Aalborg Universitet

Mental Health Among Patients with non-Hodgkin Lymphoma

a Danish Nationwide Study of Psychotropic Drug Use in 8,750Patients and 43,750 Matched Comparators

Øvlisen, Andreas Kiesbye; Jakobsen, Lasse Hjort; Kragholm, Kristian Hay; Nielsen, René Ernst; de Nully Brown, Peter; Dahl-Sørensen, Rasmus Bo; Frederiksen, Henrik; Mannering, Nikolaj; Josefsson, Pär Lars; Ludvigsen Al-Mashhadi, Ahmed; Jørgensen, Judit Mészáros; Dessau-Arp, Andriette; Clausen, Michael Roost; Pedersen, Robert Schou; Torp-Pedersen, Christian; Severinsen, Marianne Tang; El-Galaly, Tarec Christoffer

Published in:
American Journal of Hematology

DOI (link to publication from Publisher):
10.1002/ajh.26538

Creative Commons License
CC BY-NC 4.0

Publication date:
2022

Document Version
Publisher's PDF, also known as Version of record

Link to publication from Aalborg University

Citation for published version (APA):
Øvlisen, A. K., Jakobsen, L. H., Kragholm, K. H., Nielsen, R. E., de Nully Brown, P., Dahl-Sørensen, R. B., Frederiksen, H., Mannering, N., Josefsson, P. L., Ludvigsen Al-Mashhadi, A., Jørgensen, J. M., Dessau-Arp, A., Clausen, M. R., Pedersen, R. S., Torp-Pedersen, C., Severinsen, M. T., & El-Galaly, T. C. (2022). Mental Health Among Patients with non-Hodgkin Lymphoma: a Danish Nationwide Study of Psychotropic Drug Use in 8,750Patients and 43,750 Matched Comparators. *American Journal of Hematology*, *97*(6), 749-761. https://doi.org/10.1002/ajh.26538

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal -

Take down policy
If you believe that this document breaches copyright please contact us at vbn@aub.aau.dk providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from vbn.aau.dk on: December 04, 2025

Check for updates

Received: 2 November 2021 | Revised: 21 February 2022 | Accepted: 7 March 2022

DOI: 10.1002/ajh.26538

RESEARCH ARTICLE

AJH WILEY

Mental health among patients with non-Hodgkin lymphoma: A Danish nationwide study of psychotropic drug use in 8750 patients and 43 750 matched comparators

Andreas Kiesbye Øvlisen[1,2] | Lasse Hjort Jakobsen[1,2] | Kristian Hay Kragholm[3,4] | René Ernst Nielsen[2,5] | Peter de Nully Brown[6] | Rasmus Bo Dahl-Sørensen[7] | Henrik Frederiksen[8] | Nikolaj Mannering[8] | Pär Lars Josefsson[9] | Ahmed Ludvigsen Al-Mashhadi[1] | Judit Mészáros Jørgensen[10] | Andriette Dessau-Arp[11] | Michael Roost Clausen[12] | Robert Schou Pedersen[13] | Christian Torp-Pedersen[3,14] | Marianne Tang Severinsen[1,2,15] | Tarec Christoffer El-Galaly[1,2,15]

[1]Department of Hematology, Aalborg University Hospital, Aalborg, Denmark

[2]Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

[3]Unit of Epidemiology and Biostatistics, Aalborg University Hospital, Aalborg, Denmark

[4]Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark

[5]Department of Psychiatry, Aalborg University Hospital, Aalborg, Denmark

[6]Department of Hematology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

[7]Department of Hematology, Zealand University Hospital, Roskilde, Denmark

[8]Department of Hematology, Odense University Hospital, Odense, Denmark

[9]Department of Hematology, Herlev Hospital, Herlev, Denmark

[10]Department of Hematology, Aarhus University Hospital, Aarhus, Denmark

[11]Department of Hematology, Sydvestjysk Sygehus, Esbjerg, Denmark

[12]Department of Hematology, Vejle Sygehus, Vejle, Denmark

[13]Department of Hematology, Hospitalsenheden Vest, Holstebro, Denmark

[14]Department of Cardiology and Clinical Research, Nordsjællands Hospital, Hillerød, Denmark

[15]Clinical Cancer Research Unit, Aalborg University Hospital, Aalborg, Denmark

Correspondence
Andreas Kiesbye Øvlisen, Department of Hematology, Aalborg University Hospital, Mølleparkvej 4, DK-9000 Aalborg, Denmark.
Email: a.oevlisen@rn.dk

Abstract

Psychological distress following cancer diagnosis may lead to mental health complications including depression and anxiety. Non-Hodgkin lymphomas (NHLs) include indolent and aggressive subtypes for which treatment and prognosis differ widely. Incident use of psychotropic drugs (PDs—antidepressants, antipsychotics, and anxiolytics) and its correlation to lymphoma types can give insights into the psychological distress these patients endure. In this prospective matched cohort study, we used nationwide population-based registries to investigate the cumulative risk of PD use in NHL patients compared to a sex- and age-matched cohort from the Danish

