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Significantly more patients with lung cancer diagnosed during the COVID-19 pandemic were metastasized at diagnosis.

# Background

- Since the initial detection of SARS-CoV-2 cases in Germany in January 2020, the recorded COVID-19-related deaths have reached 171,411 at the time of this research [1].
- It is crucial to note that COVID-19 is seldom a standalone cause of fatality but is notably exacerbated by comorbidities [2].
- Previous research has demonstrated an increased vulnerability among cancer patients. Particularly, individuals diagnosed with lung cancer have shown an increased risk of COVID-19-related mortality [3, 4, 5].

### **Objective**

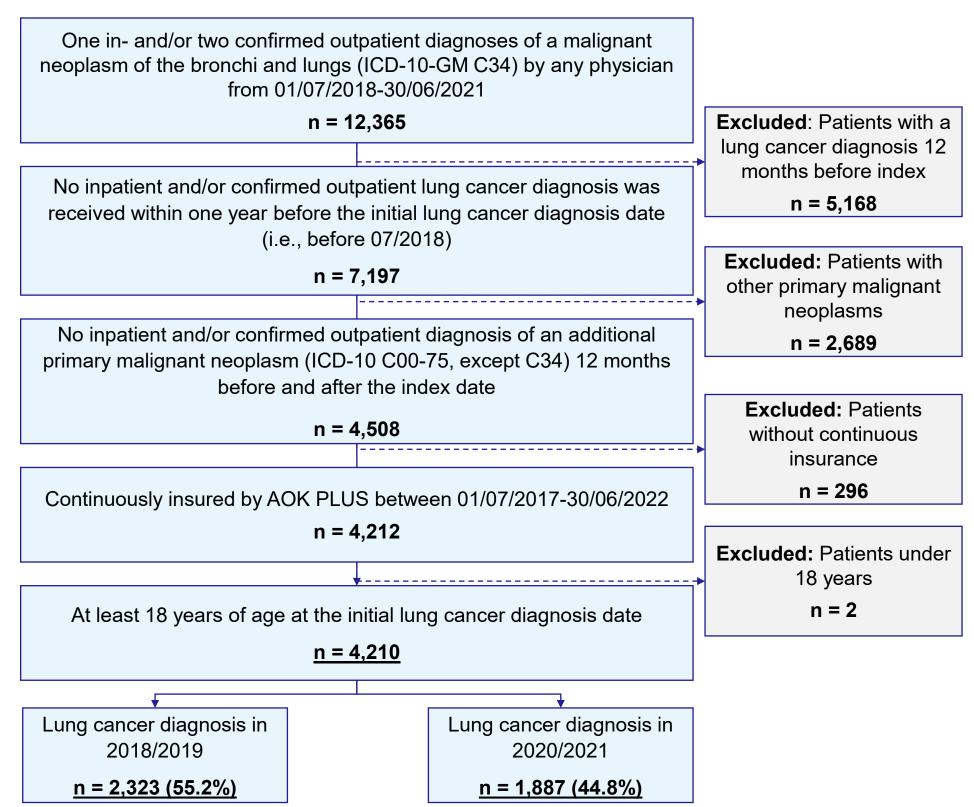
 This study examines the effects of severe COVID-19 infections on adults diagnosed with lung cancer in Germany, aiming to pinpoint factors that significantly influence patient mortality.

### Methods

#### **Patient identification**

- This retrospective study utilized anonymized German claims data from AOK PLUS, a regional statutory health insurance with approximately 3.5 million insured individuals. This database was employed to identify cases with an incident diagnosis of lung cancer (=index) from July 1, 2018, to June 30, 2021.
- Adults were included if they had at least two confirmed outpatient lung cancer diagnoses or one inpatient lung cancer diagnosis (coded as per ICD-10-GM: C34). An incident case was defined as one with a diagnosis-free period of at least 12 months before the index date.
- Patients were categorized into two groups based on whether their index year was before (2018/2019) or after (2020/2021) the outbreak of the COVID-19 pandemic in Germany.

Figure 1. Patient identification



Abbreviations: ICD-10-GM, International Classification of Diseases, 10<sup>th</sup> revision, German Modification; N, number.

