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Original article

Depression, intoxication, suicide attempt, suicide and the use of anxiolytics, hypnotics, sedatives and antidepressants following a diagnosis of non-small cell lung cancer. A population-based study (Sweden)

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ABSTRACT

Introduction: A cancer diagnosis affects quality of life, including psychological wellbeing. The risk of depression and suicide has been found to be increased in cancer patients, especially in cancers with poor prognosis. The aim of this study was to examine a broad range of indicators of psychological distress pre- and post-diagnosis in patients with non-small cell lung cancer (NSCLC).

Methods: We used data in a population-based lung cancer research database to compare diagnostic events of depression, anxiety, intoxication, suicide attempt and suicide as well as filled prescriptions for anxiolytics, hypnotics, sedatives and antidepressants between patients with NSCLC and individuals free of lung cancer (comparators).

Results: The study population encompassed 47,625 patients diagnosed with NSCLC between January 2006 and May 2022 and 236,492 lung cancer free individuals. Diagnostic rates indicating psychological distress (depression, intoxication, suicide attempt, suicide) were higher in NSCLC patients after diagnosis. Already three months prior to diagnosis, fillings of prescriptions for anxiolytics, hypnotics and sedatives were more common in patients with NSCLC than in comparators and remained higher in the cases during the first year post diagnosis. Following diagnosis, rates of prescriptions for antidepressants were also higher in cases. For all medications except antidepressants, rates of filled prescriptions correlated with severity of disease.

Conclusion: We found evidence of increased rates of both diagnostic events related to psychological distress and use of psychiatric medications after a diagnosis of NSCLC. Our findings underscore the importance of symptom monitoring post-diagnosis and preparedness to provide adequate support and treatment.

1. Introduction

A cancer diagnosis affects quality of life, including psychological wellbeing, with reports of increased rates of depression and anxiety in cancer patients compared to the general population (Dalton et al., 2009; Hung et al., 2017; Lee et al., 2021) . A review of studies on cancer patients in a palliative setting estimated the prevalence of a major depressive disorder, minor depression and anxiety to 14.3 %, 9.6 % and 9.8 %, respectively (Mitchell et al., 2011). Depression and anxiety cause suffering and may negatively affect prognosis by influencing not only

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the willingness to accept cancer treatment, but also adversely impact adherence to therapy (Shoval et al., 2019).

Lung cancer patients appear to be at increased risk of depression compared to patients with other malignancies, findings possibly explained by the poor prognosis in late-stage disease. In addition, both paraneoplastic symptoms (Hung et al., 2017) and high inflammatory activity in advanced stage lung cancer may be associated with depression (McFarland et al., 2019a). There are reports of an increased use of anxiolytics and sedatives already two years prior to diagnosis in patients with lung-, colorectal- and liver cancer (Lee et al., 2021).

Compared to the general population, the risk of suicide has been estimated to be twice as high in cancer patients, particularly within the first year of diagnosis (Fang et al., 2012). The risk has been reported to be especially high in patient with malignancies with poor prognosis such as lung-, pancreaticobiliary- and stomach cancer (Ahn et al., 2015; Calati et al., 2021; Choi and Park, 2020; Henson et al., 2019; McFarland et al., 2019b; Saad et al., 2019).

We used information in a large, population-based lung cancer research database to compare pre- and post-diagnostic events of depression, intoxication (alcohol, opioids, hypnotics & sedatives), suicide attempt and suicide as well as rates of filled prescriptions for anxiolytics, antidepressants, hypnotics & sedatives between patients with Non-Small Cell Lung Cancer (NSCLC) and individuals free of lung cancer representing the background population.

2. Methods

2.1. Data collection

This population-based matched cohort study was based on data obtained from the research database Lung Cancer Data Base Sweden (LCBaSe). The study population was defined by individuals with a record of a NSCLC diagnosis between January 1, 2006 and May 31, 2022 in the National Lung Cancer Register (NLCR). By use of the unique personal identifier assigned to all residents in Sweden, additional individual level data were obtained from other Swedish population-based registers including the Swedish Cancer Register, the National Patient Register (NPR), the National Cause of Death Register, the Longitudinal Integrated Database for Health Insurance and Labour Market Studies, the Total Population Register and the National Prescribed Drug Register (NPDR). LCBaSe also includes comparators from the general population. For each lung cancer patient, five lung cancer-free individuals were randomly chosen from the Swedish Population Register, matched on sex, birth year and region of residence at the date of the diagnosis of the case. LCBaSe has previously been described in detail (Löfling et al., 2019; Willén et al., 2022, 2019).

The NLCR, a national clinical quality register, was established in 2002 and includes detailed information on patient and tumor characteristics, performance status, smoking history and first line treatment. The completeness of NLCR exceeds 95 % when compared to the Swedish Cancer Register to which reporting is mandated. Psychiatric disorders were identified in the NPR by use of codes according to the International Classification of Diseases (ICD). The NPR reached national coverage in 1987 and includes data on in-and outpatient care from government and private hospitals and clinics, but not on primary care. During the time-period under study, both ICD-9 (up to December 31, 2010) and ICD-10 (from January 1, 2011 and onwards) were in use. To identify diagnostic events of interest the following ICD 9 codes were used: depressive disorders 296.2, 296.3, 311, anxiety disorders 300.4, for acute alcohol intoxication 2914, 2922, 3050, for acute intoxication with opioids 2922, 3055, acute intoxication with sedatives and hypnotics 2922, 3054 and for suicide and suicide attempt E950-E959 and E980-E989. The corresponding codes from ICD-10 were: depressive disorders F32, F33, anxiety disorders F34.1, for acute alcohol intoxication F10.0, for acute intoxication with opioids F11.0, acute intoxication with sedatives and hypnotics F13.0 and for suicide and suicide attempt X60-X84 and Y87. Data on suicide were also retrieved from the National Cause of Death Register.

