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Reduced delays in diagnostic pathways for non-small cell lung cancer after local and National initiatives

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A B S T R A C T

Objectives: Patients with non-small cell lung cancer (NSCLC) may experience progression and stage shift due to delays in a complex and time-consuming diagnostic work-up. We have analyzed the impact of both a local and national intervention on total time to treatment (TTT).
Material and Methods: All patients diagnosed with NSCLC at a Norwegian county hospital from 2007 to 2016 were reviewed. Logistic bottlenecks and delays were identified (2007–12) resulting in implementation of a local initiative with new diagnostic algorithm introduced by the beginning of 2013. In 2015, national diagnostic cancer pathways were implemented. TTT defined as time from received referral from the primary physician to start of treatment was compared in the three diagnostic time periods; baseline (2007–12), local (2013–14) and national (2015–16).
Results: A total of 780 patients were included. Among patients treated with curative intent the median TTT decreased by 21 days, from 64 to 43 days ($p < 0.001$) while the mean number of diagnostic procedures increased from 3.5 to 3.9. In median regression analysis, the local initiative was associated with a reduction of estimated 7.8 days (95% CI 3.2, 12.3) in TTT, while the national initiative correlated with a reduction of estimated 14.9 days (95% CI 10.2, 19.6) compared to time at baseline. Covariates associated with longer TTT were stage I, use of PET-CT, diagnostic procedure at external hospital, and number of diagnostic procedures.
Conclusion: Local and national initiatives significantly reduced TTT in NSCLC. The effect was most pronounced among patients with disease available for curative treatment.

1. Introduction

The diagnostic work-up of suspected non-small cell lung cancer (NSCLC) is a complex and logistically challenging process. NSCLC grows rapidly with median volume doubling times reported as low as 66 days [1]. Thus, a time-consuming diagnostic process may lead to deteriorating performance status, weight loss, larger treatment volumes and stage shift. That again may affect both treatment options, prognosis and ultimately survival [1–5].

In clinical practice, time spent on diagnostic work-up and awaiting treatment are often longer than guidelines recommend. Several reports address interventions to reduce time intervals, including suggestions for a rapid outpatient diagnostic program, multidisciplinary meetings, nurse coordinated cancer programs and specific diagnostic algorithms [6–9].

Guidelines address maximum acceptable waiting times for referral, diagnostic work-up and initiation of treatment for lung cancer [10–13]. The Norwegian recommendations were introduced in January 2015 defining a maximum total time to treatment (TTT) of 35 to 42 calendar days from referral to start of treatment (Fig. 1) [14].

In the present paper we analyse the impact on TTT of two separate major revisions in the lung cancer program in a cohort from a single centre hospital in Southern Norway. Firstly, in 2013 the diagnostic work-up was optimised based on a local analysis of delays. Secondly, in 2015 the national diagnostic cancer pathways (NDCP) were introduced [14]. With political incentives, recommendations were given on timeliness, with the aim to offer a more predictable diagnostic work-up for patients with suspected cancer.

2. Material and methods

2.1. Data and diagnostics

All patients diagnosed with lung cancer (ICD-10 code C34) at

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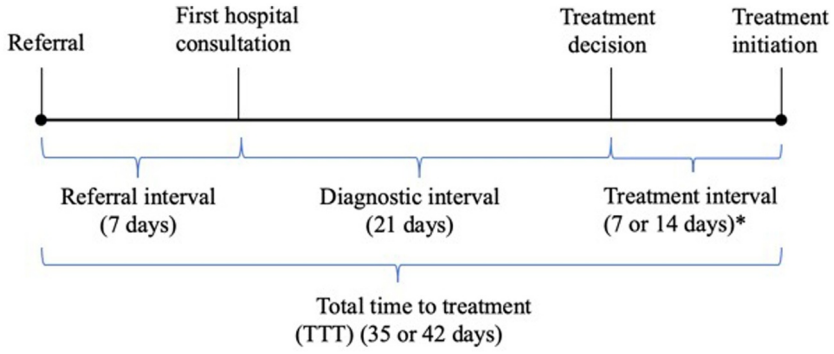

Fig. 1. Overview of intervals and recommended maximum time limits in calendar days according to Norwegian National diagnostic pathways [14]
Referral: date of receiving referral letter at department
First hospital consultation: date of first consultation in pulmonary department.
Treatment decision: date of multidisciplinary team meeting with final treatment decision. All diagnostic procedures are finished.
Treatment initiation: a) date of surgery or b) date of first fraction of radiotherapy or c) date of first day of chemotherapy/anti-tumor medication.
TTT: time in calendar days from referral due to suspicion of lung cancer to start treatment.
* Seven days when first treatment is medication (TTT 35 days), 14 days when receiving surgery or radiation therapy (TTT 42 days).