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.
© 2022 The Authors. *American Journal of Hematology* published by Wiley Periodicals LLC.

background population. In addition, contact patterns to psychiatric departments and incident intentional self-harm or completed suicide were explored. In total, 8750 NHL patients and 43 750 matched comparators were included (median age 68; male: female ratio 1.6). Median follow-up was 7.1 years. Two-year cumulative risk of PD use was higher in NHL patients (16.4%) as compared to the matched comparators (5.1%, $p < .01$); patients with aggressive NHL subtypes had the highest incidence. Prescription rates were higher in the first years after diagnosis but approached the rate of the matched population 5 years into survivorship in aggressive NHLs, whereas patients with indolent subtypes continued to be at higher risk. NHL patients had a slightly higher two-year risk of suicide/intentional self-harm (0.3%) as compared to the matched comparators (0.2%, $p = .01$). These results demonstrate that mental health complications among NHL patients are frequent. Routine assessment for symptoms of depression and anxiety should be consider as part of standard follow-up of NHL patients.

1 | INTRODUCTION

Patients diagnosed with cancer are in a stressful situation due to the uncertainties associated the diagnosis: fear of poor response to treatment, suffering, and death as well as concerns over risk of treatment complications. The fears and concerns can cause significant psychological distress and lead to poor mental health.[1–4] Mental health complications in patients with cancer cause long-term suffering and can have severe psychosocial consequences such as reduced quality of life, prolonged sick-leave, increased risk of disability pension, and even increased mortality.[5] Solid tumor patients with poor prognosis (e.g., lung and gynecological cancers) experience higher rates of depression and anxiety than solid tumor patients with more favorable prognosis (e.g., prostate and skin cancers).[6–8]

The non-Hodgkin lymphomas (NHLs) are a heterogenous group of cancers with highly variable disease course spanning from the highly proliferative, fast-growing, and potentially curable lymphomas to the chronic, indolent lymphomas.[9] Most indolent NHLs are incurable with conventional therapies, which range from use of mild- to moderate-intensity immunochemotherapy regimens to single agent rituximab, radiotherapy, or initial observation without treatment for patients without symptomatic disease. Treatments for aggressive NHLs include intensive chemotherapy regimens and, in selected cases, consolidation strategies with autologous stem cell transplantation.[9,10] Thus, NHLs are an interesting case study of the impact of prognosis, curability, and treatments on the level of psychological distress. Patients with indolent lymphomas, even those patients who do not require immediate treatment, may experience chronic stress from the fact that many of them face a lifelong cancer disease with repeated treatment intervention.[9,10] In contrast, patients with aggressive lymphomas may present with acute life-threatening disease, which require immediate treatment intervention.[9,10] However, many are cured, and for most common type of aggressive NHL, diffuse large B-cell lymphoma (DLBCL), life expectancy for survivors becomes close to normal after only few years in remission.[11] Nevertheless, a considerable risk of relapse, especially in the first years after completing therapy, may result in worry and anxiety, potentially exacerbated by the frequent hospital visits where patients are screened for disease recurrence.[12] A recent study from our group showed increased use of psychotropic drugs (PDs) in Hodgkin lymphoma (HL) patients,[12] but studies focusing on patients with NHL are very limited.[13]

The aim of this nationwide population-based study was to investigate the risk of mental health complications in various subtypes of NHLs using redeemed PD prescriptions as a proxy for symptoms of depression and anxiety. The impact of time since diagnosis on the incidence of mental health problems was also examined.

2 | MATERIALS AND METHODS

2.1 | Study- and background population

The study population was identified using the *Danish National Lymphoma registry* (LYFO), which is characterized by high completeness (92%–100%) and accuracy (positive predictive value between 87% and 100%).[14] LYFO includes detailed data about patient characteristics from the time of diagnosis (e.g., B-symptoms, age, sex, and Eastern Cooperative Oncology Group [ECOG] performance score), disease characteristics (e.g., subtype, localization, risk scores, and selected lab results), treatment information (*including if initial watchful waiting was pursued*), and treatment outcomes.

The inclusion criteria in the present study were (a) a diagnosis of any type of NHL between January 2005 and December 2015, (b) age ≥18 years at the time of diagnosis, and (c) no PD prescriptions within 10 years prior to the date of diagnosis (to describe the incident use of PDs). Subtypes of NHL were grouped into five groups based on disease characteristics (Table S1). For each NHL patient, five NHL-free individuals from the Danish background population were matched

(incidence density matching) on age (year and month of birth), sex, and country of origin using the *Danish Civil Registration System*.[15–17] Inclusion date for the matched comparators was the date of diagnosis for the index patient (index date). In addition, the matched comparators had to be alive and living in Denmark on the index date and, similarly to the NHL population, without PD prescriptions 10 years prior to the index date.