Data on filled prescriptions were obtained from the NPDR, a national register administered by the Swedish Board of Health and Welfare launched on July 1, 2005. Prescribed medications were identified by use of The Anatomical Therapeutic Chemical Code (ATC-code); Anxiolytics N05B, Hypnotics & Sedatives N05C and Antidepressants N06A. Data are reported to the NPDR when the patient collects the medication at a pharmacy. While a filled prescription does not equal actual patient use, it can be considered as an indicator of decreased psychological well-being as determined by the prescribing physician. In the following, both the terms "use" and "filled prescriptions" will be used.

By use of information in the NPR, comorbidity was estimated based on the Charlson Comorbidity Index (CCI) and categorized into no (CCI 0), mild (CCI 1–2) and severe (CCI $\geq$3) (Charlson et al., 1987). Highest attained level of education was obtained from the Longitudinal Integrated Database for Health Insurance and Labour Market Studies and categorized into low, middle and high corresponding to $\leq$9, 10–12 or $\geq$12 years of schooling.

To align with the start of the NPDR, the study was restricted to individuals diagnosed with NSCLC from 2006 and onwards.

2.2. Statistical methods

Sociodemographic data were used to characterize cases and comparators at the date of diagnosis of the case (index date). The absolute numbers of diagnosed depressions, intoxications, suicide attempt, suicides as well as filled prescriptions for anxiolytics, hypnotics & sedatives and antidepressants are presented prior and post index date for NSCLC patients and individuals free of lung cancer; prior to diagnosis: $\leq$3 months, 4–12 months and $\geq$13 months and after diagnosis: $\leq$3 months, 4–12 months, $\geq$13 months.

Post-diagnosis data are also presented as rates per 100 000 person years. Because individuals could experience multiple outcomes during follow-up, conventional time-to-event methods, such as Kaplan–Meier estimation or Cox proportional hazards regression, would not fully capture the disease course, as these methods typically model only the time to a single event and do not explicitly account for transitions between multiple states. For this reason, a multistate model was used to estimate the cumulative incidence of each outcome while treating all-cause death as a competing risk. This approach allows individuals to contribute information to several outcomes over time and provides estimates of both the cumulative incidence of each outcome and the rate ratios comparing patients with NSCLC and the matched comparators (Le-Rademacher et al., 2022).

Thus, for each outcome of interest, we presented the cumulative incidence per 10,000 person-years comparing NSCLC patients with matched comparators and further stratified by stage at diagnosis (I–II, III, and IV) versus comparators. Rate Ratios (RR) were estimated using Poisson regression models adjusted for sex, age and Charlson Comorbidity Index, and presented as a function of follow-up time.

All tests were two-sided, and a 5 % level was considered statistically significant. For statistical analyses R version 3.5.0. was used.

2.3. Research ethics

The study was performed in accordance with the ethical principles in the Declaration of Helsinki and was approved by the Research Ethics Board in Stockholm (2012–1162–31–4, 2016–1137–32, 2017–2026–32, 2017–445–32 and 2021–05–25).

3. Results

3.1. Demographics and clinical characteristics

Following exclusions due to missing data, the study encompassed a

total of 47,625 patients diagnosed with NSCLC between January 1, 2006 and May 31, 2022. The lung cancer free cohort (comparators) consisted of 236,492 individuals. Demographic characteristics are presented in Table 1. The large majority of both lung cancer patients and comparators were Swedish born. Compared to lung cancer free individuals, patients with NSCLC were less likely to have a high educational level (17.8 % vs 25.8 %) and had a higher comorbidity burden (CCI ≥2: 29.2 % vs 16.4 %).

3.2. Psychological distress prior to diagnosis

Within three months prior to a diagnosis of NSCLC, prescriptions filled for anxiolytics (15.2 % vs 6.2 %) as well as hypnotics & sedatives (23.7 % vs 12.3 %) were more common in lung cancer patients than in comparators. However, no differences were found for antidepressants nor for reported clinical diagnoses of depression, intoxication or suicide attempt. (Table 1).

Table 1
Sociodemographic characteristics, number of recorded diagnostic events of depression, suicide attempt, and filled prescriptions for anxiolytics, hypnotics & sedatives and antidepressants prior to date of diagnosis/index date in patients with non-small cell lung cancer in Sweden between January 1, 2006 – May 31, 2022 (date of non-small cell lung cancer diagnosis) compared to matched lung cancer free individuals (comparators) from the general population.