Table 1
Local and National adjustments introduced to improve timeliness for lung cancer diagnosis and start of treatment.

Local initiative (2013–14): Optimizing diagnostic work-up	National initiative (2015–16): National diagnostic cancer pathways
Plan diagnostics before 1st consultation and choose procedure(s) of highest diagnostic and staging value(s)	New recommendations of delays for referral period, diagnostic period and treatment initiation*
Designated slots for combined 1st consultation and diagnostic procedure	National reporting of delays
Referral to all other relevant procedures at 1st consultation	Internal resource shift with one extra physician to see referred cancer patients
Improved radiologic service with shorter time to CT scanning and available slots for CT guided lung biopsies 1 day a week	CT guided biopsy 2 slots 2 days a week
Improved capacity to start chemotherapy with priority for curative intent patients	

* See Fig. 1.

Sørlandet Hospital Kristiansand (SHK) in the ten-year period of 2007–16 have been registered in a local, clinical database. Demographic variables, clinical characteristics, diagnostic intervals and survival data from 2007–12 were retrieved retrospectively from the electronic patient records. Since 2013 registration of the same variables has been prospective and continuous.

SHK is a county hospital serving a population of 200 000. There is no other hospital or private alternative for lung cancer patients in the region. Norway has a universal health care insurance system covering all citizens. Thus, the database contains an unselected and complete population-based lung cancer cohort.

The hospital has the personnel, skills and equipment for a complete diagnostic work up except for Positron Emission Tomography Computer Tomography (PET-CT) which was performed at the regional centre Oslo University Hospital (OUH). Endobronchial ultrasound-guided (EBUS) fine-needle aspiration cytology has been available at SHK since 2013. Chemotherapy, radiation and chemoradiation were administered at SHK, while surgery and stereotactic beam radiation therapy (SBRT) were performed at OUH throughout the period. A local multidisciplinary team (MDT) meeting discussed all patients diagnosed with lung cancer. Patients suggestive for surgery or SBRT were discussed in a weekly teleconference MDT meeting with OUH.

In this study, all invasive and radiological procedures aimed at providing diagnosis and staging were registered and counted. Included procedures were chest CT scan, bronchoscopy, EBUS, esophageal ultrasound-guided fine needle aspiration, CT and ultrasound-guided percutaneous biopsies, surgical excision biopsies, pleural effusion cytology, PET-CT and magnetic resonance imaging (MRI). The total number of procedures assigned to each patient was noted to give a measure of the complexity of the diagnostic process. In patients where cytologic or histologic confirmation proved particularly difficult, additional EBUS or CT-guided percutaneous biopsy was performed at OUH. These planned, out-of-house procedures were registered as "external OUH procedure" in order to assess to what extent they contributed to a diagnostic delay.

2.2. Initiatives

2.2.1. Local streamlining of the diagnostic work-up (2013–14)

Delays in the diagnostic pathways for primary pulmonary carcinoma in Southern Norway have previously been reported from the region in the period 2002–2005 [15]. In 2012, a local quality improvement initiative from the hospital administration enabled registration and review of the diagnostic and treatment delays of previous lung cancer patients. Several bottlenecks in the diagnostic pathway were identified, and a new diagnostic work-up was introduced to reduce delays in the period 2013–2014 (Table 1).

2.2.2. National diagnostic cancer pathways (NDCP, 2015–16)

NDCP were launched for lung cancer in January 2015. These included new recommended maximum limits for time spent in the diagnostic process (Fig. 1) as well as mandatory reporting of the actual time intervals for all patients with suspected lung cancer. Local adaptions were introduced to comply with the new recommendations (Table 1).

