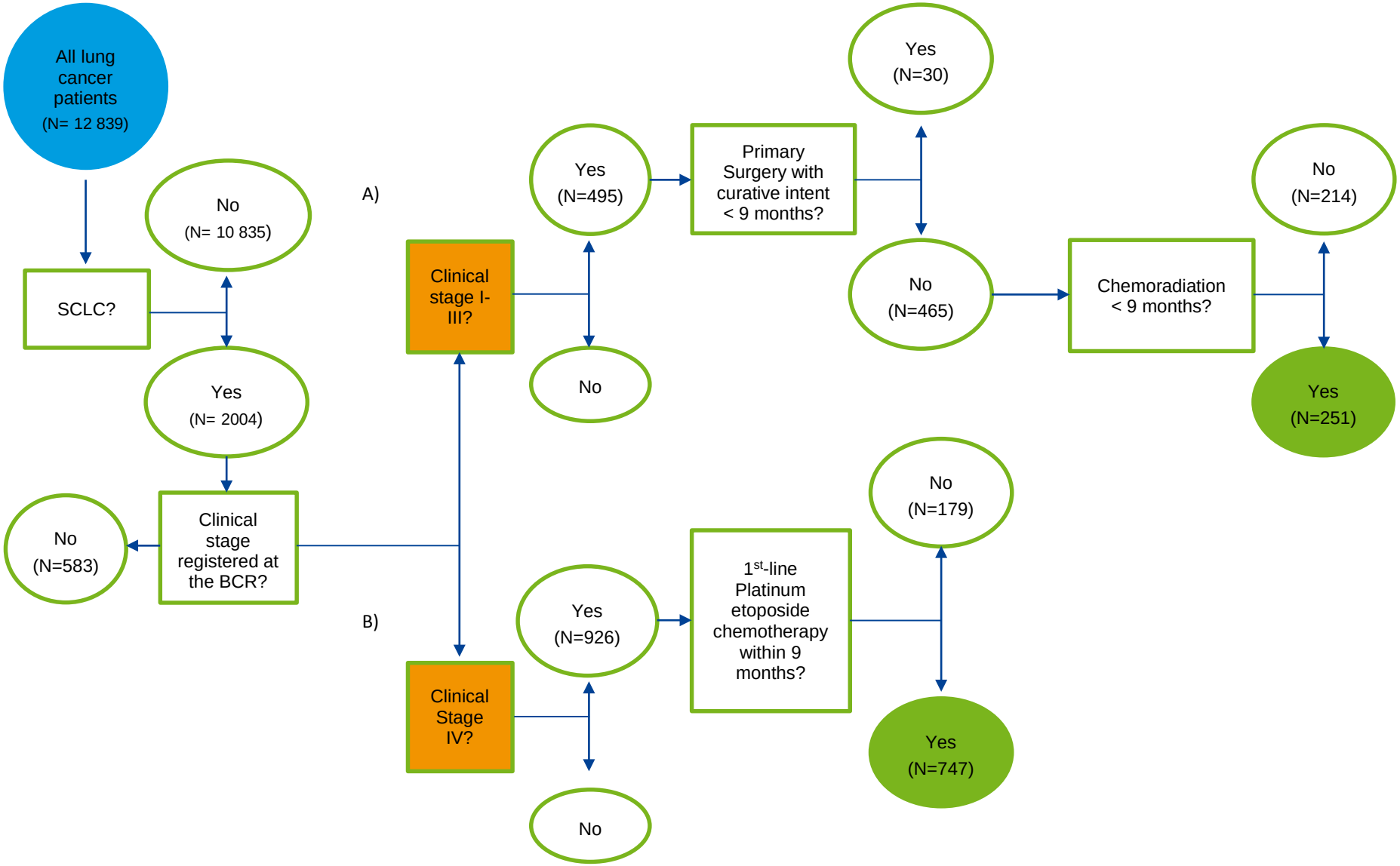
4.5.1 Documentation sheet

Title	Proportion of patients with SCLC who received chemoradiation (concurrent or sequential) for cI-III patients and platinum-etoposide combination first-line chemotherapy for cIV patients.	
Rationale	Evidence-based guidelines provide advice on treatment for lung cancer depending on clinical stage and other clinical factors, based on all available evidence from clinical trials.[19] All lung cancer patients who wish treatment and are sufficiently fit should receive treatment as recommended by recent evidence-based guidelines.	
Type of QI	Process	
Calculation	Numerator:	number of cI-III SCLC patients who received chemoradiation (concurrent or sequential) within 9 months of incidence date + number cIV SCLC patients who received platinum-etoposide combination first-line chemotherapy within 9 months of incidence date
	Denominator:	all patients with SCLC and clinical stage reported to the BCR
Target	No target	
Data source	BCR + IMA	
Technical definition	Diagnosis of SCLC: ICD-10 code C34 with ICD-O-3 morphology codes 8041-8045,8246 (BCR) (Table 103 in appendix) Radiotherapy with curative intent: billing codes (IMA) in Table 75 (appendix) Chemotherapy: billing codes (IMA) in Table 76 (appendix) Platinum-etoposide combination: maximum number of days between start platinum and start etoposide is 28 days Platinum: ATC L01XA Etoposide: ATC L01CB01	
Limitations	Clinical stage I-III does not completely overlap with the definition of limited-stage disease	
Subgroup analyses	By age, sex, by performance status, by stage, diagnostic volume	
Sensitivity analyses	Clinical stage I-III: Sequential and concurrent chemoradiation separately % of cIV patients receiving other types of chemotherapy	
Benchmarking	By centre of diagnosis	
International indicator	See **Error! Not a valid result for table.**	

Table 60 – Treatment of small cell lung cancer: international results

Author	Period covered	Country	Results
Caldarella 2012[12]	2004	Tuscany, Italy	The regional average proportion of patients with SCLC who received chemotherapy or radiochemotherapy was 88.3% (95%CI 83.2-93.4%).
National lung cancer audit report[10]	2011-2013	UK	The percentage of patients with small cell lung cancer receiving chemotherapy was 68.6% in England, 64.9% in Wales and 69.9% in Scotland.
IKNL – Longkanker in beeld[30]	2011	The Netherlands	For patients with limited-disease SCLC, treatment consisted of chemoradiation in 59% of cases and of chemotherapy alone in 19%. Sixty-four percent of patients with extensive disease were treated with chemotherapy.

4.5.2 Flowchart



4.5.3 Results

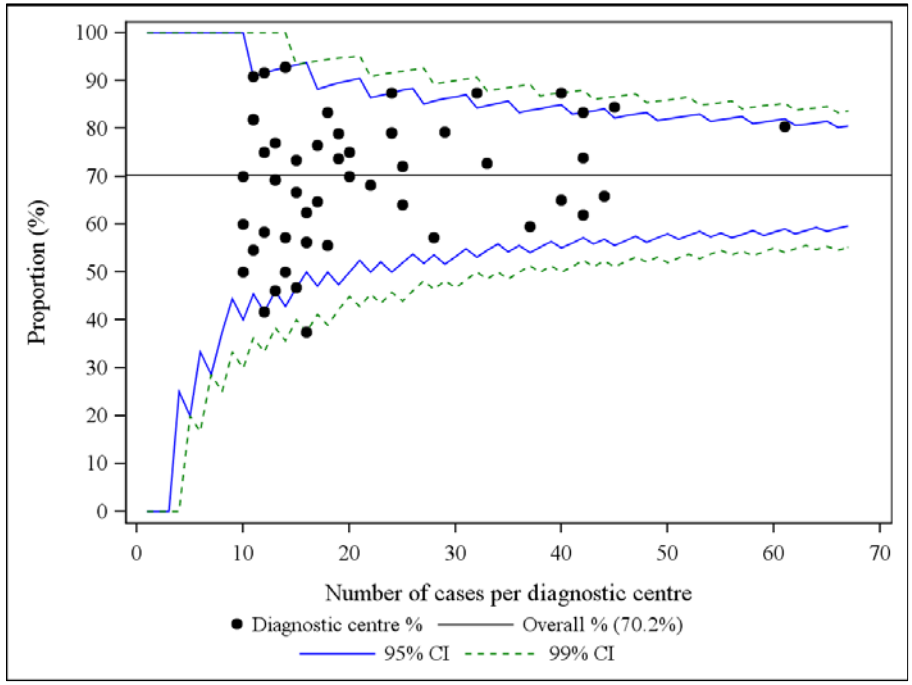
Table 61 – Proportion of cI-III SCLC patients who received chemoradiation (concurrent or sequential) and cIV SCLC patients who received platinum-etoposide first-line chemotherapy, by patient and tumour characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	1421	998	70.2
Sex			
Males	1005	701	69.8
Females	416	297	71.4
Age group			
<60 years	367	297	80.9
60-74 years	713	540	75.7
75+ years	341	161	47.2
WHO performance status			
0 – Asymptomatic	130	92	70.8
1 – Symptomatic but completely ambulatory	850	647	76.1
2 – Symptomatic, up and about more than 50% of waking hours	234	152	65.0
3 – Symptomatic, confined to bed or chair more than 50% of waking hours	73	26	35.6
4 – Completely disabled; totally confined to bed or chair	28	4	14.3
Missing	106	77	72.6
Chronic respiratory disease			
No	986	707	71.7
Yes	435	291	66.9
Cardiovascular disease			
No	606	450	74.3

Characteristic	Denominator	Numerator	Proportion (%)
Yes	815	548	67.2
Diabetes mellitus			
No	1194	849	71.1
Yes	227	149	65.6
Days of hospitalisation one year before incidence date lung cancer			
None	1049	744	70.9
1-5 days	217	161	74.2
6-15 days	96	59	61.5
More than 15 days	59	34	57.6
Clinical stage			
I*	48	16	33.3
II	69	34	49.3
III	378	201	53.2
IV	926	747	80.7

**22 patients underwent surgery within 9 months after incidence date.*
Source: BCR-IMA

Figure 25 – Proportion of SCLC patients who received guideline-concordant treatment, by diagnostic centre



Note 1: 9 patients were not shown in the figure because they could not be assigned to a diagnostic centre.

Note 2: 10 centres were not shown in the figure because they reported less than 50% of clinical stages.

Note 3: 36 centres were not shown in the figure because the denominator was smaller than 10.

Note 4: 3 centres were not shown in the figure because no SCLC patients with known stages were assigned to this centre.