Characteristics	NSCLC N = 47,625	Comparators N = 236,492
Sex		
Men	23,210 (48.7 %)	115,364 (48.8 %)
Women	24,415 (51.3 %)	121,128 (51.2 %)
Index year		
2006–2007	4649 (9.8 %)	22,783 (9.6 %)
2008–2010	7949 (16.7 %)	38,381 (16.2 %)
2011–2013	8327 (17.5 %)	40,585 (17.2 %)
2014–2016	8929 (18.7 %)	43,948 (18.6 %)
2017–2019	9390 (19.7 %)	47,639 (20.1 %)
2020–2022	8381 (17.6 %)	43,156 (18.2 %)
Age at index date*	72 (65, 77)	72 (65, 78)
Country of birth		
Nordics	3097 (6.5 %)	11,498 (4.9 %)
Other	4914 (10.3 %)	20,599 (8.7 %)
Sweden	39,614 (83.2 %)	204,395 (86.5 %)
Educational level		
Low	18,294 (38.4 %)	76,634 (32.4 %)
Middle	20,224 (42.5 %)	95,884 (40.5 %)
High	8466 (17.8 %)	60,940 (25.8 %)
Missing	641 (1.3 %)	3034 (1.3 %)
Charlson Comorbidity Index		
0	25,906 (54.4 %)	170,871 (72.3 %)
1	7790 (16.4 %)	26,945 (11.4 %)
≥2	13,929 (29.2 %)	38,676 (16.4 %)
Depression		
≤3 months prior to index date	197 (0.4 %)	228 (<0.1 %)
4–12 months prior to index date	74 (0.2 %)	359 (0.2 %)
>12 months prior to index date	1614 (3.4 %)	7676 (3.2 %)
Intoxication		
≤3 months prior to index date	24 (<0.1 %)	32 (<0.1 %)
4–12 months prior to index date	23 (<0.1 %)	80 (<0.1 %)
>12 months prior to index date	831 (1.7 %)	1873 (0.8 %)
Suicide attempt		
≤3 months prior to index date	10 (<0.1 %)	11 (<0.1 %)
4–12 months prior to index date	3 (<0.1 %)	16 (<0.1 %)
>12 months prior to index date	169 (0.4 %)	417 (0.2 %)
Anxiolytics		
≤3 months prior to index date	7219 (15.2 %)	14,568 (6.2 %)
4–12 months prior to index date	4599 (9.7 %)	18,175 (7.7 %)
>12 months prior to index date	10,885 (22.9 %)	46,836 (19.8 %)
Hypnotics & Sedatives		
≤3 months prior to index date	11,265 (23.7 %)	29,101 (12.3 %)
4–12 months prior to index date	8975 (18.8 %)	34,445 (14.6 %)
>12 months prior to index date	14,377 (30.2 %)	61,889 (26.2 %)
Antidepressants		
≤3 months prior to index date	6383 (13.4 %)	26,033 (11.0 %)
4–12 months prior to index date	6452 (13.5 %)	28,939 (12.2 %)
>12 months prior to index date	12,066 (25.3 %)	50,530 (21.4 %)
* Median (Q1, Q3)		

3.3. Psychological distress post diagnosis

Compared to lung cancer free individuals, rates of depressions were almost four times higher in lung cancer patients within 3 months of diagnosis (depression rate per 10,000 person years 523.02 vs 137.97) and remained elevated up to two years post diagnosis. The risks of intoxication, suicide attempt and suicide were also higher and remained elevated more than three years after diagnosis. Within 3 months of a NSCLC diagnosis rate per 10,000 person years for intoxication was 30.2 vs 14.4; for suicide attempt 31.3 vs 8.0 and suicide 7.0 vs 2.0. Markedly higher rates of filled prescriptions for anxiolytics, hypnotics & sedatives and antidepressants were seen within the first year of diagnosis. Rates within 3 months of NSCLC diagnosis for anxiolytics were 8630.5 vs 1384.5; hypnotics & sedatives 13,857.2 vs 3509.2; antidepressants 4119.3 vs 2987.4. The cumulative incidence of rates of filled prescriptions for anxiolytics, hypnotics & sedatives - but not för antidepressants -was higher in NSCLC-patients compared to the lung cancer free population. (Table 2, Figs. 1–4).

Following stratification by stage, the psychological effects of lung cancer were assessed in relation to severity of disease. The highest risk of suicide was observed in patients with stage IV disease, followed by lower risk in stage III and lower yet, in stage I-II disease. A similar pattern was seen in relation to the use of anxiolytics and hypnotics & sedatives. No such gradients were seen for rates of depression nor in use of antidepressants (Figs. 1–4).

4. Discussion

4.1. Summary of results

In this nationwide matched cohort study of patients with NSCLC, we found evidence of excess risks of indicators of impaired psychological well-being post diagnosis, including elevated rates of depression, intoxications, suicide attempts and suicide. Higher rates of prescriptions of anxiolytics and hypnotics & sedatives were noted already prior to diagnosis and following diagnosis also for antidepressants.

4.2. Comparisons to previous studies

Following a cancer diagnosis, psychological distress such as anxiety and depressive symptoms can be considered a normal acute crisis reaction. Over time, however, poor mental wellbeing may develop into severe depression. Results from earlier studies have found evidence of poorer survival in lung cancer patients with major depression, possibly reflecting that depressive symptoms negatively affect acceptance and adherence to treatment (Walker et al., 2021). Also, patients diagnosed with malignancies with poor prognosis have been shown to be at increased risk of suicide with a two- to thirteen-fold elevated risk reported in lung cancer patients (Ahn et al., 2015; Tang et al., 2022; Vyssoki et al., 2015). A study assessing the suicide risk within the first year following a cancer diagnosis, found the highest risk within one month followed by a decline after six months (Wang et al., 2018). We found elevated rates of depression and a higher use of antidepressants for more than two years following diagnosis. Our findings of elevated rates of intoxication, suicide attempt and suicide, especially within the first three years following diagnosis broadly corroborate results from earlier studies indicating that the increased risk of suicide in cancer patients subsides approximately 4 years after diagnosis (Klaassen et al., 2019). In addition, our results showed a correlation with severity of disease indicating that prognosis further affects the risk of suicide.