2.3. Study population and selection

From a total of 1261 patients diagnosed with lung cancer, 780 patients were included in the final analysis. The 481 patients excluded had either other histology than NSCLC (n = 204), no tissue diagnosis (n = 19) or did not receive any cancer specific treatment (n = 258). However, 42 patients lacking tissue confirmation, but receiving SBRT based on a positive PET-CT and tumour growth on repetitive CT-scans, were included. This group of patients had all stage I tumours and are in the context of this paper considered to be NSCLC.

The patients were divided into three groups according to their time of diagnostic work-up; baseline (2007–12), local (2013–14) and national (2015–16) (see above).

All patients were staged according to international staging system version 7 (TNM-7) [16].

2.4. Statistics

Descriptive statistics of the patient and tumor were presented as frequencies and percentages for categorical data and mean with standard deviation (SD) for normally distributed continuous data. Time interval variables were non-normally distributed, and thus reported as median with inter-quartile range (IQR). Comparisons of the three diagnostic time periods (2007–12, 2013–14 and 2015–16) were tested by chi-square test, one-way ANOVA or Kruskal–Wallis test, where appropriate. Further, referral, diagnostic and treatment intervals were studied in stratified analyses by treatment intent and modality.

A multivariable median regression model assessed the associations between co-variates and TTT. Age at diagnosis and number of procedures were continuous variables, while diagnostic time period (2007–12, 2013–14 and 2015–16), sex, histology (squamous cell carcinoma, non-squamous and no-biopsy), stage (I, II, III and IV), treatment (surgery, SBRT, chemoradiation of curative intent and palliative), PET-CT (yes or no), cerebral MRI (yes or no) and external OUH procedure (yes or no) were considered categorical. Treatment was not included in the multivariable model due to multicollinearity with stage at diagnosis. Results were presented as median values with 95% confidence intervals (CI).

Moreover, quantile regressions were performed at 25th, 75th and 90th percentile distributions of TTT, including the same co-variates as above, to assess the association between the diagnostic time periods (initiatives) in patients with short (25th percentile) and long (75th and 90th percentile) TTT.

A sensitivity analysis was performed to study the impact of the time-window of the baseline period. The multivariable median regression was repeated with the historical group divided into three evenly periods (2007–08, 2009–10 and 2011–12).

Differences were considered statistically significant if $p < 0.05$. All data were analysed using Stata statistical software, version 15 (StatCorp Lp, College Station, TX, USA).

Norwegian Center of Research Data approved the storage of de-identified quality data. The study was presented for the regional ethics committee that determined that the present study did not require their approval since no biomedical interventions or registrations were added for study purposes.

3. Results

3.1. Characteristics of included patients

The mean age of patients increased by nearly three years during the study period (Table 2). Approximately two-thirds of the patients were in stage I-III potential eligible for curative treatment. The proportion of patients receiving treatment with a curative intent (surgery, SBRT or chemoradiation) increased from half of the patients (49%) in 2007–12 to two-thirds (65%) in 2015–16, and mostly due to a 15% increase in SBRT. During the study period there was a significant increase in the number of patients undergoing cerebral MRI and out-of-house PET-CT as part of their diagnostic work-up. Among patients treated with curative intent, only 1% were staged with PET-CT and cerebral MRI in 2007–12, while 13% and 64% were staged with both modalities in the 2013–14 and 2015–16 periods, respectively. The mean number of diagnostic procedures increased from 3.1 to 3.7 per patient between the baseline and last diagnostic time period. Twice as many had four or more diagnostic procedures in 2015–16 (55%) as opposed to 2007–12 (28%). Similarly, in 2015–16 twice as many had four or more procedures in stages I–III (73%) compared to stage IV (35%).

3.2. Time intervals

The median TTT decreased by 11 days during the study (Table 3). This was especially evident for patients receiving treatment with curative intent. This group experienced a 21-day reduction, as compared to five days for palliative treatments. For patients receiving SBRT and those treated with curative intent chemoradiation, the median TTT decreased by about 40 days during the study period, while a more modest reduction was observed for surgical patients (16 days) (all $p < 0.001$).

The median referral interval among all patients was reduced by two days from baseline to the next time period when the local diagnostic algorithm was streamlined, with no further reductions after introduction of NDCP in 2015.