2.2 | Definition of PD prescription events and data sources for capture of events

This study investigated the following events during follow-up; (a) first redeemed PD prescription, (b) second-redeemed PD prescription (sensitivity analysis), (c) first in-patient/out-patient visit at any department of psychiatry in Denmark, and (d) completed suicide or first incident of intentional self-harm. Linking between data sources is possible using the Personal Identification Number (CPR) given to all Danish residents at time of birth or immigration.[15–17] Several registers were used in the present study. *The Danish Civil Registration System* includes demographic information such as age, sex, marital status, citizenship, and municipality of residence.[15–17] *The Danish National Patient Registry* includes data for all hospitalizations and outpatient/emergency department contacts in Danish hospitals and uses ICD-10 for register diagnoses.[18] Data from this register were used to calculate the Charlson Comorbidity Index (CCI) prior to the index date as well as capturing any events of completed suicide or intentional self-harm.[19–21] Completed suicide and intentional self-harm were captured using a Danish algorithm (DK-algorithm).[21,22] *The Danish Psychiatric Central Register* was used to identify contacts to psychiatry clinics.[23] PD prescriptions were identified using *The National Prescription Registry*, which holds information on all redeemed prescriptions from Danish pharmacies by the global Anatomical Therapeutic Chemical classification (ATC).[24,25] PDs were defined as antidepressants (ATC, N06A), antipsychotics (ATC, N05A), and anxiolytics (ATC, N05B) (for specific agents please see https://www.whocc.no/atc_ddd_index/). Since use of hypnotics (ATC, N05C, such as barbiturates and benzodiazepine derivatives) could be a potential indicator of mental stress, this was also included in a sensitivity analysis. *The Danish Education Register* holds information on the highest achieved educational level (International Standard Classification of Education [ISCED]).[26] The highest achieved educational level 1 year prior to diagnosis was used in this study.

2.3 | Statistical analysis

Categorical variables are summarized by proportions, whereas continuous variables are summarized by medians with interquartile ranges (IQRs). Differences in baseline characteristics between patients and matched comparators are provided for the entire population as well as using Pearson's chi square test or Mann–Whitney *U* test.

The follow-up period was defined as the time from the index date until first PD prescription, death from any cause, lymphoma relapse, or end of follow-up (August 2018), whichever came first. For matched comparators, follow-up was terminated if NHL was diagnosed after inclusion. Cumulative incidence of PD prescription was computed using the Aalen-Johansen estimator with deaths and relapses before PD prescriptions treated as competing events. For matched comparators, an NHL diagnosis was also considered a competing event. Two-year cumulative incidences were investigated in additional analyses with (1) PD use defined as having at least two prescriptions of PDs (follow-up until the time of the second prescription, sensitivity analysis), (2) inclusion of hypnotics in the definition of PD use, (3) hospitalization or out-patient treatment at a department of psychiatry, and (4) intentional self-harm or completed suicide. To investigate timing of PD prescriptions around diagnosis of NHL, an additional analysis of the cumulative incidence of first PD prescription was performed, in which both NHL patients and the matched comparators were allowed to have received PD prescriptions up to 5 years prior to index date.

Differences between the cumulative incidence functions were tested using Gray's test.[27] Differences in cause-specific hazard rates were tested using marginal Cox proportional hazards models with clusters defined as individual patients combined with the respective matched comparators on matching ID. Two-year hazard ratios (HRs) were calculated (in which all were censored 2 years after index date if no event, death, or relapse had occurred) and presented with 95% confidence intervals (95% CIs). To investigate potential risk changes as patients remained free of PD prescriptions, we performed a landmark analysis in which the one-year HR was computed for patients alive and without PD prescriptions one, two, and 5 years after the diagnosis. At each landmark time point, patients were rematched to five new comparators from the Danish background population who were alive and without PD prescriptions at the landmark time point.

Analyses were conducted in SAS version 9.4 (SAS Institute Inc., Gary, NC, USA), RStudio version 1.1.447 (RStudio, Inc., Boston, MA, USA), and R version 3.6.1 (R foundation for Statistical Computing, Vienna, Austria).

The study was approved by the Danish Data Protection Agency (internal ID No. 2018-88).

3 | RESULTS

3.1 | Patient characteristics

A total of 8750 NHL patients were included (3550 [40.6%] DLBCL, 3972 [45.4%] indolent NHL, and 1228 [14.0%] patients with other subtypes of NHL, Tables 1 and S2). Median age for all NHL patients was 66 years (IQR 57–75). Patients with aggressive B-cell NHL other than DLBCL (including Burkitt and lymphoblastic lymphomas) were younger (50, IQR 34–65.5). The male:female ratio in NHL patients was 1.6. Median follow-up for the total patient population was 7.1 years (subtypes ranges from 6.8–7.3 years; reverse Kaplan–Meier method).