Source: BCR-IMA

Table 62 – Proportion of cI-III SCLC patients who were treated with sequential versus concurrent chemoradiation

	Denominator	Numerator	Proportion (%)
Concurrent chemoradiotherapy	251	137	54.6
Sequential chemoradiotherapy	251	114	45.4

Source: BCR-IMA

Table 63 – Proportion of cIV SCLC patients by type of chemotherapy

	Denominator	Numerator	Proportion (%)
Combination Platinum-Etoposide	926	747	80.7
Platinum only	926	13	1.4
Etoposide only	926	19	2.1
Other chemoproducts	926	2	0.2
No chemo treatment	926	145	15.7

Source: BCR-IMA

4.5.4 Discussion and proposed actions

Overall, 70% of SCLC patients received guideline-concordant therapy in first-line, which appears a similar or higher proportion of patients in other countries (seeTable 60). However, comparison remains difficult because indicators are defined slightly differently. Older patients and patients with poor performance status or confirmed comorbidities (cardiovascular or respiratory disease, diabetes mellitus) were less likely to receive guideline-concordant treatment.

Older patients, often with (multi-)comorbidity, and patients with poor performance status were not included in the clinical trials leading to the recommendations, limiting the external validity of the clinical evidence. Tumour related factors may also play a role, as cI-III disease does not completely overlap with limited-stage disease. Not all tumours may be suitable for radiation therapy, due to size or location of the tumour. Combined chemoradiation was administered concurrently or sequentially each in about half of the treated cases (Table 62). Only very few cIV SCLC patients received chemotherapy other than the platinum-etoposide combination (Table 63).

Overall, variability between centres appears to be limited, with only very few outliers. For the relationship with centre volume, we refer to the specific chapter in the report.

Key Points

- **The proportion of SCLC patients who received guideline-concordant treatment is in line with proportions reported in other countries.**
- **Older patients and patients with comorbidity or poor performance status are less likely to have received guideline concordant care. Not all clinical stage I-III tumours may be eligible for radiation treatment.**

4.6 Safety of care: 60-day mortality after treatment (SAF-1 and SAF-2)

4.6.1 Documentation sheet

Title	Proportion of lung cancer patients who died within 60 days after primary treatment, by treatment modality
Rationale	Short-term mortality is a marker of the quality and safety of the therapeutic care provided. Treatment should only be offered to patients for whom the benefits are likely to balance the risks. All treatments should be provided in a safe environment so that toxicity and mortality are as low as possible.
Type of QI	Outcome
Calculation	**Indicator A: 60-day post-operative mortality** Numerator: NSCLC patients who died within 60 days after resection Denominator : NSCLC patients with primary resection with curative intent within 9 months after incidence date **Indicator B: 60-day post radiotherapy mortality** Numerator: cI-III NSCLC or SCLC patients who died within 60 days after end of radiotherapy Denominator : cI-III NSCLC or SCLC patients treated with primary (chemo)radiation with curative intent within 9 months after incidence date
Target	The Scottish Cancer taskforce[11] proposes the following targets for 30-day and 90-day mortality: Surgery, Radical Radiotherapy, Adjuvant Chemotherapy and Radical chemoradiotherapy: <5% Palliative Chemotherapy/Biological Therapy: <10%
Data source	BCR + IMA
Technical definition	Diagnostic of lung cancer: ICD-10 codes C34.0-C34.9 (BCR) in Table 103 (appendix) Treatment included: Surgery with curative intent: billing codes (IMA) in Table 74 (appendix) Radiotherapy with curative intent: billing codes (IMA) in Table 75 (appendix) Chemotherapy: billing codes (IMA) in Table 76 (appendix)
Subgroup analyses	By treatment modality By clinical and combined stage, age at diagnosis, sex, performance status, histological type, comorbidity, number of days of hospitalization prior to lung cancer, tumour localization, laterality. Indicator A: subgroup analysis adjuvant chemotherapy or not Indicator B: concurrent/sequential chemotherapy or not

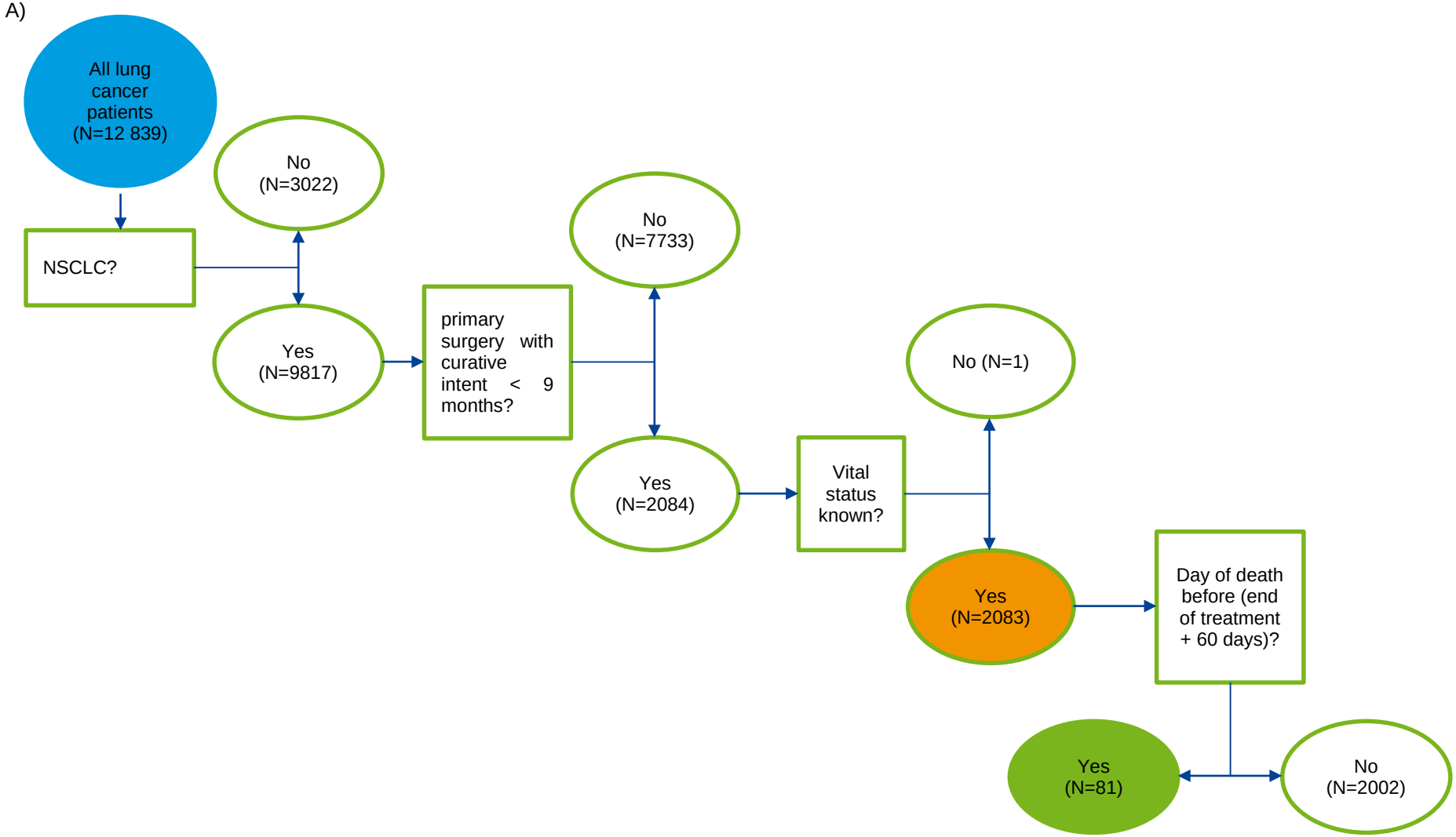
Sensitivity analyses	Post treatment mortality within 30 and 90 days of end of treatment
Benchmarking	Analyses by treatment centre Adjustment for case mix: by age, stage, PS, comorbidity, histological type
International indicator	Yes, see Table 64

Table 64 – Short-term mortality after surgery: international results

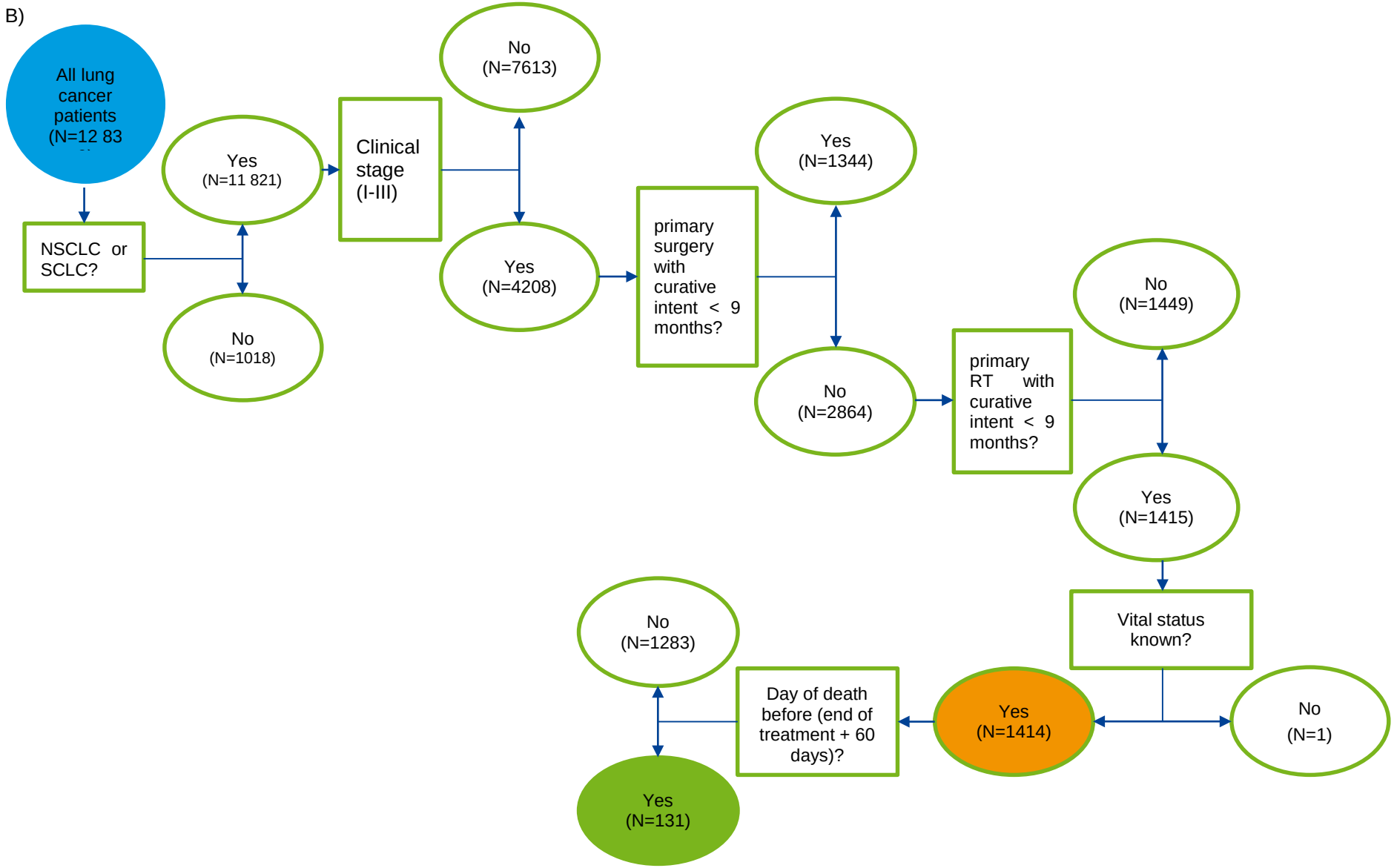
Author	Period covered	Country	Results
Caldarella 2012[12]	2004-2006	Italy	The average proportion of patients who died within 30 days after surgery was 2.8% (range 1.1-4.5%) in 2004 and 1.1% (range 0-3.3%) in 2006.
Cassivi 2008[15]	2005	USA	Overall in-hospital and 30-day mortality was 2.1%.
Freixinet 2011[32]	2007	Spain	The median mortality during the surgery admission episode was 3.4%, ranging from 1.6% to 6.6%.
Jakobsen 2009[33]	2000-2007	Denmark	The percentage of all lung cancer patients receiving surgery, who died within 30 days after surgery, has decreased from 5.2% in 2000 to 3.6% in 2007.