Results from population-based studies show that approximately 80 % of individuals committing suicide had a health care contact in the year prior to suicide, and approximately 60 % within one month prior to suicide. However, for only half of these patients, medical records

Table 2
Number of recorded diagnostic events of depression, suicide attempt and suicide, and filled prescriptions for anxiolytics, hypnotics & sedatives and antidepressants post date of diagnosis/index date in patients with non-small cell lung cancer in Sweden between January 1, 2006 – May 31, 2022 (date of non-small cell lung cancer diagnosis) compared to matched lung cancer free individuals (comparators) from the general population.

Outcome	Group	N	Number of cases	Person years (py)	Rate per 10,000 py (95 % CI)
Suicide					
≤3 months post diagnosis	NSCLC	47,625	6	8622.929	7.0 (3.1 - 15.5)
	Comparators	236,492	13	66,536.780	2.0 (1.1 - 3.4)
4–12 months post diagnosis	NSCLC	34,549	11	17,671.595	6.2 (3.5 - 11.2)
	Comparators	234,024	34	147,868.695	2.3 (1.6 - 3.2)
>12 months post diagnosis	NSCLC	23,138	26	61,266.131	4.2 (2.9 - 6.2)
	Comparators	226,093	235	1231,471.564	1.9 (1.7 - 2.2)
Sucicide attempt					
≤3 months post diagnosis	NSCLC	47,625	27	8622.929	31.3 (21.5 - 45.7)
	Comparators	236,492	53	66,536.780	8.0 (6.1 - 10.4)
4–12 months post diagnosis	NSCLC	34,549	22	17,671.595	12.5 (8.2 - 18.9)
	Comparators	234,024	63	147,868.695	4.3 (3.3 - 5.5)
>12 months post diagnosis	NSCLC	23,138	55	61,266.131	9.0 (6.9 - 11.7)
	Comparators	226,093	440	1231,471.564	3.6 (3.3 - 3.9)
Intoxication					
≤3 months post diagnosis	NSCLC	47,625	26	8622.929	30.2 (20.5 - 44.3)
	Comparators	236,492	96	66,536.780	14.4 (11.8 - 17.6)
4–12 months post diagnosis	NSCLC	34,549	36	17,671.595	20.4 (14.7 - 28.2)
	Comparators	234,024	146	147,868.695	9.9 (8.4 - 11.6)
>12 months post diagnosis	NSCLC	23,138	86	61,266.131	14.0 (11.4 - 17.3)
	Comparators	226,093	906	1231,471.564	7.36 (6.89 - 7.9)
Depression					
≤3 months post diagnosis	NSCLC	47,625	451	8622.929	523.0 (477 - 573.6)
	Comparators	236,492	918	66,536.780	138.0 (129.3 - 147.2)
4–12 months post diagnosis	NSCLC	34,549	264	17,671.595	149.4 (132.4 - 168.6)
	Comparators	234,024	950	147,868.695	64.3 (60.3 - 68.5)
>12 months post diagnosis	NSCLC	23,138	416	61,266.131	67.9 (61.7 - 74.8)
	Comparators	226,093	4711	1231,471.564	38.3 (37.2 - 39.4)
Anxiolytics					
≤3 months post diagnosis	NSCLC	47,625	7442	8622.929	8630.5 (8436.6 - 8828.8)
	Comparators	236,492	9212	66,536.780	1384.5 (1356.5 - 1413.1)
4–12 months post diagnosis	NSCLC	34,549	1330	17,671.595	752.6 (713.2 - 794.2)
	Comparators	234,024	3688	147,868.695	249.4 (241.5 - 257.6)
>12 months post diagnosis	NSCLC	23,138	1353	61,266.131	220.8 (209.4 - 232.9)
	Comparators	226,093	13,230	1231,471.564	107.4 (105.6 - 109.3)
Hypnotics & sedatives					
≤3 months post diagnosis	NSCLC	47,625	11,949	8622.929	13,857.2 (13,611.0 - 14,107.9)
	Comparators	236,492	23,349	66,536.780	3509.2 (3464.5 - 3554.5)
4–12 months post diagnosis	NSCLC	34,549	1685	17,671.595	953.5 (909.1 - 1000.1)
	Comparators	234,024	7513	147,868.695	508.1 (496.7 - 519.7)
>12 months post diagnosis	NSCLC	23,138	1393	61,266.131	227.4 (215.7 - 239.6)
	Comparators	226,093	19,640	1231,471.564	159.5 (157.3 - 161.7)
Antidepressants					
≤3 months post diagnosis	NSCLC	47,625	3552	8622.929	4119.3 (3986.0 - 4257.0)
	Comparators	236,492	19,877	66,536.780	2987.4 (2946.1 - 3029.2)
4–12 months post diagnosis	NSCLC	34,549	641	17,671.595	362.7 (335.7 - 391.9)
	Comparators	234,024	3851	147,868.695	260.4 (252.3 - 268.8)
>12 months post diagnosis	NSCLC	23,138	828	61,266.131	135.2 (126.3 - 144.7)
	Comparators	226,093	14,123	1231,471.564	114.7 (112.8 - 116.6)