## Analysis periods and outcomes determination

- Baseline characteristics were assessed during the 12 months preceding the patient-individual index date, and patients were followed for 12 months after the index or until the time of death, whichever came earlier.
- Overall survival (OS) following the incident diagnosis was calculated using Kaplan-Meier estimation and compared between the two groups within a Cox regression model, considering key patient characteristics, including metastasis status at the time of the index.

#### Results

#### Patient demographics

- The analysis involved a total of 4,210 incident lung cancer patients, with 2,323 (55.2%) diagnosed in 2018/2019 and 1,887 (44.8%) in 2020/2021 (**Figure 1**).
- Baseline characteristics hardly differed between the two patient groups. Patients diagnosed in 2018/2019 had a mean age of 69.2 years (vs. 2020/2021: 69.1 years), a mean Elixhauser Comorbidity Index (ECI) of 9.3 (vs. 2020/2021: 8.9), and 66.5% of patients were male (vs. 2020/2021: 66.6%).
- However, significantly more patients diagnosed in 2020/2021 were metastasized at diagnosis (38.8% versus 2018/2019: 33.1%) (**Table 1**).

#### **OS** outcomes

- The median OS for patients diagnosed in 2020/2021 was 11.9 months, whereas the median was not reached for patients diagnosed in 2018/2019 (**Figure 2/3**).
- Cox regression confirmed the tendency of shorter OS in patients with incident diagnosis in 2020/2021 but without statistical significance (hazard ratio [HR]: 1.05; p=0.318).
- Higher age (HR: 1.03), female sex (HR: 0.77), being diagnosed in an outpatient setting (HR: 0.33), being metastasized at index (HR: 3.25), and having any care level (HR low/medium: 1.52, HR high: 2.40) significantly increase the hazard of death (**Table 2**).

Table 1: Patient characteristics and comorbidities

	Index 2018/2019 n = 2,323		p-value	
Age, mean (SD), years	69.2 (11.5)	69.1 (11.27)	0.863	
<b>Male,</b> n (%)	1,544 (66.5)	1,256 (66.6)	0.948	
Outpatient index diagnosis, n (%)	212 (9.13)	121 (6.41)	0.001	
CCI, mean (SD)	3.1 (2.8)	2.9 (2.8)	0.079	
ECI, mean (SD)	9.3 (9.8)	8.9 (9.8)	0.139	
Care level*, n (%)				
None	78.5	77.3		
Low/medium	10.8	11.2	0.651	
High	10.8	11.5		
Metastasized at index, n (%)	769 (33.1)	733 (38.8)	<0.001	
Observation period, mean (SD), months	19.4 (16.3)	12.3 (9.7)	<0.001	
Deaths within 12-month FU, n (%)	1,074 (46.2)	947 (50.2)	0.011	
Time to death, median (IQR), months	NE	11.9 (2.83-NE)	-	

Abbreviations: SD, Standard Deviation; n, number; CCI, Charlson Comorbidity Index; ECI, Elixhauser Comorbidity Index; FU, Follow-Up, IQR, Inter Quartile Range; NE, Not Estimable.

\* The German care level determines the disability grade of a patient and decides which subsidies insured patients receive from their care insurance fund. The higher the level of care, the higher the level of monetary and material benefits.

**Table 2.** Cox proportional hazards model comparing OS of LC patients diagnosed in 2020/2021 vs. 2018/2019

Variable	Hazard Ratio	Standard Error	p-value	95% CI		
Lung cancer diagnosis in 2020/2021, binary	1.05	0.05	0.318	0.96-1.14		
Age, continuous	1.03	0.00	<0.001	1.02-1.03		
Female sex, binary	0.77	0.04	<0.001	0.70-0.85		
ECI, continuous	1.00	0.00	0.460	1.00-1.01		
Outpatient index, binary, compared to inpatient index	0.33	0.04	<0.001	0.25-0.42		
Metastasized at index, binary	3.25	0.15	<0.001	2.97-3.55		
Care level, categorical, compared to no care level						
Low/medium care level	1.52	0.11	<0.001	1.32-1.74		
High care level	2.40	0.16	<0.001	2.12-2.73		
Abbreviations: CI, Confidence Interval; ECI, Elixhauser Comorbidity Index.						