TABLE 1 Baseline characteristics of patients with the most common subtypes of non-Hodgkin lymphoma (NHL) and the matched comparators

	All NHL			DLBCL			Indolent NHL		
	Patients	Matched comparators	*p*-value	Patients	Matched comparators	*p*-value	Patients	Matched comparators	*p*-value
Overall	8750 (100%)	43 750 (100%)		3550 (100%)	17 750 (100%)		3972 (100%)	19 860 (100%)	
Age									
Median (IQR)	66 (57–75)	66 (57–75)	1.00	67 (57–75)	67 (57–75)	1.00	66 (58–75)	66 (58–75)	1.00
18–45 years	816 (9.3%)	4080 (9.3%)	1.00	369 (10.4%)	1845 (10.4%)	1.00	259 (6.5%)	1295 (6.5%)	1.00
46–70 years	4427 (50.6%)	22 135 (50.6%)		1725 (48.6%)	8625 (48.6%)		2137 (53.8%)	10 685 (53.8%)	
≥71 years	3507 (40.1%)	17 535 (40.1%)		1456 (41.0%)	7280 (41.0%)		1576 (39.7%)	7880 (39.7%)	
Sex									
Females	3417 (39.1%)	17 085 (39.1%)	1.00	1403 (39.5%)	7015 (39.5%)	1.00	1655 (41.7%)	8275 (41.7%)	1.00
Males	5333 (60.9%)	26 665 (60.9%)		2147 (60.5%)	10 735 (60.5%)		2317 (58.3%)	11 585 (58.3%)	
Charlson Comorbidity Index									
0	6268 (71.6%)	35 135 (80.3%)	<.01*	2494 (70.3%)	14 244 (80.2%)	<.01*	2885 (72.6%)	15 918 (80.2%)	<.01*
≥1	2482 (28.4%)	8615 (19.7%)		1056 (29.7%)	3506 (19.8%)		1087 (27.4%)	3942 (19.8%)	
Educational level (ISCED)									
Primary education	3228 (36.9%)	16 395 (37.5%)	<.01*	1369 (38.6%)	6669 (37.6%)	.11	1426 (35.9%)	7353 (37.0%)	.02*
Secondary/tertiary education	5091 (58.2%)	24 829 (56.8%)		1987 (56%)	9958 (56.1%)		2363 (59.5%)	11 422 (57.5%)	
Missing	431 (4.9%)	2526 (5.8%)		194 (5.5%)	1123 (6.3%)		183 (4.6%)	1085 (5.5%)	
Country of origin									
Danish	8271 (94.5%)	41 355 (94.5%)	1.00	3339 (94.1%)	16 695 (94.1%)	1.00	3762 (94.7%)	18 810 (94.7%)	1.00
Western country	≤240 (≤2.7%)[a]	≤1230 (≤2.7%)[a]		102 (2.9%)	510 (2.9%)		121 (3.0%)	605 (3.0%)	
Nonwestern country	≤238 (≤2.7%)[a]	≤1190 (≤2.7%)[a]		109 (3.1%)	545 (3.1%)		89 (2.2%)	445 (2.2%)	
Civil status									
Married	5632 (64.4%)	27 713 (63.3%)	.08	2234 (62.9%)	11 101 (62.5%)	.83	2616 (65.9%)	12 818 (64.5%)	.07
Divorced	937 (10.7%)	4579 (10.5%)		365 (10.3%)	1839 (10.4%)		449 (11.3%)	2142 (10.8%)	
Widowed	1118 (12.8%)	5768 (13.2%)		491 (13.8%)	2413 (13.6%)		504 (12.7%)	2641 (13.3%)	
Unknown	1063 (12.1%)	5690 (13.0%)		460 (13%)	2397 (13.5%)		403 (10.1%)	2259 (11.4%)	
ECOG performance status									
0	5132 (58.7%)	-	-	1731 (48.8%)	-	-	2807 (70.7%)	-	-
1–4	3586 (41.0%)	-		1806 (50.9%)	-		1150 (29%)	-	
Missing	32 (0.4%)	-		13 (0.4%)	-		15 (0.4%)	-	

TABLE 1 (Continued)

	All NHL			DLBCL			Indolent NHL		
	Patients	Matched comparators	*p*-value	Patients	Matched comparators	*p*-value	Patients	Matched comparators	*p*-value
Disease stage									
Limited stage (I-II)	2778 (31.7%)	-	-	1521 (42.8%)	-	-	985 (24.8%)	-	-
Advanced stage (III-IV)	≤5767 (≤65.9%)	-		1951 (55.0%)	-		2878 (72.5%)	-	
Missing	≤211 (≤2.4%)	-		78 (2.2%)	-		109 (2.7%)	-	
B-symptoms at diagnosis									
Yes	2862 (32.7%)	-		1444 (40.7%)	-		855 (21.5%)	-	-
No	5638 (64.4%)	-		1988 (56.0%)	-		3033 (76.4%)	-	
Missing	250 (2.9%)	-		118 (3.3%)	-		84 (2.1%)	-	
LDH level above normal threshold									
No	5345 (61.1%)	-	-	1672 (47.1%)	-	-	3033 (76.4%)	-	-
Yes	≤3087 (≤35.3%)[a]	-		1746 (49.2%)	-		797 (20.1%)	-	
Missing	≤320 (≤3.7%)[a]	-		132 (3.7%)	-		142 (3.6%)	-	
Planned treatment									
Yes	6814 (73.4%)	-	-	3341 (94.1%)	-	-	2162 (54.4%)	-	-
Wait-and-watch	2382 (25.7%)	-		187 (5.3%)	-		1776 (44.7%)	-	
Unknown	89 (1.00)	-		22 (0.6%)	-		34 (0.9%)	-	
IPI-score									
Low	2872 (32.8%)	-	-	1184 (33.4%)	-	-	1385 (34.9%)	-	-
Low-intermediate	2792 (31.9%)	-		820 (23.1%)	-		1605 (40.4%)	-	
High-intermediate	1656 (18.9%)	-		747 (21.0%)	-		598 (15.1%)	-	
High	893 (10.2%)	-		588 (16.6%)	-		125 (3.1%)	-	
Missing	537 (6.1%)	-		211 (5.9%)	-		259 (6.5%)	-	
FLIPI-score									
Low	662 (7.6%)	-	-	-	-	-	662 (16.7%)	-	-
Intermediate	564 (6.4%)	-		-	-		564 (14.2%)	-	
High	577 (6.6%)	-		-	-		577 (14.5%)	-	
Missing	6947 (79.4%)	-		-	-		2169 (54.6%)	-	