The median diagnostic interval for patients receiving curative treatments was longer than for patients receiving palliative treatments in all three diagnostic time periods. After the two initiatives in 2013 and 2015, the diagnostic intervals were reduced by a total of 15 days (from 36 to 21) in the curative group, while there was no change in the time spent on palliative patients (13–14 days). Thus, the difference between the curative and palliative treated groups of patients decreased from 23 to seven days. The shortening of the diagnostic interval was seen for all three curative treatment modalities, with 11 days for surgery, 21 days for SBRT and 19 days for curative chemoradiation ($p < 0.001$).

Table 2
Patient and cancer characteristics within the three time periods in a cohort of non-small cell lung cancer patients ($N = 780$).

	Baseline 2007–2012 $n = 446$	Local initiative 2013–2014 $n = 145$	National initiative 2015–2016 $n = 189$	p-value
Age, years (mean ± SD)	65.8 (9.7)	66.9 (10.2)	68.6 (8.7)	0.003[1]
Sex (%)				0.14[2]
Male	55.6	46.2	53.4	
Female	44.4	53.8	46.6	
Stage (%)				0.145[2]
I	28.3	27.6	34.4	
II	10.5	16.6	13.8	
III	21.8	24.1	17.5	
IV	39.5	31.7	34.4[3]	
Histology (%)				< 0.001[2]
Squamous	25.8	25.5	25.9	
non-squamous	72.0	67.6	63.5	
No histologic confirmation	2.2	6.9	10.6	
Treatment (%)				< 0.001[2]
Surgery	34.1	27.6	31.2	
Stereotactic beam radiation therapy	5.4	15.2	20.6	
Chemoradiation of curative intent*	9.2	12.4	12.7	
Palliative treatments**	51.4	44.8	33.5	
PET-CT (%)	41.5	64.1	75.7	< 0.001[2]
Magnetic resonance imaging (%)	12.8	16.6	58.2	< 0.001[2]
Number of procedures (mean ± SD)***	3.1 (1.1)	3.2 (1.1)	3.7 (1.1)	< 0.001[1]

PET-CT: Positron emission tomography – computed tomography.

* Concurrent and sequential chemoradiotherapy and fractionated radiotherapy where radiation dose ≥ 60 Gy.

** Includes chemotherapy, radiation, combinations of chemotherapy and radiation where (radiation dose < 60 Gy), personalized treatment (EGFR TKI etc.).

*** Included procedures, chest CT scan, bronchoscopy, EBUS, esophageal ultrasound-guided fine needle aspiration, CT and ultrasound-guided percutaneous biopsies, surgical excision biopsies, pleural effusion cytology, PET-CT and magnetic resonance imaging (MRI).

[1] ANOVA.

[2] Chi-square test.

[3] Four patients with limited brain metastasis received treatment with curative intent for both metastasis and primary tumour.

Table 3
Observed time intervals at baseline (2007–12) and after local (2013–14) and national initiative (2015–16) stratified by treatment intent and modality.

	Baseline 2007–2012		Local initiative 2013–2014		National initiative 2015–2016		p-value[1]
	n	Median (IQR)	n	Median (IQR)	n	Median (IQR)	
Total time to treatment							
All patients	446	46(27–67)	145	40(25–57)	189	35(24–50)	<0.001
Palliative treatments	229	28(19–43)	65	25(20–42)	67	23(18–33)	0.13
Curative treatments	217	64(49–89)	80	50(35–69)	122	43(32–56)	<0.001
• Surgery	152	58(47–81)	40	47(35–57)	59	42(34–56)	<0.001
• SBRT	24	91(70–116)	22	74(65–78)	39	51(40–61)	<0.001
• Chemoradiation of CI	41	67(54–84)	18	35(28–47)	24	28(24–35)	<0.001
*Referral interval**							
All patients	330	6 (4–9)	115	4(2–7)	162	4 (2–6)	<0.001
Palliative treatments	136	6(3–8)	41	4(2–6)	53	3(1–5)	<0.001
Curative treatments	194	7(4–11)	74	4(2–7)	109	4(2–7)	<0.001
• Surgery	137	7(4–11)	38	4(2–7)	55	4(2–8)	<0.001
• SBRT	23	7(5–10)	18	4(2–7)	34	4(2–6)	0.02
• Chemoradiation of CI	34	6(4–11)	18	5(2–7)	20	4(3–6)	0.03
*Diagnostic interval***							
All patients	434	23(12–41)	145	23(13–34)	189	19(12–29)	0.04
Palliative treatments	217	13(7–25)	60	16(8–28)	67	14(7–23)	0.48
Curative treatments	217	36(22–50)	80	29(19–38)	122	21(13–34)	<0.001
• Surgery	152	34(22–48)	40	27(19–35)	59	23(13–35)	<0.001
• SBRT	24	43(28–59)	22	34(30–45)	39	22(15–36)	<0.001
• Chemoradiation of CI	41	38(27–55)	18	23(15–32)	24	19(14–22)	<0.001
*Treatment interval****							
Palliative treatments	215	8(5–14)	64	8(6–14)	66	6(4–12)	0.10
Curative treatments	216	20(11–32)	80	15(7–26)	122	15(8–21)	<0.001
• Surgery	152	19(11–27)	40	14(8–20)	59	14(12–20)	0.06
• SBRT	24	37(27–44)	22	33(26–41)	39	21(19–26)	<0.001
• Chemoradiation of CI	40	25(12–33)	18	6(2–7)	24	6(5–7)	<0.001