4.6.2 Flowchart

A)



B)


All lung cancer patients (N=12 83
NSCLC or SCLC?
Yes (N=11 821)
No (N=1018)
Clinical stage (I-III)
No (N=7613)
Yes (N=4208)
primary surgery with curative intent < 9 months?
Yes (N=1344)
No (N=2864)
primary RT with curative intent < 9 months?
No (N=1449)
Yes (N=1415)
Vital status known?
No (N=1)
Yes (N=1414)
Day of death before (end of treatment + 60 days)?
No (N=1283)
Yes (N=131)

4.6.3 Results

4.6.3.1 Short-term mortality after surgical resection (SAF-1)

Table 65 – Proportion of NSCLC patients who died within 30, 60 and 90 days after primary surgery

	Denominator	Numerator	Proportion (%)
30 days	2083	42	2.0
60 days	2083	81	3.9
90 days	2083	100	4.8

Source: BCR-IMA

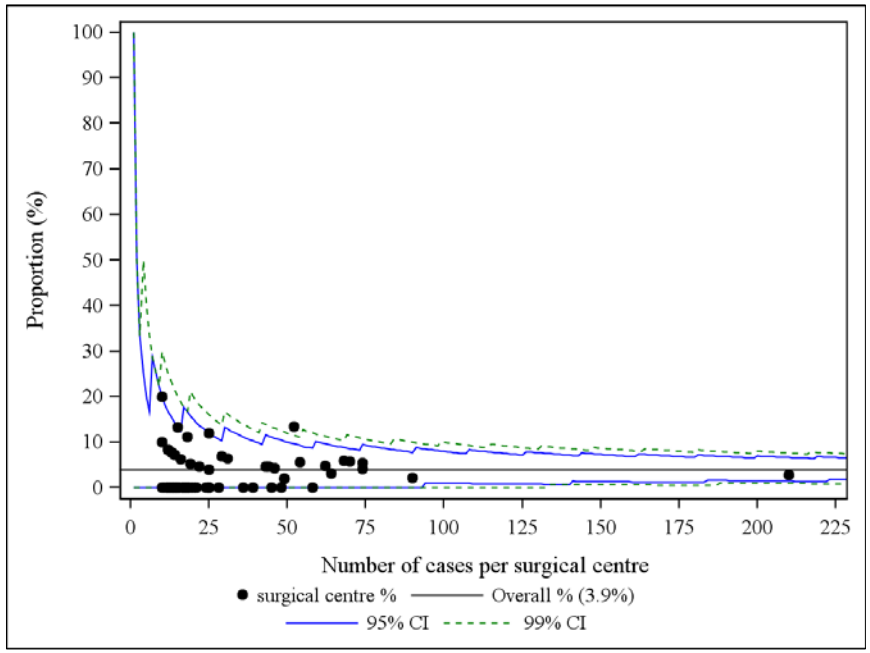
Table 66 – Proportion of NSCLC patients who died within 60 days after primary surgery, by patient, tumour and treatment characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	2083	81	3.9
Sex			
Male	1404	71	5.1
Female	679	10	1.5
Age group			
<50 years	135	1	0.7
50-59 years	489	9	1.8
60-69 years	782	25	3.2
70-79 years	596	39	6.5
80+ years	81	7	8.6
WHO performance status			
0 – Asymptomatic	519	13	2.5
1 – Symptomatic but completely ambulatory	1079	45	4.2
2 – Symptomatic, up and about more than 50% of waking hours	47	3	6.4
3 – Symptomatic, confined to bed or chair more than 50% of waking hours	6	2	33.3
4 – Completely disabled; totally confined to bed or chair	5	0	0.0
Missing	427	18	4.2
Chronic respiratory disease			
No	1482	59	4.0
Yes	601	22	3.7
Cardiovascular disease			
No	943	30	3.2
Yes	1140	51	4.5
Diabetes mellitus			
No	1826	69	3.8
Yes	257	12	4.7
Days of hospitalisation one year before incidence date lung cancer			
None	1427	53	3.7

Characteristic	Denominator	Numerator	Proportion (%)
1-5 days	421	19	4.5
6-15 days	147	5	3.4
More than 15 days	88	4	4.5
Histological subtype			
Adenocarcinoma	1094	27	2.5
Squamous cell carcinoma	730	40	5.5
Large cell carcinoma	60	6	10.0
Other	199	8	4.0
Sublocalisation (ICD-10)			
C34.0 Main bronchus	29	0	0.0
C34.1 Upper lobe, bronchus or lung	994	38	3.8
C34.2 Middle lobe, bronchus or lung	89	3	3.4
C34.3 Lower lobe, bronchus or lung	557	21	3.8
C34.8 Overlapping lesion of bronchus and lung	2	1	50.0
C34.9 Bronchus or lung, unspecified	412	18	4.4
Laterality			
Pair organ, laterality unknown	78	0	0.0
Left	855	29	3.4
Right	1150	52	4.5
Combined stage			
I	1038	27	2.6
II	524	21	4.0
III	303	22	7.3
IV	114	7	6.1
X	104	4	3.8
Type of surgery			
Total or partial lung excision with lymphadenectomy (nomenclature codes 227216/227220)	1594	58	3.6
Total or partial lung excision (nomenclature codes 227253/227264)	356	14	3.9
Excision with anastomosis (sleeve lobectomy) (nomenclature codes 227275/227286)	133	9	6.8
Adjuvant chemotherapy			
No	1429	77	5.4
Yes	654	4	0.6

Source: BCR-IMA

Figure 26 – Proportion of NSCLC patients who died within 60 days after primary surgery, by surgical centre



Note 1: 13 centres were not shown in the figure because the denominator was 0.
Note 2: 31 centres were not shown in the figure because the number of denominator was smaller than 10.
Source: BCR-IMA

Discussion

National result for 60-day mortality after surgery is good compared to international results reported for 30-day mortality. For 30-, 60- and 90- day mortality, results remain below the pre-set target of 5%. As expected, the risk of postoperative death increases with age, clinical stage, poor performance status and comorbidity. Men have a considerably higher risk of postoperative mortality than women. The risk of postoperative death also depends on the type of surgery, with a higher risk after sleeve lobectomy. Similar risk factors (older age, significant cardiopulmonary comorbidity, and greater extent of surgical resection) were reported in previous publications.[34, 35] A very recent publication reported results from a multivariable analysis on 161 255 lung cancer patients aiming to identify the clinical and nonclinical variables that might be predictive of 30-day mortality after lung cancer resection. Results demonstrate that clinical variables, including older age, male sex, higher comorbidity score, increased cancer stage, pneumonectomy, positive surgical margins, use of preoperative radiation therapy, and increased tumour size, were associated with higher rates of 30-day mortality after lung cancer resection. Results also showed that nonclinical variables, such as living in low-income neighbourhoods and communities with a lesser proportion of high school graduates, were also factors independently associated with greater 30-day mortality after lung cancer surgery.[36] Such variables could not be evaluated in this study using our databases.

The funnel plot of results for individual surgical centres shows only few outliers, but 31 centres were not included due to small sample size (less than ten cases).

As lobectomy and pneumonectomy have an identical billing code in Belgium, we cannot differentiate results by type of surgery. Differences in proportion of pneumonectomy or sleeve lobectomy may partially explain differences in outcomes between hospitals.

For the volume-outcome analysis, we refer to the “volume outcome” chapter in the report.