Abbreviations: DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; FLIPI, Follicular Lymphoma International Prognostic Index; IQR, interquartile range; IPI, International Prognostic Index; ISCED, International Standard Classification of Education; LDH, lactate dehydrogenase; NHL, non-Hodgkin lymphoma.

[a]To comply with Statistics Denmark's policies and regulations, we cannot report the exact number, as there are few in each group.

*Statistically significant (*p*-value < .05).

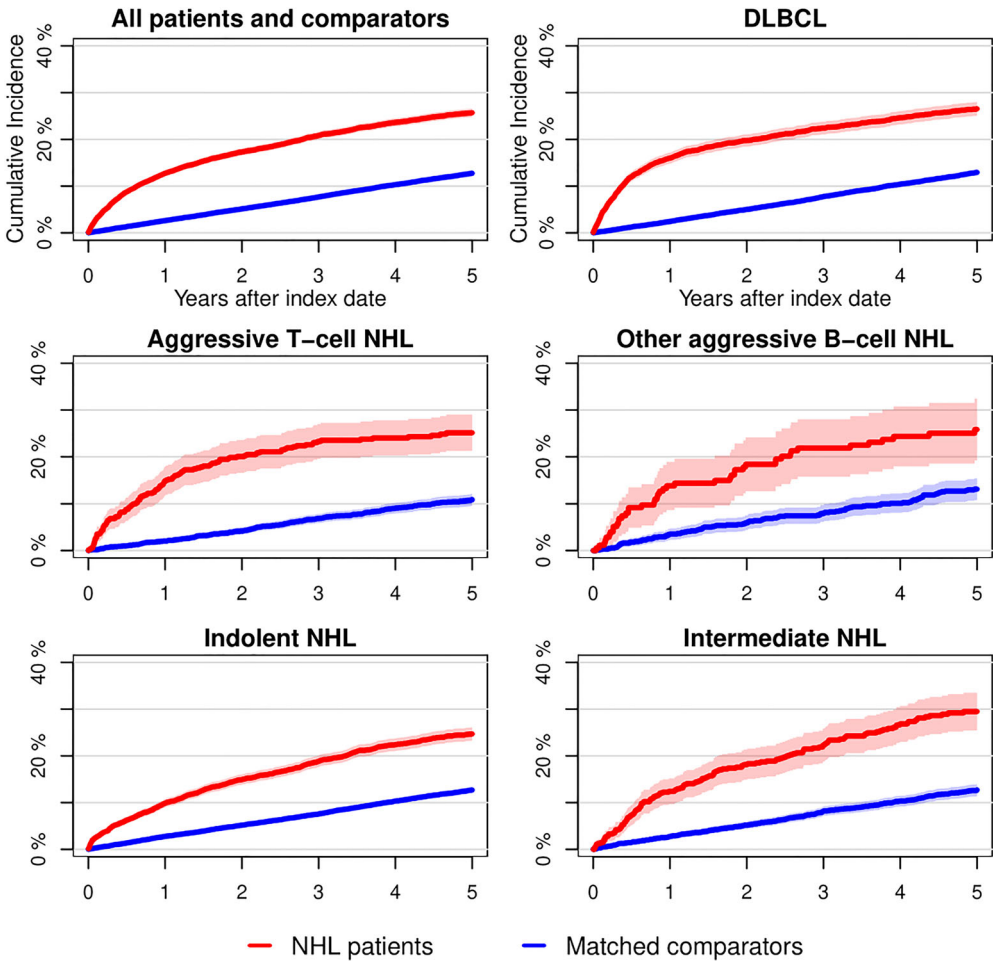

FIGURE 1 Cumulative incidence plots of time to first prescription of any psychotropic drug (PD, antidepressants, antipsychotics, anxiolytics) stratified by non-Hodgkin lymphoma (NHL) patients and the matched cohort. Gray's test was used to investigate difference between cumulated incidences for NHL patients and the background population. For all, the cumulative incidence of time to first PD prescription was significantly higher in NHL patients as compared to the matched comparators [Color figure can be viewed at wileyonlinelibrary.com]