IQR: inter-quartile range; SBRT: stereotactic beam radiation therapy; CI: curative intent.
[1] p-value from Kruskal–Wallis test.
* Referral interval was not given when patient was directly admitted to hospital.
** Diagnostic interval was not registered when referral was based on histologic confirmed lung cancer and no further diagnostic procedures were performed.
*** Treatment interval was not registered when treatment was started before diagnostics were finished.

In general, the longest treatment intervals were seen in patients receiving curative treatment. However, there was a shortening of the interval from 20 to 15 days during the study period ($p < 0.001$). The largest reduction was seen in patients receiving curative intent chemoradiation where the median treatment interval decreased by 19 days ($p < 0.001$). For the two out of house treatment modalities, SBRT and surgery, the reduction was 16 days (from 37 to 21) ($p < 0.001$) and five days (from 19 to 14) ($p = 0.06$), respectively.

In contrast, there was only a small, nonsignificant decrease in the palliative group with a median treatment interval reduction from eight to six calendar days ($p = 0.10$).

3.3. Regression analysis

In the adjusted model, the local optimized diagnostic process was associated with an estimated reduction of 7.8 days (95% CI −12.3, −3.2) in TTT, while the NDCP experienced an estimated reduction of 14.9 days (95% CI −19.6, −10.2) compared to the baseline period (Table 4).

Studying the 25th percentile, the adjusted reduction in TTT associated with the local initiative, was four days (95% CI −6.9, −1.1; $p = 0.01$) compared to the baseline period. Correspondingly, the additional reduction in TTT of NDCP was 6.8 days CI (95% CI −11.3, −2.2; $p < 0.001$). At the 75th percentile, adjusted reduction related to local initiative was 12.7 days (95% CI −16.9, −8.5; $p < 0.001$) and national initiative 9.3 (95% CI −16.5, −2.1; $p = 0.01$). At the 90th percentile corresponding numbers for local and national were 17.7 days and 9.2 days, respectively, the sum being close to four weeks.

In the multivariate regression analysis, several other covariates significantly changed median TTT. The following factors increased TTT: low stage (I–III), being diagnosed without histologic confirmation (no-biopsy), increasing age and number of diagnostic procedures or out-of-house invasive procedures and PET-CT ($p < 0.05$). The largest delay (21 days) was observed for stage I compared to stage IV. In contrast, receiving MRI reduced TTT ($p < 0.05$) (Table 4).

Sensitivity analysis, changing the time-window of the baseline period from the six-year period 2007–2012 to a smaller time interval did not alter the changes in TTT (data not shown). Only non-significant variations in median TTT was observed within the baseline period when splitting it into three separate two-year periods.

3.4. Timely treatment

The national guidelines of January 2015 set standards for maximum recommended time limits for both referral, diagnostic and total time to treatment (Fig. 1). The percentage of patients receiving timely treatment within the maximum recommended TTT, increased from 43% via 49% to 64% through the three time periods (Fig. 2). Such increase was most evident in the group of patients receiving curative treatment. The national guidelines also set a goal of 70% for the fraction of patients that should receive treatment within the new standard time limits. Among the NSCLC patients following the NDCP (2015–16), only patients receiving palliative treatment (85%) and curative intent chemoradiation (85%) reached this goal, both being in-house treatments.