Key points

- **Mortality within 60 days after surgical resection with curative intent in NSCLC patients was 3.9%, which is below the 5% target.**
- **The following factors are predictive of 60 days mortality: type of surgery; sex (males have higher mortality), age, stage and histology (adenocarcinoma have lower mortality).**

4.6.3.2 *Short-term mortality after primary (chemo)radiation (SAF- 2)*

Table 67 – Proportion of cI-III lung cancer patients who died within 30, 60 and 90 days after primary (chemo)radiation

	Denominator	Numerator	Proportion (%)
30 days	1414	81	5.7
60 days	1414	131	9.3
90 days	1414	174	12.3

Source: BCR-IMA

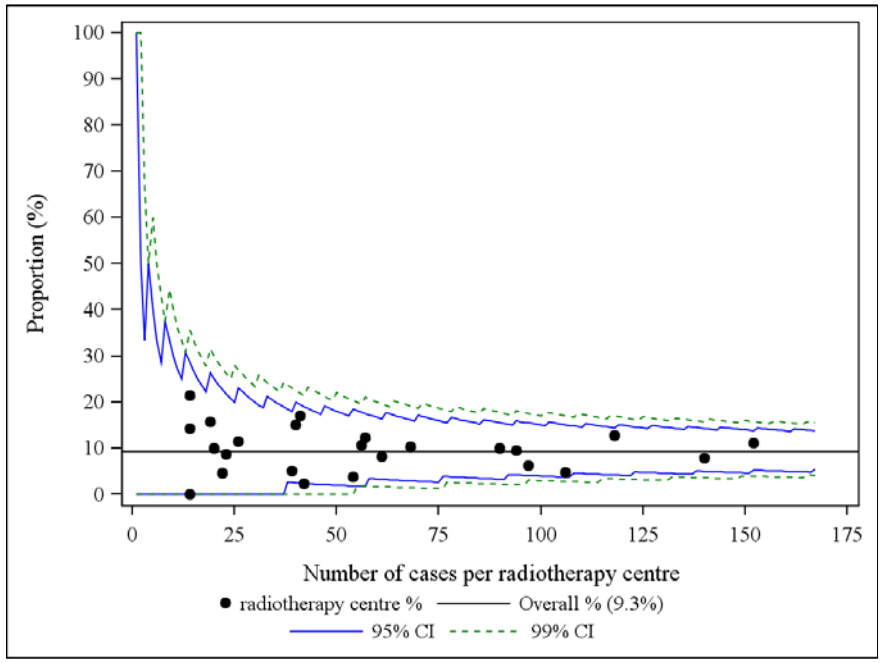
Table 68 – Proportion of cI-III lung cancer patients who died within 60 days after primary radiotherapy, by patient, tumour and treatment characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	1414	131	9.3
Sex			
Male	1036	100	9.7
Female	378	31	8.2
Age group			
<50 years	60	7	11.7
50-59 years	282	10	3.5
60-69 years	461	37	8.0
70-79 years	413	48	11.6
80+ years	198	29	14.6
Performance Status			
0 – Asymptomatic	210	13	6.2
1 – Symptomatic but completely ambulatory	973	88	9.0
2 – Symptomatic, up and about more than 50% of waking hours	107	15	14.0
3 – Symptomatic, confined to bed or chair more than 50% of waking hours	16	2	12.5
4 – Completely disabled; totally confined to bed or chair	4	2	50.0
Missing	104	11	10.6
Chronic respiratory disease			
No	939	96	10.2
Yes	475	35	7.4
Cardiovascular disease			
No	597	42	7.0
Yes	817	89	10.9
Diabetes mellitus			
No	1218	106	8.7
Yes	196	25	12.8
Days of hospitalisation one year before incidence date lung cancer			

Characteristic	Denominator	Numerator	Proportion (%)
None	1046	91	8.7
1-5 days	210	23	11.0
6-15 days	95	8	8.4
More than 15 days	63	9	14.3
Histological subtype			
Adenocarcinoma	430	38	8.8
Squamous cell carcinoma	581	58	10.0
Large cell carcinoma	53	9	17.0
Small cell carcinoma	258	13	5.0
Other	92	13	14.1
Sublocalisation			
C34.0 Main bronchus	97	12	12.4
C34.1 Upper lobe, bronchus or lung	614	54	8.8
C34.2 Middle lobe, bronchus or lung	47	4	8.5
C34.3 Lower lobe, bronchus or lung	274	28	10.2
C34.8 Overlapping lesion of bronchus and lung	1	0	0.0
C34.9 Bronchus or lung, unspecified	381	33	8.7
Laterality			
Pair organ, laterality unknown	53	2	3.8
Left	555	55	9.9
Right	806	74	9.2
Combined stage			
I	232	14	6.0
II	171	16	9.4
III	1009	101	10.0
IV*	2	0	0.0
Type of radiotherapy (according to IMA data)			
Category 2	13	3	23.1
Category 3	1054	110	10.4
Category 4	347	18	5.2
Concurrent/Sequential chemotherapy			
Concurrent chemoradiotherapy	409	23	5.6
Sequential chemoradiotherapy	604	53	8.8
No chemotherapy	401	55	13.7

Source: BCR-IMA
**Patients with clinical stage I-III (cfr inclusion) but combined stage IV*

Figure 27 – Proportion of cI-III lung cancer patients who died within 60 days after primary radiotherapy, by radiotherapy centre



Note: 1 centre was not shown in the figure because the number of denominator was smaller than 10.
Source: BCR-IMA

Discussion

Results for short-term mortality after (chemo)radiation are higher than expected and did not remain below the pre-set target of 5%.

The Scottish Cancer Taskforce suggested a target of 5% for both 30-day and 90-day mortality, but no results for Scotland were published yet. We did not find similar results published in the international literature.

Some published survival curves for non-trial populations can be informative. The survival curve of patients treated with chemoradiation (with the etoposide-cisplatin or carboplatin-paclitaxel combination) identified in the Veterans Health Administration (USA) shows a survival of approximately 90%, four to five months after diagnosis (may approximate duration of chemoradiation plus 60 days).[37] Results from the National Cancer Data Base, a database including patients from more than 1500 accredited cancer institutes in the US, show a survival of approximately 80% after six months in stage III NSCLC patients treated with definitive chemoradiation.[38]

The results may in the first place be an indication of the poor prognosis and frail general health of many cIII NSCLC patients. The higher short-term mortality in the group of patients who received sequential chemoradiotherapy or radiotherapy alone, although counterintuitive, may further reflect the fact that many cIII lung cancer patients have poor general fitness and have difficulties supporting intensive treatment. A population-based study published in 2009 has shown that more than half of patients with stage III lung cancer are (theoretically) not eligible for concurrent chemoradiation due to age or co-morbidity.[39] Our results show that even less toxic treatment options such as sequential chemoradiation or radiotherapy alone have significant short term mortality. Further research into predictors of short term mortality and measures to reduce toxicity of treatment would enable treatment delivery with a better benefit-risk balance and better value for all patients. Information on toxicity and short-term mortality by patient characteristics can also be helpful for patients and medical doctors when making treatment decisions taking into account patient preferences and values.

For analysis of the volume-outcome relationship, we refer to the “volume outcome” chapter of the report.

Key points

- **Mortality within 60 days after the end of primary radiotherapy in SCLC and NSCLC patients was 9.3%, which is above a pre-set target of 5% proposed by the Scottish Cancer Taskforce.**
- **The following factors are predictive of 60 days mortality: age, stage and WHO performance status. Patients with chronic respiratory disease seem to have a lower mortality rate, which is somewhat counterintuitive.**

4.7 Chemotherapy or targeted therapy near the end-of-life (EOL-1)

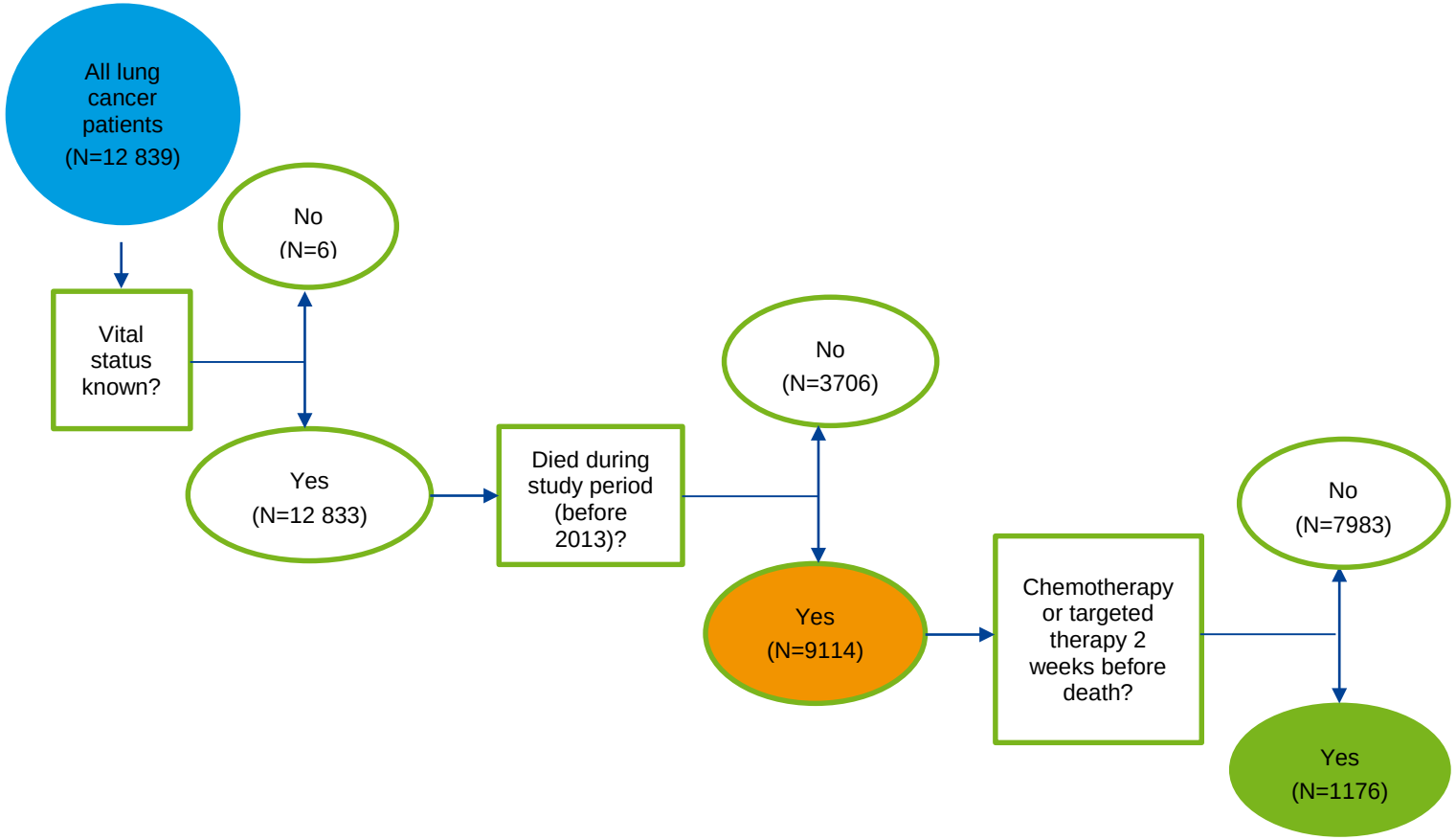
4.7.1 Documentation sheet

Title	Proportion of lung cancer patients who received chemotherapy or targeted therapy within 2 weeks of death
Rationale	As prognosis of advanced and recurrent lung cancer is limited, it is recommended to implement advance care planning early in the disease process and obtain patient's preferences timely. Patients' quality of life should be prioritized and anticancer therapy should be offered only when there is a reasonable chance that it will provide a meaningful clinical benefit. Continuing cancer-directed treatment at the end of life should be avoided.[19, 40, 41]
Type of QI	Process
Calculation	Numerator: Number of lung cancer patients who received chemotherapy, targeted therapy within 2 weeks of death Denominator: Number of lung cancer patients who died during the study period
Target	No target
Data source	BCR + IMA
Technical definition	Diagnostic of lung cancer: ICD-10 codes C34 (BCR) (Table 103) Treatment: Chemotherapy: billing codes (IMA) in Table 76 Targeted therapy: billing codes in Table 77
Limitations	Date of death can be determined by end-of-life decisions such as euthanasia, shortening the time interval between last systemic therapy and day of death.
Subgroup analyses	Sex, age, combined stage, per treatment modality received before death
Sensitivity analyses	Within 60 days, 30 days and 7 days of death
Benchmarking	No analysis per centre
International indicator	See Table 69