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Figure 2. Kaplan-Meier curve: OS in 2018/2019

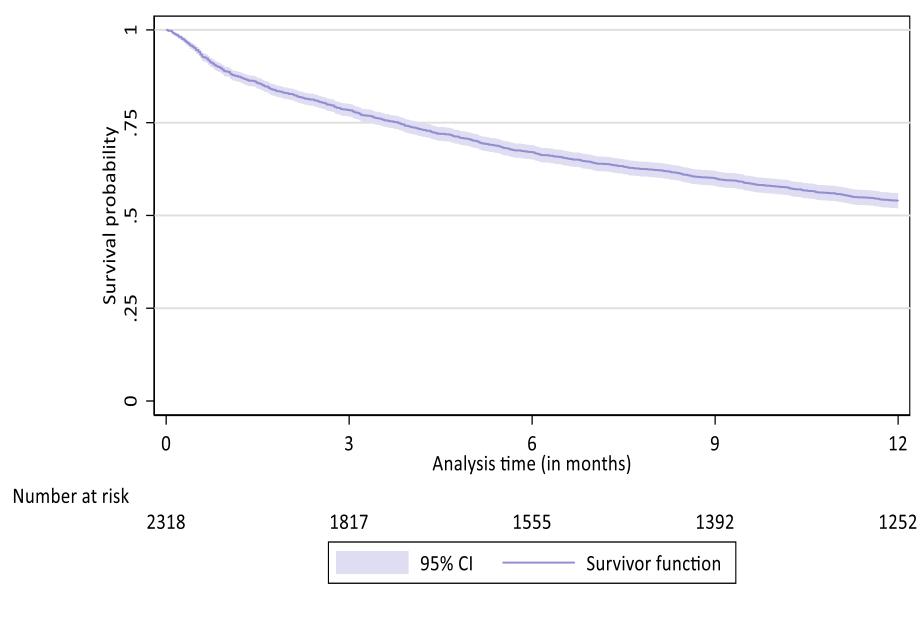
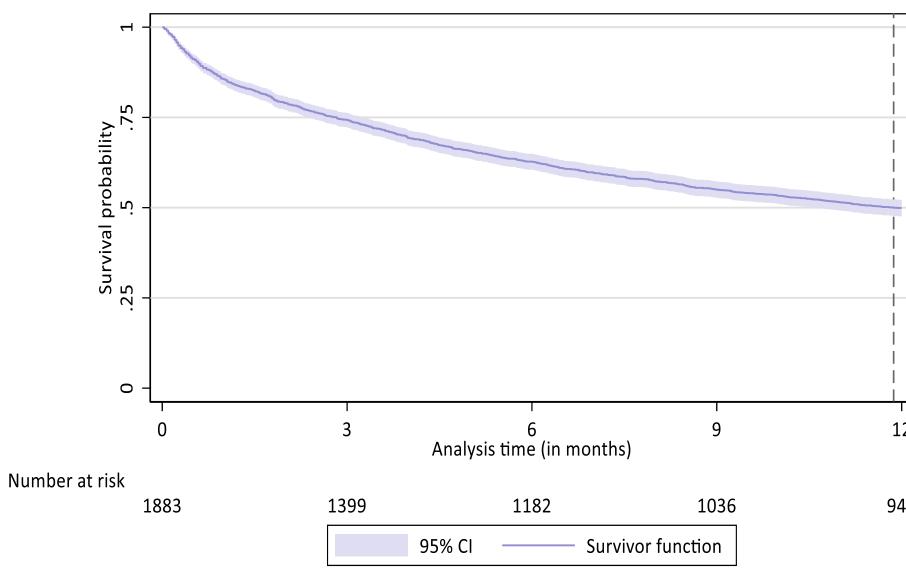


Figure 3. Kaplan-Meier curve: OS in 2020/2021



## Conclusions

This analysis showed that, generally, fewer cases were diagnosed during the pandemic. However, those that were detected were more likely in an advanced stage, which was reflected in worse OS outcomes. Further research is needed to investigate the pandemic's underlying factors and impact on real-world outcomes in lung cancer patients.

## References

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## Disclosures

Julia Krieger is an employee of Cytel Inc. and has no conflicts of interest to declare. Sabrina Mueller and Philipp Hahn participated in this study as members of IPAM e.V. and have no conflict of interest to declare. Andreas Fuchs works for a statutory insurance fund (AOK PLUS), which provided the data used in this study.





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