4. Discussion

The introduction of both local and national initiatives were associated with significant reductions in TTT for NSCLC-patients. This reduction was most evident among patients with tentatively curable disease, stage I-III, and was experienced despite an increasing number of diagnostic procedures performed.

Table 4
Univariable and multivariable median regression of total time to treatment (TTT) in lung cancer patients, 2007–2016 (N = 780).

	Unadjusted difference (days) in median TTT (95% CI)	Adjusted difference (days) in median TTT (95% CI)
Diagnostic time period		
2007–12 (baseline)	Ref	Ref
2013–14 (local initiative)	−6 (−12.7, 0.7)	**−7.8 (−12.3, −3.2)**
2015–16 (national initiative)	**−11 (−17.0, −5.0)**	**−14.9 (−19.6, −10.2)**
Age		
per 10-years	**4.8 (2.4, 7.2)**	**4.1 (2.3, 5.9)**
Sex		
Female	Ref	Ref
Male	−4 (−9.0, 1.0)	−1.7 (−5.0, 1.8)
Histology		
Squamous cell c.	Ref	Ref
Non-squamous cell c.	**−9 (−14.2, −3.7)**	−1.0 (−5.0, 2.9)
No-biopsy	**16 (5.0, 27.0)**	**12.8 (3.2, 21.0)**
Procedure numbers		
no.	**8 (5.9, 10.1)**	**5.3 (3.3, 7.4)**
Stage		
I	**36 (31.7, 40.3)**	**21.3 (15.9, 26.7)**
II	**25 (19.3, 30.7)**	**7.9 (1.4, 14.4)**
III	**18 (13.2, 22.8)**	**5.9 (0.8, 11.0)**
IV	Ref	Ref
Treatment		*
Surgery	**27 (23.2, 30.8)**	
SBRT	**39 (33.5, 44.5)**	
Chemoradiation	**20 (14.4, 25,6)**	
Palliative	Ref	
PET-CT		
Yes	**26 (22.5, 29.5)**	**10.6 (5.5, 15.7)**
No	Ref	Ref
MRI		
Yes	**−10 (−15.4, −4.6)**	**−9.7 (−14.3, −5.0)**
No	Ref	Ref
External OUH procedure		
Yes	**28 (20.2, 35.8)**	**13.0 (6.9, 19.1)**
No	Ref	Ref

Significant values in bold.
CI: confidence interval; SBRT: stereotactic beam radiation therapy; PET-CT: positron emission tomography – computed tomography; MRI: magnetic resonance imaging; OUH: Oslo University Hospital.
* Not included in multivariable regression model due to multi-collinearity with stage.

4.1. Initiatives and association with TTT

Lung cancer is a complex and multifaceted disease reflected in an intricate path from referral to treatment, involving multiple procedures and clinical specialties. The increasing number of procedures, like PET-CT, EBUS and a more elaborate pathological work-up, has made the diagnostic process prone to more delays.

Several studies report interventions to reduce time to treatment or diagnosis. In The- Time-to-Treat program in Canada [9], optimization and coordination of care as well as use of a coordinator was associated with reduced unadjusted time from abnormal X-ray to diagnosis (128 to 20 days). Similarly, implementation of a coordinator nurse at a cancer centre in Ohio was found to reduce the unadjusted TTT from 64 to 45 days [17]. The introduction of a cancer care program was associated with reduced time from abnormal x-ray image to treatment by 25 days (from 126 days to 101 days; $p < 0.02$) when corrected for confounders in a multivariate analysis [7]. In our cohort, reduced TTT was associated with the introduction of both the local and national initiatives, when adjusting for known covariates. Additionally, it seems very plausible that the introduction of the new algorithms benefitted patients at a broad range, as shown through regression analyses at different percentiles. We found that the longer the initial TTT, the more pronounced was the reduction in TTT associated with the initiatives. To the best of our knowledge, this association has not been reported in a lung cancer population previously.