Table 69 – Chemotherapy or targeted therapy near the end of life: international results

Author	Period covered	country	Results
Earle 2008[42]	1993-1999	USA	9.7% and 11.6% of all patients who died of (any) malignancy received chemotherapy within 14 days of death (unclear if targeted treatment was included).
Nakano 2012[43]	2002-2007	Japan	Rates of patients with metastatic NSCLC receiving chemotherapy within the last two weeks of life were 28% in patients who died in general wards and 0% in patients who died in palliative care units. The mean number of days between the last chemotherapy and death was 78.3 days in general wards and 94.2 days in palliative care units.
Murillo 2006[44]	2000-2003	USA	20% of stage IIIB-IV NSCLC patients received chemotherapy within 2 weeks of death, 41% received chemotherapy within 1 month of death.
Tokito 2014[45]	2010-2012	Japan	For stage IV NSCLC patients who received chemotherapy, median time from last day of chemotherapy to death was 64 days (range 0-164 days), more specifically 72 days (6-614 days) for intravenous chemotherapy, 40 days (5-247 days) for oral cytotoxic agents and 50 days (0-524 days) for patients who received TKIs.
Calderalla 2012[12]	2004	Tuscany, Italy	24.2% of patients received chemotherapy within one month of death.
Fasola 2012[6]	2008	Italy	16% of patients with NSCLC received active medical treatment within 30 days of death (benchmark value was put at 20%).

4.7.2 Flowchart



4.7.3 Results

Table 70 – Proportion of lung cancer patients who received chemotherapy or targeted therapy within 2 weeks of death, by patient and tumour characteristics

Characteristic	Denominator	Numerator	Proportion (%)
Overall	9114	1176	12.9
Sex			
Males	6670	885	13.3
Females	2444	291	11.9
Age group			
<50 years	395	67	17.0
50-59 years	1578	286	18.1
60-69 years	2582	394	15.3
70-79 years	2855	339	11.9
80+ years	1704	90	5.3
Combined stage			
I	452	36	8.0
II	412	28	6.8
III	1772	204	11.5
IV	4 668	653	14.0
X	1795	255	14.2
NA	15	0	0.0

Source: BCR-IMA

Table 71 – Type of treatment received by lung cancer patients who received chemotherapy or targeted therapy within 2 weeks of death

Treatment modality within 2 weeks of death	Denominator	Numerator	Proportion (%)
Chemo only	1176	927	78.83
Chemo + targeted therapy	1176	5	0.43
Targeted therapy only	1176	244	20.75

Source: BCR-IMA

Table 72 – Sensitivity analysis: Proportion of lung cancer patients who received chemotherapy or targeted therapy within 7 days, 14 days, 30 days and 60 days of death

Number of days before death	Denominator	Numerator	Proportion (%)
Within 7 days	9114	545	6.0
Within 14 days	9114	1176	12.9
Within 30 days	9114	2128	23.3
Within 60 days	9114	3303	36.2

Source: BCR-IMA

Table 73 – Proportion of patients who received chemotherapy in the last 2 weeks of life, by tumour type (2006-2012)

	Total	N with palliative care	
	N	N	%
Acute	58 479	6275	10.7
Oesophagus	3506	251	7.2
Stomach	4979	261	5.2
Liver, primary	2555	133	5.2
Gallbladder and biliary Tract	1624	77	4.7
Pancreas	6820	686	10.1
Lung, bronchus and trachea	33 091	4171	12.6
Pleura	1181	51	4.3
Brain	3090	105	3.4
Acute myeloid leukaemia	1633	540	33.1
Chronic	8352	1153	13.8
Head and Neck	3544	402	11.3
Small Intestine	432	19	4.4
Nasal cavities and sinuses	260	11	4.2
Ovary and uterine adnexa	2189	264	12.1
Multiple Myeloma	1399	259	18.5
Acute lymphatic leukaemia	176	65	36.9
Chronic myeloid leukaemia	352	133	37.8
Total	66 831	7428	11.1

Source: Performance of the Belgian Health System – Report 2015[41]

4.7.4 Discussion

Overall, 13% of the patients who died during the study period received systemic therapy (chemotherapy, targeted therapy) during the 2 weeks before death. Patients with advanced (or not reported) stage at diagnosis received systemic therapy near the end of life more often than patients who were diagnosed with early stage disease. Older patients (especially ≥80 years old) were treated less frequently during the 2 weeks before death. Results reported internationally for the last 14 and 30 days before death were within the same range or even higher (see Table 69 and Table 72). International results for other types of cancer suggest that the use of chemotherapy near the end of life differs depending on tumour type, with lung cancer in the group of more frequently treated tumours near the end of life (seeTable 73).

Death within 2 weeks after the last administration of systemic therapy may be due to fatal toxicity, disease progression or causes not related to lung cancer or its treatment. In addition, end of life decisions such as euthanasia, can shorten the time interval between last treatment and death. Good patient selection, limiting toxicity and adequate end of life care are important parts of high quality care.

To reduce the number of patients receiving tumour-directed therapy near the end of life, the following measures can thus be proposed:

- To avoid 'aggressive' care and overuse of cancer-directed treatment at the end of life, early integration of palliative care and discussions about the patient's preferences regarding care at the end of life appear to be essential.[42, 46 47]
- Careful clinical evaluation of the general condition of the patient before initiating therapy is necessary to invidualize the benefit-harm balance.

Third-line and further therapy maybe beneficial for a limited number of patients only.

- Close monitoring and timely and adequate treatment of adverse events related to therapy can reduce the number of fatal toxicity.

Key Points

- **Nearly 13% of the patients who died during the study period received systemic therapy (chemotherapy, targeted therapy) during the last 2 weeks before death.**
- **To limit the use of tumour-directed treatment near the end of life, careful patients selection and early integration of palliative care and advance care planning are recommended.**

SUPPLEMENT: BILLING CODES (NOMENCLATURE)

APPENDIX 1. DEFINITION OF ACTIVE TREATMENT

Appendix 1.1. Surgery with curative intent

Table 74 – Nomenclature Codes Surgery with curative intent

Outpatient	Inpatient	Dutch Description	French Description
227216	**227220**	Uitgebreide totale of gedeeltelijke longexerese met klierevidement voor oncologische aandoening	Exérèse totale élargie ou partielle du poumon avec évidement ganglionnaire pour affection oncologique
227275	**227286**	Resectie met anastomose (broncho-bronchiaal of tracheo-bronchiaal) van een stambronchus of van de trachea via thoracotomie	Résection d'une bronche souche ou de la trachée avec anastomose (broncho-bronchique ou trachéo-bronchique) par thoracotomie
227253	**227264**	Totale of gedeeltelijke longexeresis	Exérèse totale ou partielle d'un poumon

Appendix 1.2. Radiotherapy with curative intent

Table 75 – Nomenclature Codes Radiotherapy with curative intent

Outpatient	Inpatient	Dutch Description	French Description
444135	**444146**	Forfaitair honorarium voor een eenvoudige uitwendige bestralingsreeks van minstens 11 tot 35 fracties voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 2	Honoraires forfaitaires pour une série d'irradiations externes simples de 11 à 35 fractions chez un patient qui répond aux critères ou pathologie repris en catégorie 2
444150	**444161**	Forfaitair honorarium voor een complexe uitwendige bestralingsreeks voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 3, 5 of 6	Honoraires forfaitaires pour une série d'irradiations externes complexes chez un patient qui répond aux critères ou pathologie repris en catégorie 3
444172	**444183**	Forfaitair honorarium voor een complexe uitwendige bestralingsreeks voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 4	Honoraires forfaitaires pour une série d'irradiations externes complexes chez un patient qui répond aux critères ou pathologie repris en catégorie 4

Appendix 1.3. Chemotherapy and targeted therapy

Table 76 – ATC-3, ATC-4 and ATC-5 codes for chemotherapy

ATC Code	Name
L01A	ALKYLATING AGENTS
L01B	ANTIMETABOLITES
L01C	PLANT ALKALOIDS AND OTHER NATURAL PRODUCTS
L01D	CYTOTOXIC ANTIBIOTICS AND RELATED SUBSTANCES
L01XA	OTHER ANTINEOPLASTIC AGENTS, Platinum compounds
L01XB	METHYLHYDRAZINES
L01XD	OTHER ANTINEOPLASTIC AGENTS, sensitizers used in photodynamic/radiation therapy
L01XX05	hydroxycarbamide
L01XX11	estramustine
L01XC17	topotecan
L01XC19	irinotecan

Table 77 – ATC-4 and ATC-5 codes for targeted therapy

ATC Code	Name
L01XC	OTHER ANTINEOPLASTIC AGENTS, Monoclonal antibodies
L01XE	OTHER ANTINEOPLASTIC AGENTS, Protein kinase inhibitors
L01XX32	bortezomib

APPENDIX 2. DEFINITION OF DIAGNOSTIC CENTRE

Appendix 2.1. MDT meeting

Table 78 – Nomenclature Codes Multidisciplinary Team Meeting (MDT)