3.2 | PD use overall and relative to the matched comparators

The overall two-year cumulative risk of incident PD prescriptions was 16.4% (95% CI 15.7%–17.2%) for NHL patients and 5.1% (95% CI 4.9%–5.3%, $p < .01$) for the matched comparators (Figure 1). Within the group of lymphoma patients, DLBCL-, aggressive T-cell NHL-, and other aggressive B-cell NHL patients had the highest two-year cumulative incidences (19.7%, 19.9%, and 18.4%, respectively, Figure 1), whereas the lowest two-year cumulative incidence was observed for indolent NHL patients (13.1%). For all subtypes of NHLs, the cumulative incidence was significantly higher than the matched comparator group (absolute difference in two-year risk in the range 8.2%–15.7%, the lowest being observed for indolent NHL patients and the highest being observed for aggressive T-cell NHL patients). The significant differences were verified in Cox regression analyses (Table 2, Table S3). Results were robust in a sensitivity analysis where PD use was defined as at least two prescriptions of PD (Figure S2).

Additional analyses in which both NHL patients and matched comparators could receive PDs prior to inclusion were performed to investigate when prescription rate among patients departed from comparators. These analyses showed that the increase in prescriptions rate occurred in the months following the diagnosis date for all subtypes of NHL (Figure S3).

The most commonly used PDs in NHL subtypes were antidepressants (two-year cumulative incidence, 9.0%, 95% CI 8.4–9.6) and anxiolytics (8.9%, 95% CI 8.3–9.4), whereas antipsychotics were less commonly prescribed (2.7%, 95% CI 2.3–3.0) (Figures S4–S6. The two-year cumulative risk of incident hypnotics use was 24.1% (95% CI 23.2%–25.1%) as compared to 7.9% (95% CI 7.6%–8.1%) within the matched comparators (Figure S7). Analyses of the association between PD use and patient characteristics comparing NHL patients with their matched comparators were conducted using Cox-proportional hazards regression in which follow-up was limited to 2 years. HRs with 95% CIs and P-values are presented in Tables 2 and S3. All subtypes of NHL showed higher risk of PD prescriptions as compared to the matched comparators for all variables investigated.

3.3 | Risk factors for PD use among lymphoma patients

Cox-proportional hazards regression analyses were performed to investigate clinical risk factors within the NHL patients (Tables 3 and

TABLE 2 Cox regression analysis of the association between use of psychotropic drugs (PDs) in non-Hodgkin lymphoma (NHL) patients and demographic variables relative to the matched comparators (reference)

	DLBCL		Indolent NHL	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Overall	2.32 (2.2–2.5)	<.01*	1.89 (1.8–2.0)	<.01*
Age				
18–45 years	2.13 (1.7–2.7)	<.01*	1.74 (1.3–2.3)	<.01*
46–70 years	2.83 (2.6–3.1)	<.01*	2.10 (1.9–2.3)	<.01*
≥71 years	2.13 (1.9–2.4)	<.01*	1.80 (1.6–2.0)	<.01*
Sex				
Females	2.33 (2.1–2.6)	<.01*	1.86 (1.7–2.1)	<.01*
Males	2.33 (2.1–2.6)	<.01*	1.93 (1.8–2.1)	<.01*
Charlson Comorbidity Index				
0	2.32 (2.2–2.5)	<.01*	1.89 (1.8–2.0)	<.01*
≥1	2.32 (2.1–2.5)	<.01*	1.80 (1.7–2.0)	<.01*
Educational level (ISCED)				
Primary education	2.39 (2.2–2.6)	<.01*	1.92 (1.8–2.0)	<.01*
Secondary/tertiary education	2.36 (2.2–2.5)	<.01*	1.91 (1.8–2.1)	<.01*
Country of origin				
Danish	2.33 (2.2–2.5)	<.01*	1.92 (1.8–2.1)	<.01*
Western country	2.72 (1.8–4.1)	<.01*	1.46 (1.0–2.2)	.07
Nonwestern country	1.77 (1.1–2.8)	.01*	1.45 (0.9–2.4)	.14
Civil status				
Married	2.35 (2.2–2.5)	<.01*	1.90 (1.8–2.0)	<.01*
Divorced	2.43 (2.2–2.5)	<.01*	1.85 (1.7–2.0)	<.01*
Widowed	2.40 (2.2–2.7)	<.01*	1.75 (1.6–1.9)	<.01*

Abbreviations: DLBCL, diffuse large B-cell lymphoma; HR, hazard ratio; ISCED, International Standard Classification of Education; NHL, non-Hodgkin lymphoma; PDs, psychotropic drugs.
*Statistically significant (*p*-value < .05).

S4). For most NHL subtypes, the risk for PD prescriptions was higher in patients >70 years, CCI ≥1, ECOG performance score >1, and higher IPI-score (for aggressive lymphomas). On the contrary, higher educational level was associated with lower risk of PD prescriptions.