4.2. Significant covariates

Patients surmised to have curable disease often wait longer for diagnosis and treatment initiation than patients with non-curative treatment options. This has been explained by the increased number of diagnostic procedures necessary for accurate staging in early lung cancer [18]. This was confirmed in our study where twice as many patients in curative stages I-III needed four or more diagnostic procedures compared with patients in stage IV. When correcting for number of procedures and other covariates, low staging still remained a factor associated with delayed diagnosis and treatment (Table 4). This finding is supported by Ezer et al. [19], concluding in a multivariate model that stage (I/II vs III/IV) was associated with longer TTT. Patients with stage IV disease are more often admitted to hospital presenting a symptomatic disease, which often contributes to a quicker diagnosis and thereby shorter TTT.

Out-of-house procedures were also associated with longer TTT. Staging with PET-CT (adding 10.6 days) and external OUH procedure (adding 13 days) were independent factors of delay. Transferring information, including diagnostic imaging and additional discussion in once weekly MDT meetings with the referral hospital might explain some of the experienced delay.

The finding of delay associated with the “no-biopsy” group can be explained by the fact that these patients were exclusively treated with SBRT, the treatment category with longest treatment interval. Treatment could not be included in the regression analysis due too high correlation with stage. It was also surprising that performing an MRI was associated with shorter TTT. The most likely explanation is that we made no distinction between cerebral MRI as a screening modality of asymptomatic brain metastasis and MRI ordered due to emergency symptoms. In the latter case, for instance in spinal cord affection, the MRI was followed by quick initiation of treatment.

4.3. Intervals and guideline recommendations

Recent consensus based expert guidelines are fairly in alignment with the Norwegian with a recommended 40 to 45 days from referral to start of treatment depending on treatment given [11,12].

In the baseline period we found long TTT-intervals for all patients, but especially for patients where curative treatment was intended. Median TTT for surgery, SBRT and chemoradiation was reduced by approximately two weeks in the period following the local initiative (2013–2014). Interestingly there was a further median reduction of approximately one week in TTT for all patients treated with curative intent after the introduction of the NDCP in January 2015, i.e. 5 days, 13 days and 7 days for surgery, SBRT and chemoradiation, respectively. The additional effect of NDCPs, could be explained by the clear incentives from the government and hospital administrators to make conjoint efforts to reach recommended time limits. The entire diagnostic chain including pulmonary, radiologic, nuclear medicine and pathologic services was primed and streamlined.

However, all improvements were performed without additional national resources or funding.

The reasons for the various time intervals constituting the TTT vary markedly. While the covariates discussed above mostly influence the time spent in the diagnostic interval, the referral and treatment intervals are more dependent on organizational and capacity factors.

Referral interval was median six days, at baseline, before implementation of our local initiative in 2013 (Table 3). Careful daily evaluation of referrals and having available prioritized slot times for cancer diagnostics, enabled a reduced time to first consultation to four

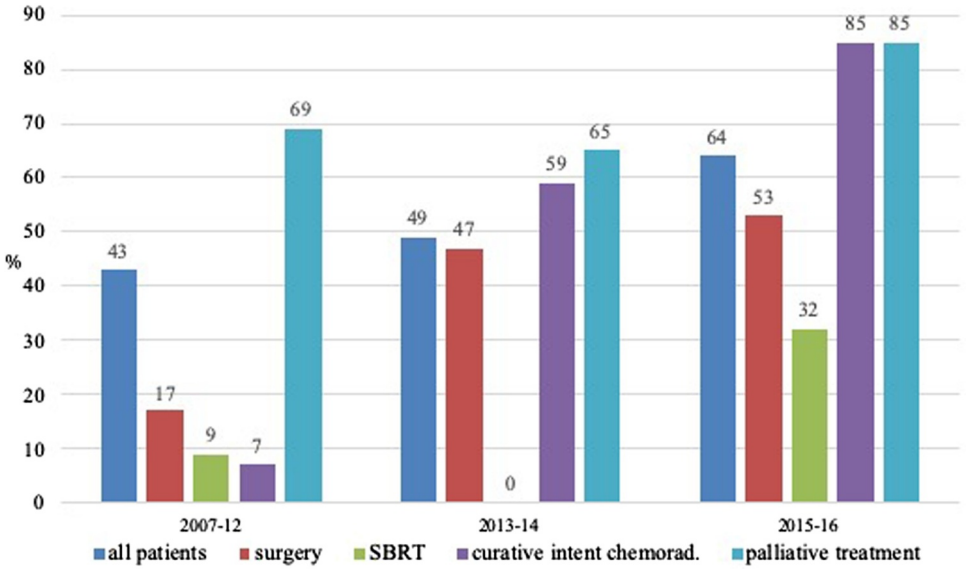

Fig. 2. Percentage of patients receiving timely treatment according to recommendations in Norwegian diagnostic cancer pathways.
A TTT of 35 days or less is regarded as timely for chemotherapy and 42 days or less for surgery or radiotherapy. SBRT: stereotactic bean radiation therapy.

days in 2013–14. This referral interval of four days is short compared to other reports. In the review article by Jacobsen et al. [20] the median referral interval was seven days with a range from 1–17 in the nine studies reported.