Outpatient	Inpatient	Dutch Description	French Desription
350372	**350383**	Schriftelijk verslag van een multidisciplinair oncologisch consult met deelname van minstens drie geneesheren van verschillende specialismen onder leiding van een geneesheer-coördinator, met beschrijving van de diagnose en van het behandelingsplan (until 31/10/2010) Eerste multidisciplinair oncologisch consult (eerste MOC), geattesteerd door de geneesheer-coördinator	Rapport écrit d'une concertation oncologique multidisciplinaire avec la participation d'au moins trois médecins de spécialités différentes sous la direction d'un médecin-coordinateur et reprenant la description du diagnostic et du plan de traitement (until 31/10/2010) Première consultation oncologique multidisciplinaire (première COM), attestée par le médecin-coordinateur (since 1/11/2010)
350394	**350405**	Deelname aan multidisciplinair oncologisch consult	Deelname aan multidisciplinair oncologisch consult
350416	**350420**	° Deelname aan het multidisciplinair oncologisch consult door een arts die geen deel uitmaakt van de staf van ziekenhuisgeneesheren	° Participation à la concertation oncologique multidisciplinaire par un médecin qui n'est pas membre de l'équipe de médecins hospitaliers
350276	**350280**	Opvolgings-multidisciplinair oncologisch consult (opvolgings-MOC), geattesteerd door de geneesheer-coördinator	Concertation oncologique multidisciplinaire de suivi (COM de suivi), attestée par le médecin-coordinateur
350291	**350302**	Bijkomend multidisciplinair oncologisch consult (bijkomende MOC) in een ander ziekenhuis dan dit van het eerste MOC, op doorverwijzing, geattesteerd door de geneesheer-coördinator	Concertation oncologique multidisciplinaire supplémentaire (COM supplémentaire) dans un hôpital autre que celui de la première COM, sur renvoi, attestée par le médecin-coordinateur
350475	**350486**	Bijkomend honorarium bij de verstrekking 350394-350405 of 350416-350420 aanrekenbaar door de geneesheer-specialist in de medische oncologie, of houder van de bijzondere beroepstitel in de klinische hematologie of in de pediatrische hematologie en oncologie, wanneer deze het multidisciplinair oncologisch consult bijwoont	Supplément d'honoraires à la prestation 350394-350405 ou 350416-350420, attestable par le médecin spécialiste en oncologie médicale ou porteur du titre professionnel particulier en hématologie clinique ou en hématologie et oncologie pédiatriques, lorsque celui-ci assiste à la consultation oncologique multidisciplinaire
350453	**350464**	Bijkomend honorarium bij de verstrekking 350372-350383, 350276-350280 en 350291-350302 aanrekenbaar door de geneesheer-specialist in de medische oncologie, of houder van	Supplément d'honoraires à la prestation 350372-350383, 350276-350280 et 350291-350302, attestable par le médecin spécialiste en oncologie médicale ou porteur du titre professionnel particulier en hématologie clinique ou en

Outpatient	Inpatient	Dutch Description	French Desription
		de bijzondere beroepstitel in de klinische hematologie of in de pediatrische	hématologie et oncologie pédiatriques, lorsque celui-ci coordonne la consultation oncologique multidisciplinaire

Appendix 2.2. Bronchoscopy

Table 79 – Nomenclature Codes Bronchoscopy

Outpatient	Inpatient	Dutch Description	French Description
257294	**257305**	Bronchoscopie zonder afname voor biopsie en/of bronchoscopie met therapeutische aspiratie	Bronchoscopie sans prélèvement biopsique, et/ou bronchoscopie avec aspiration thérapeutique
257316	**257320**	Bronchoscopie met afname voor biopsie en/of verwijderen van tumors en/of coagulatie van letsels	Bronchoscopie avec prélèvement biopsique, et/ou ablation de tumeurs, et/ou coagulation de lésions
471715	**471726**	Bronchoscopie zonder afname voor biopsie	Bronchoscopie sans prélèvement biopsique
471730	**471741**	Bronchoscopie met afname voor biopsie, en/of verwijderen van tumors, en/of coagulatie van letsels	Bronchoscopie avec prélèvement biopsique, et/ou ablation de tumeurs, et/ou coagulation de lésions
471752	**471763**	Bronchoscopie met transcarinale punctie en eventuele radioscopische controle	Bronchoscopie avec ponction transcarinale et contrôle radioscopique éventuel
471774	**471785**	Bronchoscopie met bronchoalveolair wassen (min. 100 ml)	Bronchoscopie avec lavage broncho-alvéolaire (minimum 100 ml)
471796	**471800**	Bronchoscopie met extractie van vreemde lichamen of plaatsing van een prothetisch element	Bronchoscopie avec extraction de corps étrangers ou mise en place d'un élément prothétique
471811	**471822**	Bronchoscopie met perifere pulmonaire afnamen voor biopsie (ofwel veelvuldige afnamen, minimum 5, ofwel geleide afname in geval van perifere tumor), inclusief de eventuele radioscopische controle	Bronchoscopie avec prélèvement de biopsies pulmonaires périphériques (soit prélèvements multiples minimum 5, soit prélèvement dirigé en cas de tumeur périphérique) y compris le contrôle radioscopique éventuel

Appendix 2.3. Biopsy

Table 80 – Nomenclature Codes Punction Biopsy

Outpatient	Inpatient	Dutch Description	French Description
355434	**355445**	Punctie bij ascites of borstvliesontsteking	Ponction d'ascite ou de pleurésie
355456	**355460**	Punctie voor evacuatie bij ascites of borstvliesontsteking, inclusief de eventuele inspuitingen en spoelingen	Ponction évacuatrice d'ascite ou de pleurésie, y compris les injections et lavages éventuels
355633	**355644**	Pleurabiopsie met naald	Biopsie pleurale à l'aiguille
355655	**355666**	Punctiebiopsie van een longletsel onder radiologische controle	Ponction biopsique d'une lésion pulmonaire sous contrôle radiologique

Appendix 2.4. CT

Table 81 – Nomenclature Codes CT

Outpatient	Inpatient	Dutch Description	French Description
458813	**458824**	Computergestuurde tomografie van de hals (weke delen) of van de thorax of van het abdomen, met en/of zonder contrastmiddel, met registreren en clichés, minimum 15 coupes, voor het hele onderzoek	Tomographie commandée par ordinateur, du cou (parties molles) ou du thorax, ou de l'abdomen,avec et/ou sans moyen de contraste, avec enregistrement et clichés, 15 coupes au minimum, pour l'ensemble de l'examen
459550	**459561**	Computergestuurde tomografie van de thorax met of zonder contrastmiddel, met registreren en clichés, minimum 15 coupes, voor het hele onderzoek	Tomographie commandée par ordinateur, du thorax avec/ou sans moyen de contraste, avec enregistrement et clichés, 15 coupes au minimum, pour l'ensemble de l'examen
459594	**459605**	Computergestuurde tomografie van de hals en de thorax, met of zonder contrastmiddel, met registreren en clichés, minimum 30 coupes voor het hele onderzoek	Tomographie commandée par ordinateur du cou et du thorax, avec/ ou sans moyen de contraste, avec enregistrement et clichés, 30 coupes au minimum, pour l'ensemble de l'examen
459616	**459620**	Computergestuurde tomografie van de thorax en het abdomen, met of zonder contrastmiddel, met registreren en clichés, minimum 30 coupes voor het hele onderzoek	Tomographie commandée par ordinateur du thorax et de l'abdomen, avec/ou sans moyen de contraste, avec enregistrement et clichés, 30 coupes au minimum, pour l'ensemble de l'examen
459631	**459642**	Computergestuurde tomografie van de hals, de thorax en het abdomen, met of zonder contrastmiddel, met registreren en clichés, minimum 30 coupes voor het hele onderzoek	Tomographie commandée par ordinateur du cou, du thorax et de l'abdomen, avec/ou sans moyen de contraste, avec enregistrement et clichés, 30 coupes au minimum, pour l'ensemble de l'examen
459572	**459583**	Computergestuurde tomografie van het abdomen, met of zonder contrastmiddel, met registreren en clichés, minimum 15 coupes, voor het hele onderzoek	Tomographie commandée par ordinateur, de l'abdomen, avec/ou sans moyen de contraste, avec enregistrement et clichés, 15 coupes au minimum, pour l'ensemble de l'examen

Appendix 2.5. Pulmonary Function

Table 82 – Nomenclature Codes Pulmonary Function

Outpatient	Inpatient	Dutch Description	French Desription
471251	**471262**	Volledige spirografie met bepalen van maximum adem minuten volume	Spirographie globale avec détermination du volume expiratoire maximum seconde
471273	**471284**	Spirografie met bronchodilatatieproef	Spirographie avec épreuve de bronchodilatation
471295	**471306**	Spirografie met pharmacodynamische provocatieproef al dan niet gevolgd van bronchodilatatie	Spirographie avec épreuve pharmaco-dynamique, de provocation, suivie ou non de bronchodilatation
471310	**471321**	Bepalen van het residuair volume	Détermination du volume résiduel
471354	**471365**	Meten van diffusiecapaciteit	Mesure de la capacité de diffusion
471376	**471380**	Studie van de ventilatiemechaniek	Etude de la mécanique ventilatoire
471391	**471402**	Ergospirometrie	Ergospirométrie

APPENDIX 3. OTHER DIAGNOSTIC AND STAGING PROCEDURES

Appendix 3.1. Histology-Cytology-Pathology-Molecular Diagnostic

Table 83 – Nomenclature Codes Histological Diagnosis

Outpatient	Inpatient	Dutch Description	French Description
588011	**588022**	Honorarium voor het pathologisch-anatomische onderzoek door inclusie en coupe van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen en met inbegrip van het eventueel macroscopisch onderzoek van operatiestukken, voor die prelevementen die niet overeenkomen met de prestaties 588232 - 588243, 588254 - 588265, 588276 - 588280 of 588291 - 588302	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires, pour les prélèvements ne correspondant pas aux prestations 588232 - 588243, 588254 - 588265, 588276 - 588280 ou 588291 - 588302
588254	**588265**	Honorarium voor het pathologisch-anatomisch onderzoek door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen, en met inbegrip van het eventueel macroscopisch onderzoek, voor volgende prelevementen : Biopten van volgende diepe organen : - lever, - nier, - nierbekken, - bijnier, - prostaat, - borst, - lymfeklier, - beenmerg, - bot, - schildklier, - speekselklier, - pleura, - long, - testikel, - peritoneum, - retroperitoneum, - mediastinum, - hersenen	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe, d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, et y compris l'examen macroscopique éventuel, pour les prélèvements suivants : Biopsies des organes profonds suivants : - foie, - rein, - bassinet, - surrénale, - prostate, - sein, - ganglion lymphatique, - moelle osseuse, - os, - glande thyroïde, - glande salivaire, - plèvre, - poumon, - testicule, - péritoine, - rétropéritoine, - médiastin, - cerveau
588276	**588280**	Honorarium voor het pathologisch-anatomisch onderzoek, door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen, en met inbegrip van het eventueel macroscopisch onderzoek voor volgende operatiestukken : - lymfeklierexerese, - eenzijdige lymfeklier okselevidement, - eenzijdige lymfeklier liesevidement, - heelkundige longbiopsie, - totale of partiële thymectomie, - resectie van subaponeurotische tumoren, - partiële pancreatectomie, - partiële hepatectomie, - cholecystectomie, - splenectomie, - mesenteriale tumorectomie, - retroperitoneale tumorectomie, - oogbol resectie, - speekselklierresectie (met uitzondering van de accessoire speekselklieren), - partiële of totale glossectomie, -	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe, d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires suivantes : - exérèse de ganglion lympathique, - évidement ganglionnaire axillaire unilatéral, - évidement ganglionnaire inguinal unilatéral - biopsie pulmonaire chirurgicale, - thymectomie totale ou partielle, - résection de tumeur subaponévrotique, - pancréatectomie partielle, - hépatectomie partielle, - cholécystectomie , - splénectomie, - tumorectomie mésentérique, - tumorectomie rétropéritonéale, - résection du globe oculaire, - résection d'une glande salivaire (à l'exception des glandes salivaires accessoires), - glossectomie