Abbreviations: Person-years (PY) represent the total amount of follow-up time contributed by all individuals. Rates are presented as the number of events per 100,000 person-years.

included diagnostic information indicating psychological distress or mental problems (Ahmedani et al., 2014; Laanani et al., 2020) Also, self-reporting of depressive symptoms and use of antidepressants has been found to identify fewer depressive events in cancer patients compared to when validated depression surveys are used for screening (Martinez et al., 2024). This highlights the importance for health care staff to identify depressive symptoms and psychological distress. An improved understanding and consideration of risk factors for suicide is of importance also in an oncological care setting, such as documented elevated risks of suicide in males, in widowed and unmarried individuals, in the elderly and in patients with advanced stage cancer with poor prognosis (Ravaioli et al., 2020; Tang et al., 2022; Vyssoki et al., 2015). Also, cancer patients with a prior history of mental disorders are at increased risk of suicide compared both to the general population and to cancer patients without a history of psychiatric care and treatment (Choi and Park, 2020; Klaassen et al., 2019). Furthermore, potent medications are often prescribed to relieve cancer symptoms, drugs that also may be used for self-harm. The optimal treatment of depressive symptoms in cancer patients remains debated. A Cochrane meta-analysis concluded that studies on treatment of depression in cancer patients are few and of low quality (Vita et al., 2023).

4.3. Strengths and limitations

Strengths of our study included the use of a large nation-wide population-based data set. For this reason, selection bias was not an issue. Data on lung cancer free individuals allowed for comparisons to the background population. In addition, the data set at hand included individual level information on comorbidity and socioeconomic status. As opposed to most previous studies in this area, we are able to indirectly assess psychological distress by leveraging data on filled prescriptions of anxiolytics, hypnotics & sedatives and antidepressants.

Limitations included the likely underreporting to the National Patient Register of diagnoses of depression and anxiety made in inpatient