3.4 | Use of PDs use in NHL patients after relapse

In total, 1861 (20.0%) NHL patients experienced relapse after treatment during follow-up. Indolent NHL (699, 17.6%), DLBCL (798, 22.5.%), and intermediate NHL patients (178, 32.7%) had the highest numbers of relapses. In addition, 793 (20.0%) indolent NHL patients who were managed initially by watchful waiting experienced progression. NHL patients with relapse/progression had higher two-year cumulative use of PD compared to the matched comparators. Patients with relapsed DLBCL (two-year cumulative incidence for PD use 20.8%), aggressive T-cell NHL (25.0%), and other aggressive B-cell NHL (26.3%) showed the highest two-year cumulative incidence of PD use. Moreover, the cumulative incidence of PD prescriptions rose at the time of relapse for all NHL types by visual inspection of the plots (Figure S8).

Following relapse, a total of 1080 NHL patients died (58.4%). During the last 12 months prior to death, the cumulative incidence of PD use was high among all subtypes of NHL (overall 36%, range 32.2%–40.4% according to subtype, not presented).

3.5 | Normalization of PD as a function of time

The time effect on incident PD use was investigated. Results showed elevated one-year risk of incident PD use across all subtypes of NHL as compared to the matched comparators; however, the risk decreased as time elapsed from diagnosis (Figure 2). After 5 years, the risk of incident PD use in NHL patients was similar to that of the matched comparators for all NHL subtypes except for indolent NHL patients. Among patients with indolent NHL, the PD prescription rate remained elevated after 5 years.

3.6 | Incidence of other mental health complications

The two-year cumulative risk of psychiatric hospital admissions/out-patient visits and completed suicide/intentional self-harm are shown in Figures 3 and 4. For psychiatric hospital admissions/out-patient

TABLE 3 Cox-regression analysis of the association between use of psychotropic drugs (PDs) and clinicopathological variables in non-Hodgkin lymphoma (NHL) patients

	DLBCL		Indolent NHL	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Age				
18–45 years	1.0 (Ref)		1.0 (Ref)	
46–70 years	1.42 (1.1–1.8)	<.01*	1.09 (0.8–1.4)	.52
≥71 years	1.99 (1.6–2.5)	<.01*	1.86 (1.4–2.4)	<.01*
Sex				
Females	1.0 (Ref)		1.0 (Ref)	
Males	0.82 (0.7–0.9)	<.01*	0.84 (0.8–1.0)	<.01*
Charlson Comorbidity Index				
0	1.0 (Ref)		1.0 (Ref)	
≥1	1.41 (1.2–1.6)	<.01*	1.37 (1.2–1.6)	<.01*
Educational level (ISCED)				
Primary education	1.0 (Ref)		1.0 (Ref)	
Secondary/tertiary education	0.83 (0.7–0.9)	<.01*	0.73 (0.7–0.8)	<.01*
Country of origin				
Danish	1.0 (Ref)		1.0 (Ref)	
Western country	1.04 (0.7–1.5)	.84	0.83 (0.6–1.2)	.32
Nonwestern country	0.76 (0.5–1.1)	.17	0.89 (0.6–1.3)	.57
Civil status				
Married	1.0 (Ref)		1.0 (Ref)	
Divorced	1.17 (1.0–1.4)	.12	1.14 (1.0–1.4)	.17
Widowed	1.36 (1.1–1.6)	<.01*	1.44 (1.2–1.7)	<.01*
ECOG performance status				
0	1.0 (Ref)		1.0 (Ref)	
1–4	1.71 (1.5–2.0)	<.01*	1.71 (1.5–1.9)	<.01*
Disease stage				
Limited stage (I-II)	1.0 (Ref)		1.0 (Ref)	
Advanced stage (III-IV)	1.20 (1.1–1.4)	<.01*	1.15 (1.0–1.3)	.05*
B-symptoms at diagnosis				
Yes	1.0 (Ref)		1.0 (Ref)	
No	0.89 (0.8–1.0)	.07	0.81 (0.7–0.9)	<.01*
LDH level above normal threshold				
No	1.0 (Ref)		1.0 (Ref)	
Yes	1.18 (1.0–1.3)	<.01*	1.01 (0.9–1.2)	.93
Planned treatment				
Yes	1.0 (Ref)		1.0 (Ref)	
Wait-and-watch	1.2 (0.9–1.6)	.21	0.79 (0.7–0.9)	<.01*
IPI-score				
Low	1.0 (Ref)		1.0 (Ref)	
Low intermediate	1.33 (1.1–1.6)	<.01*	1.29 (1.1–1.5)	<.01*
High intermediate	1.41 (1.2–1.7)	<.01*	1.34 (1.1–1.6)	<.01*
High	1.68 (1.4–2.0)	<.01*	2.54 (1.8–3.5)	<.01*
FLIPI-score				
Low	1.0 (Ref)		1.0 (Ref)	

TABLE 3 (Continued)

	DLBCL		Indolent NHL	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Intermediate	-	-	1.13 (0.9–1.5)	.36
High	-	-	1.74 (1.4–2.2)	<.01*

Abbreviations: DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; FLIPI, Follicular Lymphoma International Prognostic Index; HR, hazard ratio; IPI, International Prognostic Index; ISCED, International Standard Classification of Education; LDH, lactate dehydrogenase; NHL, non-Hodgkin lymphoma; PDs, psychotropic drugs.
*Statistically significant (*p*-value < .05).