Outpatient	Inpatient	Dutch Description	French Description
		thyroidectomie, - parathyroidectomie, - pharyngectomie, - incisionele borstbiopsie, - borsttumorectomie, - partiële cystectomie (met uitzondering van de endoscopische blaasresectie), - heelkundige of endoscopische prostaatadenomectomie, - epididymectomie, - orchidectomie, - partiële penis amputatie, - diepe hals tumorectomie, - partiële nefrectomie, - uni- of bilaterale adnexectomie, - ovariectomie, - totale salpingectomie, - partiële vulvectomie, - baarmoederhals conisatie of -resectie, - bijnier resectie, - zenuwbiopsie, - spierbiopsie, - hersen-, ruggemerg- of hypofysetumor resectie, - bottumor resectie, - tonsillectomie (> 18 jaar), - adenoidectomie (> 18 jaar)	partielle ou totale, - thyroïdectomie,- parathyroïdectomie, - pharyngectomie, - biopsie par incision du sein, - tumorectomie du sein, - cystectomie partielle (à l'exception de la résection vésicale endoscopique), - adénomectomie prostatique chirurgicale ou endoscopique , - épididymectomie, - orchidectomie, - amputation partielle du pénis, - tumorectomie profonde du cou, - néphrectomie partielle, - annexectomie uni- ou bilatérale, - ovariectomie, - salpingectomie totale, - vulvectomie partielle, - conisation ou résection du col de l'utérus, - résection de la glande surrénale, - biopsie nerveuse- biopsie musculaire, - résection d'une tumeur du cerveau, de la moelle épinière ou de l'hypophyse, - résection de tumeur osseuse, - amygdalectomie (> 18 ans), - adénoïdectomie (> 18 ans)
588291	**588302**	Honorarium voor het pathologisch-anatomisch onderzoek, door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen en met inbegrip van het eventueel macroscopisch onderzoek, voor volgende operatiestukken : - partiële mammectomie met okselklier uitruiming, - totale mammectomie met of zonder okselklier uitruiming, - partiële of totale pneumectomie, - partiële of totale slokdarmresectie, - bilaterale lies klierevidement, - lymfeklierevidement van 2 of meerdere groepen halsklieren, - tumorectomie van de mondbodem met of zonder mandibulectomie, - tumorectomie van het verhemelte met of zonder maxillectomie, - totale maxillectomie, - partiële of totale gastrectomie, - dunne darm resectie, - partiële of totale colectomie, - duodenopancreatectomie, - radicale, totale of subtotale hysterectomie, - abdominoperineale resectie, - partiële of totale laryngectomie, - totale cystectomie, - totale penisamputatie, - totale nefrectomie, - totale prostatectomie (met zaadblaasjes), - hartresectie, - hart long blok, - totale hepatectomie, - totale pelvectomie, - totale vulvectomie, - foetus van 14 tot en met 24 weken	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe d'autant de prélèvements que nécessaire quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires suivantes : - mammectomie partielle avec évidement ganglionnaire, - mammectomie totale avec ou sans évidement ganglionnaire, - pneumectomie partielle ou totale, - résection partielle ou totale de l'oesophage, - évidement ganglionnaire inguinal bilatéral, - évidement de deux ou plusieurs groupes de ganglions du cou, - tumorectomie du plancher buccal avec ou sans mandibulectomie, - tumorectomie du palais avec ou sans maxillectomie, - maxillectomie totale, - gastrectomie partielle ou totale, - résection de l'intestin grêle, - colectomie partielle ou totale, - duodénopancréatectomie, - hystérectomie radicale, totale ou subtotale, - résection abdominopérinéale, - laryngectomie partielle ou totale, -
588033	**588044**	Peroperatoir pathologisch-anatomisch extempore onderzoek, ongeacht het aantal afnamen volgens de vriesmethode en	Examen peropératoire extemporané quel que soit le nombre de prélèvements examinés par la technique de congélation et quel

Outpatient	Inpatient	Dutch Description	French Description
		ongeacht het aantal verrichte controle-onderzoeken na inclusie en coupe	que soit le nombre de contrôles effectués après inclusion et coupe

Table 84 – Nomenclature Codes Cytology

Outpatient	Inpatient	Dutch Description	French Description
588416	**588420**	Honorarium voor het cytopathologisch onderzoek voor het opzoeken van neoplastische cellen (zowel na uitstrijken en/of insluiten), van afnamen niet gespecificeerd in de verstrekkingen 588350 - 588361 en 588394 - 588405, ongeacht het aantal uitstrijkpreparaten en/of insluiten per afname (588350 is inderdaad voor cervicovaginale afnames)	Honoraires pour l'examen cytopathologique pour la recherche de cellules néoplasiques (après frottis et/ou inclusion), de prélèvements non précisés dans les prestations 588350 - 588361 et 588394 - 588405, quel que soit le nombre de frottis et/ou d'inclusions, par prélèvement

Table 85 – Nomenclature Codes Immunohistochemistry anti-EGFR treatment: immuno-histology article 32

Outpatient	Inpatient	Dutch Description	French Description
588976	**588980**	Honorarium voor de immunohistologische onderzoeken voor het aantonen van farmaco-diagnostiche antigenen in de coupes na incubatie met antisera, per gebruikt antiserum, in het kader van het voorschrijven van tumor-specifieke medicatie bij oncologische patiënten (*EGFR-bepaling wanneer men bij de toepassing van deze nomenclatuur gaat kijken, Art. 32)*	Honoraires pour les examens immuno-histologiques pour la mise en évidence d'antigènes pharmaco-diagnostiques au niveau des coupes, après incubation avec antisérums, par antisérum utilisé, dans le cadre de la prescription d'une médication spécifique à la tumeur pour des patients oncologiques (*specifique EGFR, article 32)*)

Table 86 – Nomenclature Codes Molecular Diagnosis (article 33 et 33bis)

Outpatient	Inpatient	Dutch Description	French Description
588534	**588545**	Opsporen van een verworven chromosoom of genafwijking door middel van een moleculair biologische methode, in de diagnostiche investigatiefase van een niet-lymfoïde en niet-myeloïde vaste tumor (Diagnoseregel 1, 8)	Dépistage d'anomalies chromosomiques ou géniques acquises au moyen d'une méthode de biologie moléculaire, dans la phase d'investigation diagnostique d'une tumeur solide non-lymphoïde et non-myéloïde (Règle diagnostique 1, 8)
588696 ***(supressed 01/01/2013)***	**588700**	Opzoeken van genetische anomalieën volgens de methoden van hybridisatie van DNA-fragmenten,	Recherche d'anomalies génétiques par les méthodes d'hybridation de fragments d'A.D.N.

Appendix 3.2. Endoscopy

Table 87 – Nomenclature Codes EBUS and EUS

Outpatient	Inpatient	Dutch Description	French Description
EBUS			
471833	**471844**	Echo-endoscopie van de bronchi	Echoendoscopie bronchique
471855	**471866**	Echo-endoscopie van de bronchi met punctie van extramuraal weefsel (disposable materiaal niet inbegrepen)	Echo-endoscopie bronchique avec ponction de tissu extramural (matériel disposable non compris)
EUS			
473852	**473863**	Echo-endoscopie van de bovenste gastro-intestinale tractus	Echoendoscopie du tube digestif supérieur
473874	**473885**	Echo-endoscopie met punctie van extramuraal weefsel (disposable materieel niet inbegrepen)	Echoendoscopie avec ponction de tissu extramural (matériel disposable non compris)

Table 88 – Nomenclature Codes Tracheoscopy

Outpatient	Inpatient	Dutch Description	French Description
471612	**471623**	Tracheoscopie met verwijderen van tumors en/of coagulatie van letsels	Trachéoscopie avec ablation de tumeurs et/ou coagulation de lésions
351035	**351046**	Tracheo- en/of laryngoscopie, met of zonder afname voor biopsie	Trachéo- et/ou laryngoscopie, avec ou sans prélèvement biopsique

Table 89 – Nomenclature Codes Gastro-Intestinal Scopy

Outpatient	Inpatient	Dutch Description	French Description
472356	**472360**	Oesofagoscopie	Oesophagoscopie
472415	**472426**	Fibrogastroscopie en/of fibrobulboscopie	Fibro-gastroscopie et/ou fibro-bulboscopie
473056	**473060**	Fibroduodenoscopie (2e en 3e duodenum)	Fibro-duodénoscopie (2ème et 3ème duodénum)
472231	**472242**	Duodenum- of dunne darmbiopsie met sonde, inclusief radioscopie	Biopsie du duodénum ou de l'intestin grêle, par sonde, radioscopie comprise

Outpatient	Inpatient	Dutch Description	French Description
472555	**472566**	Oesofagoscopie met wegnemen van tumors en/of coagulatie van letsels	Oesophagoscopie avec ablation de tumeurs et/ou coagulation de lésions
472570	**472581**	Fibrogastroscopie en/of fibrobulboscopie met wegnemen van tumors en/of coagulatie	Fibro-gastroscopie et/ou fibro-bulboscopie avec ablation de tumeurs et/ou coagulation de lésions
473793	**473804**	Wegnemen van tumors en/of coagulatie van letsels (2e en 3e duodenum)	Ablation de tumeurs et/ou coagulation de lésions (2e et 3e duodénum)

Appendix 3.3. Invasive mediastinal staging (surgery)

Table 90 – Nomenclature Codes Mediastinoscopy

Outpatient	Inpatient	Dutch Description	French Description
228152	**228163**	Mediastinoscopie	Médiastinoscopie