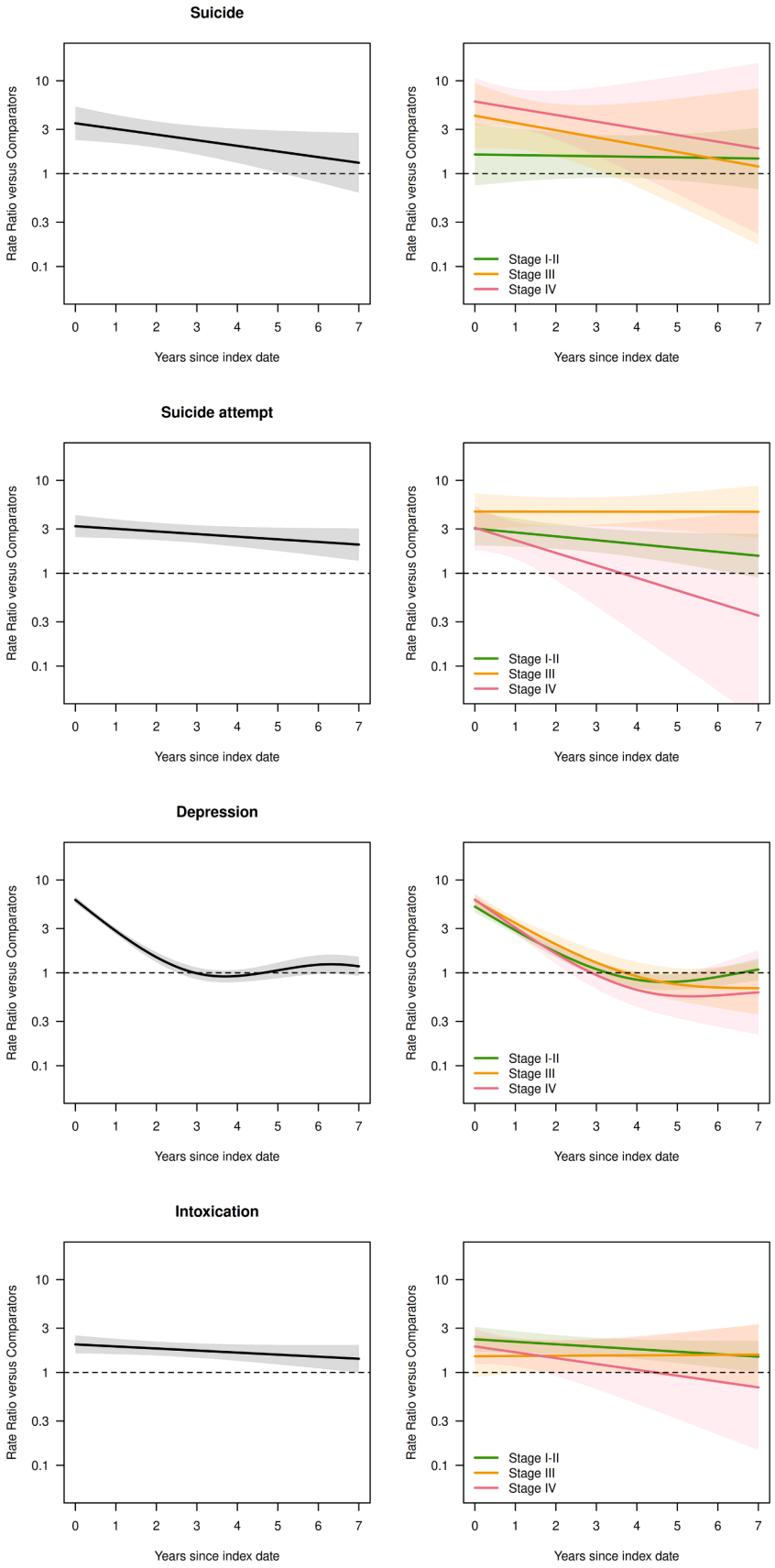

Fig. 1. Estimated rate ratios of suicide, suicide attempt, depression and intoxication in patients with non-small cell lung cancer in Sweden between 2006–2022, for all patients and stratified by cancer stage. Adjusted for sex, age and Charlson Comorbidity Index. Comparators: lung cancer free individuals.

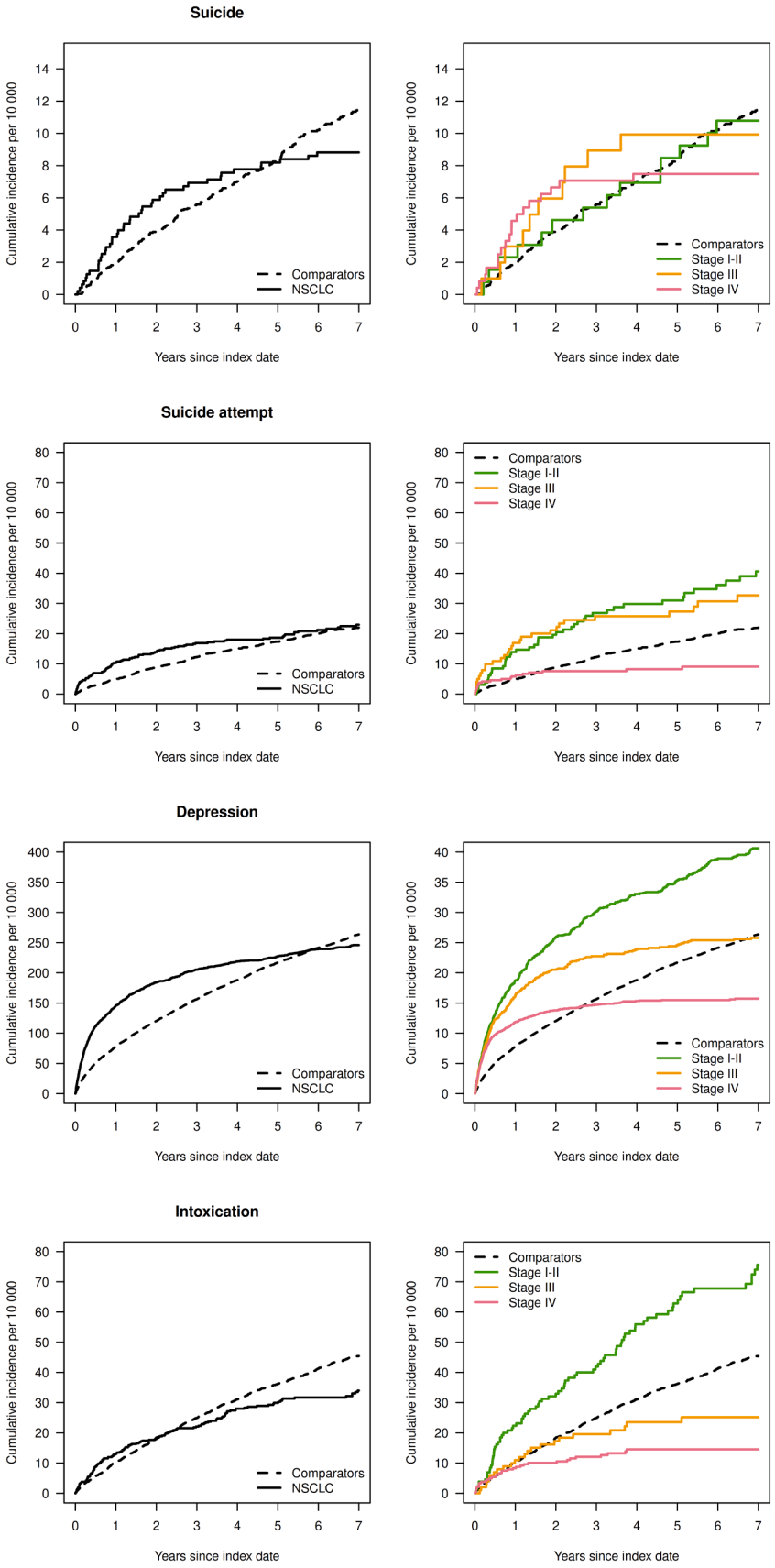

Fig. 2. Estimated cumulative incidence of death, suicide, suicide attempt, depression and intoxication in individuals with non-small cell lung cancer in Sweden between 2006–2022, for all patients and stratified by cancer stage. Comparators: lung cancer free individuals.