While there was no difference in referral interval for patients ending up receiving curative or palliative treatment, we found a marked difference between the two groups in the diagnostic interval (Table 3). The shorter diagnostic time period of palliative patients often involves only one CT scanning and one invasive diagnostic procedure. The two weeks spent on the diagnostic work-up in this group did not change during our study period. The longer diagnostic interval seen in curative patients was however reduced from 36 to 21 days. This reduction occurred despite an increase in mean number of diagnostic procedures from 3.5 in the baseline period to 3.9 after the national initiative. The reduced delays in 2013–14 and 2015–16, is considered to be related to improved coordination and the introduction of a logistically more efficient path to treatment. More specifically, unnecessary diagnostic procedures were avoided through preplanning the diagnostic work-up at referral. Furthermore, procedures with presumed highest yields and staging values were prioritized, and these procedures were often performed at the day of the first consultation.

Despite the referral and diagnostic intervals being fairly similar among the curative treatment modalities, there was a marked difference in TTT ranging from 28 days for chemoradiation of curative intent to 51 days for SBRT. Most of these differences were due to the treatment interval varying from six to 21 days. The longer delays were seen in the out-of-house modalities surgery and SBRT. These delays in the treatment interval depend highly upon the capacity of the separate treatment modalities. The ability to adapt to and vary the number of treatments to be initiated every week is important in order to avoid capacity delays. Overall the mean treatment interval of six days in case of chemoradiation with curative intent, 14 days of surgery and 21 days of SBRT are in the low range of reported values in other studies, ranging 14–33 days [8,18,21].

The NDCP states that a typical diagnostic interval should be maximum 21 calendar days. This goal was achieved for 75% of the palliative patients, but only for 50% for patients treated with curative intent in the 2015–16 diagnostic period. Still this was an improvement from the 22% achieved in 2007–12

Comparison with other studies is made difficult by the lack of consensus as to what intervals are reported. A diagnostic interval of 2–37 days has been reported [8]. In many of these studies the diagnostic interval was defined by date of biopsy, while additional staging procedures and final treatment decision were not included. This was also the case in a recent study from the Norwegian Cancer Registry with national data for 2007–16. Here the time interval from diagnosis (date of biopsy) to surgery or start curative intent radiotherapy for lung cancer was found to decrease from 2010 before and after introduction of national cancer pathways in 2015 [22]. The capacity to initiate treatment, i.e. treatment interval, was not measured in the national study.

4.4. Strengths

The study cohort is based on a complete, unselected lung cancer population spanning a period of 10 years. This gives an overview of the effects of the diagnostic periods and should comply with a sound external validity for other hospitals treating lung cancer. A quantile regression model, enabling us to estimate the impact of initiatives on different lengths of TTT, gives added understanding to interpretation of delays.

4.5. Weaknesses

Although data from 2013 were prospectively collected, the patient data prior to this were retrieved using electronic records. This makes them susceptible to bias. Our diagnostic chain involves two hospitals for most of the patients treated with curative intent, either through diagnostic PET-CT or treatment with surgery or SBRT. Thus, generalizability may also be limited in set ups were all diagnostics and treatments are located in the same hospital.

5. Conclusions

This study demonstrates that it is possibly to shorten both time spent on diagnostic work-up and the successive time spent waiting for treatment. Our experience shows that this can be done by rather small logistic changes by focusing on removing unnecessary delays. Both local and national initiatives regarding time intervals are of importance in this process. More importantly, this reduction can be achieved even in a period where new diagnostic procedures and a more aggressive attitude to tissue sampling and staging are introduced. This is especially

important in a time where more effective treatment options are becoming available.

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Declaration of Competing Interests

None.

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