Table 91 – Nomenclature Codes Surgery for staging

Outpatient	Inpatient	Dutch Description	French Description
227452	**227463**	Exploratieve thoracotomie, inclusief long- of lymfknoopbiopsie	Thoracotomie exploratrice ou thoracoscopie y compris la biopsie pulmonaire ou ganglionnaire

Table 92 – Nomenclature Codes Lymphadenectomy (1 Lymph Node)

Outpatient	Inpatient	Dutch Description	French Description
220356	**220360**	Exeresis van ganglion	Exérèse ganglionnaire
258333	**258344**	Excisie voor biopsie van een diep gelegen halsklier	Excision pour biopsie d'un ganglion profond du cou
312535	**312546**	Excisie voor biopsie van een kleine diep gelegen halsklier	Excision pour biopsie d'un petit ganglion profond du cou
258311	**258322**	Excisie voor biopsie van een oppervlakkige halsklier	Excision pour biopsie d'un ganglion superficiel du cou
312513	**312524**	Excisie voor biopsie van een oppervlakkige halsklier	Excision pour biopsie d'un ganglion superficiel du cou

Appendix 3.4. Imaging

Table 93 – Nomenclature Codes RX Thorax

Outpatient	Inpatient	Dutch Description	French Description
452690	**452701**	Radiografie van de thorax en de inhoud ervan, één cliché	Radiographie du thorax et de son contenu, un cliché
452712	**452723**	Radiografie van de thorax en de inhoud ervan, minimum twee clichés	Radiographie du thorax et de son contenu, minimum 2 clichés
463691	**463702**	Radiografie van de thorax en de inhoud ervan, één cliché	Radiographie du thorax et de son contenu, un cliché
463713	**463724**	Radiografie van de thorax en de inhoud ervan, minimum 2 clichés	Radiographie du thorax et de son contenu, minimum 2 clichés

Table 94 – Nomenclature Codes CT Brain

Outpatient	Inpatient	Dutch Description	French Description
458673	**458684**	Computergestuurde tomografie van de schedel met en/of zonder contrastmiddel, met registreren en clichés, minimum 10 coupes, voor het hele onderzoek	Tomographie du crâne commandée par ordinateur, avec et/ou sans moyen de contraste, avec enregistrement et clichés, 10 coupes au minimum pour l'ensemble de l'examen
458732	**458743**	Computergestuurde tomografie van de rotsbeenderen en/of sella torsica met of zonder contrastmiddel, met registreren en clichés, in een opeenvolgende reeks coupes, gelijk aan of minder dan 2 mm : minimum 20 coupes	Tomographie des rochers et/ou de la selle turcique, commandée par ordinateur, avec ou sans moyen de contraste, avec enregistrement et clichés, dans une série successive de coupes égales ou inférieures à 2 mm : 20 coupes au minimum

Table 95 – Nomenclature Codes MRI Body

Outpatient	Inpatient	Dutch Description	French Description
459410	**459421**	NMR-onderzoek van de hals of van de thorax of van het abdomen of van het bekken, minstens drie sequenties, met of zonder contrast, met registratie op optische of elektromagnetische drager	Examen d'IRM du cou ou du thorax ou de l'abdomen ou du bassin, minimum 3 séquences, avec ou sans contraste, avec enregistrement sur support soit optique, soit électromagnétique

Table 96 – Nomenclature Codes MRI Brain

Outpatient	Inpatient	Dutch Description	French Description
459395	**459406**	NMR-onderzoek van het hoofd (schedel, hersenen, rotsbeen, hypofyse, sinussen,orbita(e) of kaakgewrichten), minstens drie sequenties, met of zonder contrast, met registratie op optische of elektromagnetische drager	Examen d'IRM de la tête (crâne, encéphale, rocher, hypophyse, sinus, orbite(s) ou articulations de la mâchoire), minimum 3 séquences avec ou sans contraste, avec enregistrement soit sur support optique, soit électromagnétique

Table 97 – Nomenclature Codes PET

Outpatient	Inpatient	Dutch Description	French Description
442595	**442606**	Functionele scintigrafische test die twee opeenvolgende tomografische onderzoeken omvat, met verwerking op computer, die ten minste twee niet-parallelle reconstructievlakken omvat, met protocol en iconografische documenten, niet cumuleerbaar met de verstrekkingen 442411 - 442422, 442455 - 442466, 442610 - 442621 en 442632 - 442643 voor het onderzoek van een zelfde functie dat met een zelfde gemerkt produkt wordt verricht	Test scintigraphique fonctionnel comportant deux examens tomographiques successifs avec traitement par ordinateur comprenant au moins deux plans non parallèles de reconstruction, avec protocole et documents iconographiques, non cumulable avec les prestations 442411 - 442422, 442455 - 442466, 442610 - 442621 et 442632 - 442643 pour l'examen d'une même fonction effectué au moyen d'un même produit marqué
442971	**442982**	Positronentomografisch onderzoek door coïncidentiedetectie met protocol en documenten, voor het geheel van het onderzoek	Tomographie à positrons par détection en coïncidence avec protocole et documents, pour l'ensemble de l'examen

Table 98 – Nomenclature Codes Bone Scan

Outpatient	Inpatient	Dutch Description	French Description
442514	**442525**	Tomografisch onderzoek van een streek van het lichaam tijdens een scintigrafie van het ganse lichaam, met computerverwerking, dat ten minste twee niet parallelle reconstructievlakken omvat, met protocol en iconografische documenten	Examen tomographique d'une région du corps lors d'une scintigraphie du corps entier, avec traitement par ordinateur comprenant au moins deux plans non parallèles de reconstruction, avec protocole et documents iconographiques
442455	**442466**	Scintigrafie van het ganse lichaam (de scintillogrammen moeten ten minste betrekking hebben op het hoofd, de romp, het abdomen, de schouder- en bekkengordels)	Scintigraphie du corps entier (les scintillogrammes doivent comporter la tête, le tronc, l'abdomen, les ceintures scapulaires et pelviennes au minimum)

Table 99 – Nomenclature Codes Other Nuclear Imaging Techniques

Outpatient	Inpatient	Dutch Description	French Description
442411	**442422**	Scintigrafie van een orgaan, van een stelsel of van een deel van het lichaam	Scintigraphie d'un organe, d'un système ou d'une partie du corps
442610	**442621**	Functionele scintigrafische test van een orgaan of stelsel van organen, met sequentele inzameling van de gegevens, kwantitatieve analyse met telsysteem (computer) die activiteitscurven in de tijd en/of tabellen met cijfergegevens en/of parametrische beelden omvat, met protocol en iconografische documenten	Test scintigraphique fonctionnel d'un organe ou système d'organes, avec acquisition séquentielle des données, analyse quantitative par calculateur (ordinateur) comprenant des courbes d'activité dans le temps et/ou des tableaux de données chiffrées et/ou des images paramétriques, avec protocole et documents iconographiques
442396	**442400**	Tomografisch onderzoek tijdens een scintigrafie, met verwerking op computer die ten minste twee niet-parallelle reconstructievlakken omvat, met protocol en iconografische documenten, niet cumuleerbaar met de verstrekkingen 442411-442422, 442455-442466, 442610-442621 en 442632-442643 voor het onderzoek van een zelfde orgaan of stelsel van organen dat met een zelfde gemerkt produkt wordt verricht	Examen tomographique lors d'une scintigraphie, avec traitement par ordinateur comprenant au moins deux plans non parallèles de reconstruction, avec protocole et documents iconographiques, non cumulable avec les prestations 442411-442422, 442455-442466, 442610-442621 et 442632-442643 pour l'examen d'un même organe ou système d'organes effectué au moyen d'un même produit marqué

APPENDIX 4. DEFINITION OF RADIOTHERAPY WITH PALLIATIVE INTENT

Table 100 – Nomenclature Codes Radiotherapy with palliative intent

Outpatient	Inpatient	Dutch Description	French Description
444113	**444124**	Forfaitair honorarium voor een eenvoudige uitwendige bestralingsreeks van 1 tot 10 fracties voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 1	Honoraires forfaitaires pour une série d'irradiations externes simples de 1 à 10 fractions chez un patient qui répond aux critères ou pathologie repris en catégorie 1

APPENDIX 5. DEFINITION OF OTHER ACTIVE TREATMENTS

Appendix 5.1. Other surgery

Table 101 – Nomenclature codes for other types of surgery

Outpatient	Inpatient	Dutch Description	French Description
227194	**227205**	Pleuropneumonectomie, pleurolobectomie of costopleuropneumonectomie wegens chronische pleuritis	Pleuro-pneumonectomie, pleuro-lobectomie ou costopleuro-pneumonectomie pour pleurésie chronique
227334	**227345**	Exeresis van de pleura wegens chronische infectie of tumor, met of zonder thoracoplastiek, in één operatietijd	Exérèse de la plèvre pour infection chronique ou tumeur, avec ou sans thoracoplastie, en un temps unique
227570	**227581**	Heelkunde voor een- of tweezijdige vermindering van het longvolume, exclusief het viscerosynthesemateriaal	Chirurgie de réduction du volume pulmonaire uni ou bilatérale, non compris le matériel de viscérosynthèse
228115	**228126**	Behandeling van mediastinumtumors en -infecties langs thoracale weg	Traitement des tumeurs et des infections du médiastin par voie thoracique
259033	**259044**	Resectie van een expansief letsel van de luchtwegen en/of van het bovenste gedeelte van het spijsverteringskanaal dat het sluiten van een huid- of slijmvliesdefect met een huidlap, een myocutane of een wandelende ent vereist	Résection d'une lésion expansive des voies respiratoires et/ou des voies digestives supérieures nécessitant la fermeture d'un défect cutané ou muqueux par un lambeau cutané, myocutané ou une greffe libre

Table 102 – Nomenclature Codes Aborted surgery

Outpatient	Inpatient	Dutch Description	French Description
227371	**227382**	Thoracotomie met poging tot exeresis	Thoracotomie avec tentative d'exérèse

APPENDIX 6. DEFINITION OF LUNG CANCER

Table 103 – ICD-10-CM Diagnosis Codes for Malignant neoplasm of bronchus and lung (C34)

Code	Label
C34.0	Malignant neoplasm of main bronchus
C34.1	Malignant neoplasm of upper lobe, bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.3	Malignant neoplasm of lower lobe, bronchus or lung
C34.8	Malignant neoplasm of overlapping sites of bronchus and lung
C34.9	Malignant neoplasm of unspecified part of bronchus or lung

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