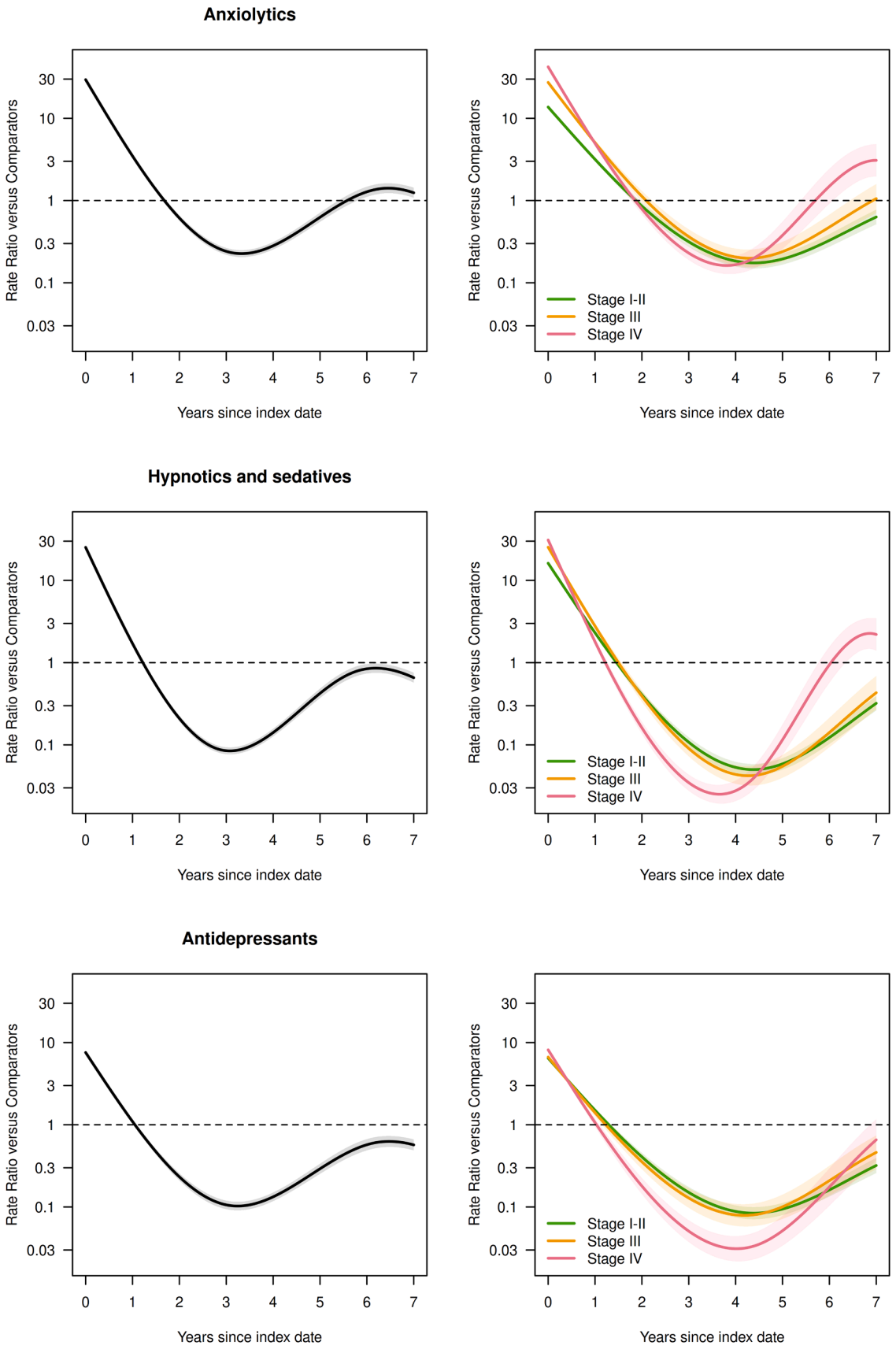

Fig. 3. Estimated rate ratios of the use of anxiolytics, hypnotics & sedatives and antidepressants in patients with non-small cell lung cancer in Sweden between 2006–2022, for all patients and stratified by cancer stage. Adjusted for sex, age and Charlson Comorbidity Index. Comparators: lung cancer free individuals.

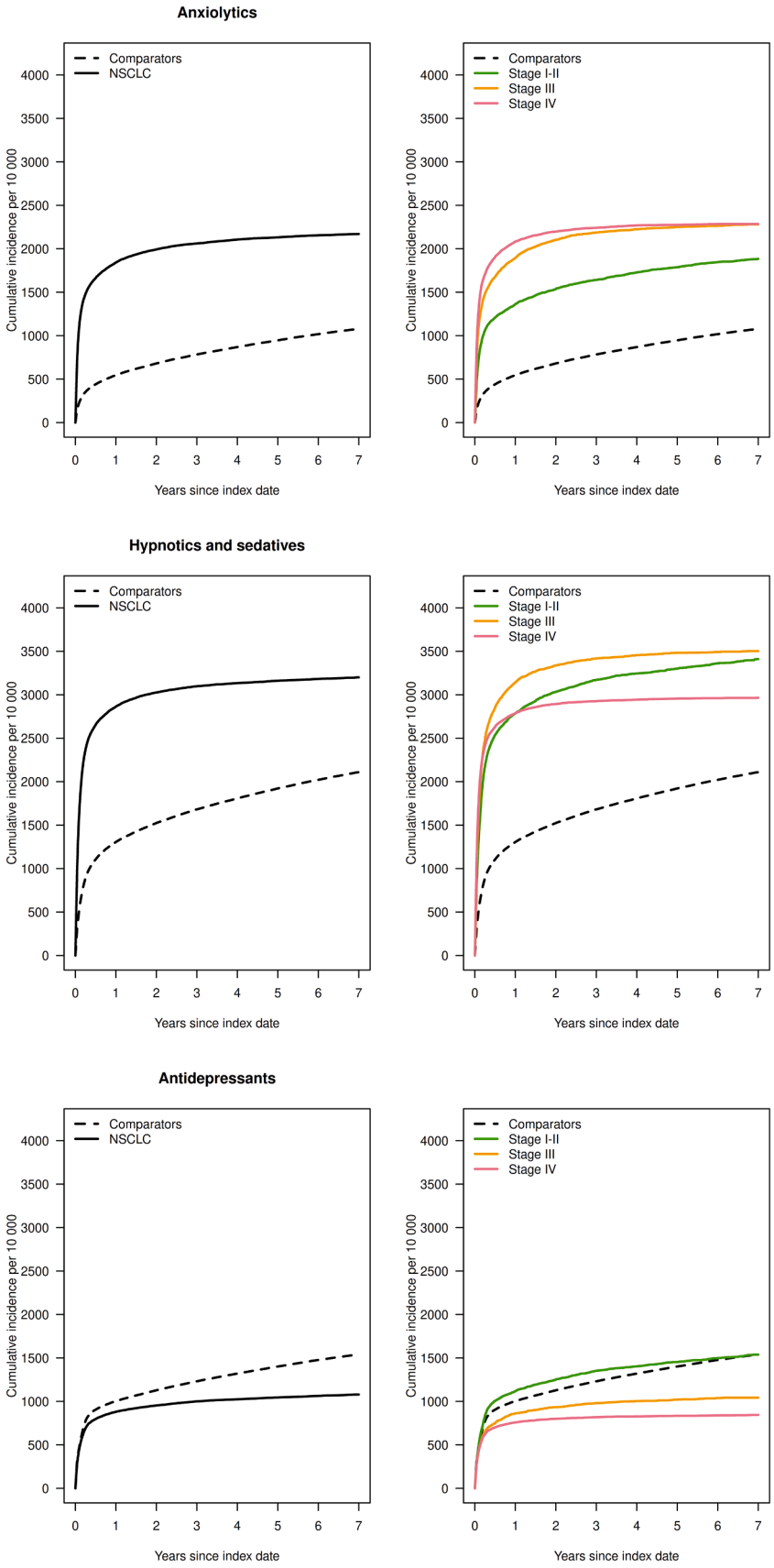

Fig. 4. Estimated cumulative incidence of anxiolytics, hypnotics & sedatives and antidepressants in individuals with non-small cell lung cancer in Sweden between 2006–2022, for all patients and stratified by cancer stage. Comparators: lung cancer free individuals.

and outpatient hospital settings. While diagnostic information was unavailable from primary care, the reporting of prescribed medications for depressive and dysthymic disorders in all health care settings should compensate for this. Although rates of filled prescriptions may differ from actual patient use, particularly for psychiatric medications, a prescription (intention to treat) represents an indicator of the presence of psychological distress as assessed by the prescribing physician. The data at hand did not include information on use of cognitive therapy or severity of depression.

It cannot be excluded that elevated risks of depression and suicide may be influenced by characteristics of NSCLC patients that differ from the background population, including a lower educational level and a higher comorbidity burden. (Grose et al., 2014; Pizzato et al., 2022), factors which may be independently associated with an increased risk of substance abuse and suicide. (Agerbo et al., 2006; Charitonidi et al., 2016).

It is worth noting that the number of reported suicides and suicide attempts was relatively low in the population under study, possibly reflecting underreporting and difficulties to determine cause of death. While the rates of suicide were estimated on data based on ICD-codes for confirmed suicides, the reporting and registration in the Cause of Death Register has not been systematically validated. It is known that deaths coded as self-injury with undetermined intent, such as intoxications, drowning or accidents, in many cases also represent suicide.(Ohberg and Lonnqvist, 1998; Tøllefsen et al., 2016) Another factor that may have contributed to an underestimation of the number of suicides is a decline in the use of post-mortem autopsies. Despite these limitations, it is unlikely that the magnitude of underreporting suicide differs between lung cancer patients and comparators. Because of concerns of events not recorded as suicide or suicide attempts, rates of intoxications post diagnosis were compared in a separate step, also yielding higher rates in NSCLC patients. While we included ICD-codes for intoxications, it can not be excluded that underreporting affected our results. (Tøllefsen et al., 2016, 2012).

5. Conclusion

We found evidence of increased rates of depression, anxiety, intoxication, suicide attempt and suicide post-diagnosis in patients with NSCLC compared to individuals free of lung cancer representing the general population. Our findings underscore the need not only to monitor newly diagnosed lung cancer patients for severe psychological distress, but also preparedness to initiate adequate support and treatment.

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CRediT authorship contribution statement

Linda Willén: Writing – original draft, Methodology, Funding acquisition, Conceptualization. **Anders Berglund:** Writing – review & editing, Visualization, Software, Resources, Methodology, Formal analysis, Data curation. **Stefan Bergström:** Writing – review & editing, Supervision, Conceptualization. **Johan Isaksson:** Writing – review & editing, Conceptualization. **Michael Bergqvist:** Writing – review & editing, Conceptualization. **Gunnar Wagenius:** Writing – review & editing, Conceptualization. **Mats Lambe:** Writing – review & editing, Supervision, Project administration, Methodology, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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