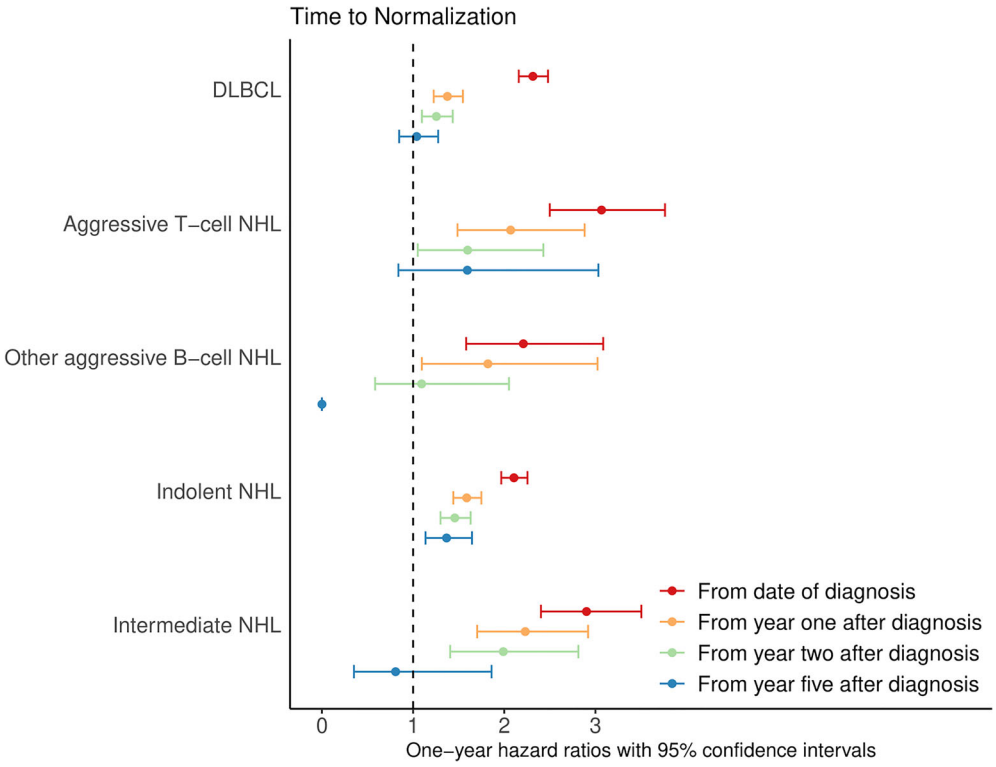

FIGURE 2 One-year hazard ratios (HRs) with matched comparators as reference group identified using Cox proportional hazard regression analysis for all subtypes of non-Hodgkin lymphoma (NHL). The HRs are calculated from index date and later time points (every year after index date, at which NHL patients still alive without relapse and without any prescription of PDs were rematched by age and sex to the Danish background population) [Color figure can be viewed at wileyonlinelibrary.com]

visits, there were no statistically significant difference in two-year cumulative incidences for any type of NHL patients (range 0.9%–2.0%) as compared to the matched comparators (range 0.6%–0.9%, Figure 3).

Completed suicide and intentional self-harm were investigated for the total NHL population due to small numbers. NHL patients had a significantly higher two-year cumulative incidence of completed suicide and intentional self-harm (0.3%, 95% CI 0.2–0.5; Figure 4) as compared to the matched comparators (0.2%, 95% CI 0.1–0.2, $p = .01$), although absolute risk increase was minimal. A Cox regression analysis comparing NHL patients with the matched comparators showed consistent results (HR 1.64, 95% CI 1.30–2.10, *p*-value < .001).

4 | DISCUSSION

This nationwide matched cohort study demonstrated that PD treatments and hospital-based psychiatric treatment as a measure of mental health complications were more common in Danish NHL patients than in the Danish background population. The two-year cumulative incidences were high for all subtypes of NHL, especially for the more aggressive subtypes. Moreover, cumulative incidence plots revealed a sharp increase during the first 6 months following index date for aggressive NHL subtypes, whereas the increase in PD use for indolent and intermediate NHL patients occurred in a more protracted fashion (Figure 1). Interestingly, risk of incident PD use normalized over time for aggressive NHL patients, but not for indolent NHL patients, where risk of incident PD use remained higher throughout the observation period (5 years). The risk of incident PD use was particularly high for patients older than 70 years, high CCI, high ECOG performance score, high IPI-score, and low educational status. PD use was high for patients with relapsed NHL and in the last 12 months of life for deceased patients. Contacts to Danish psychiatric hospitals were not more frequent than in the background population, but there was a small increase in completed suicide and intentional self-harm among NHL patients.

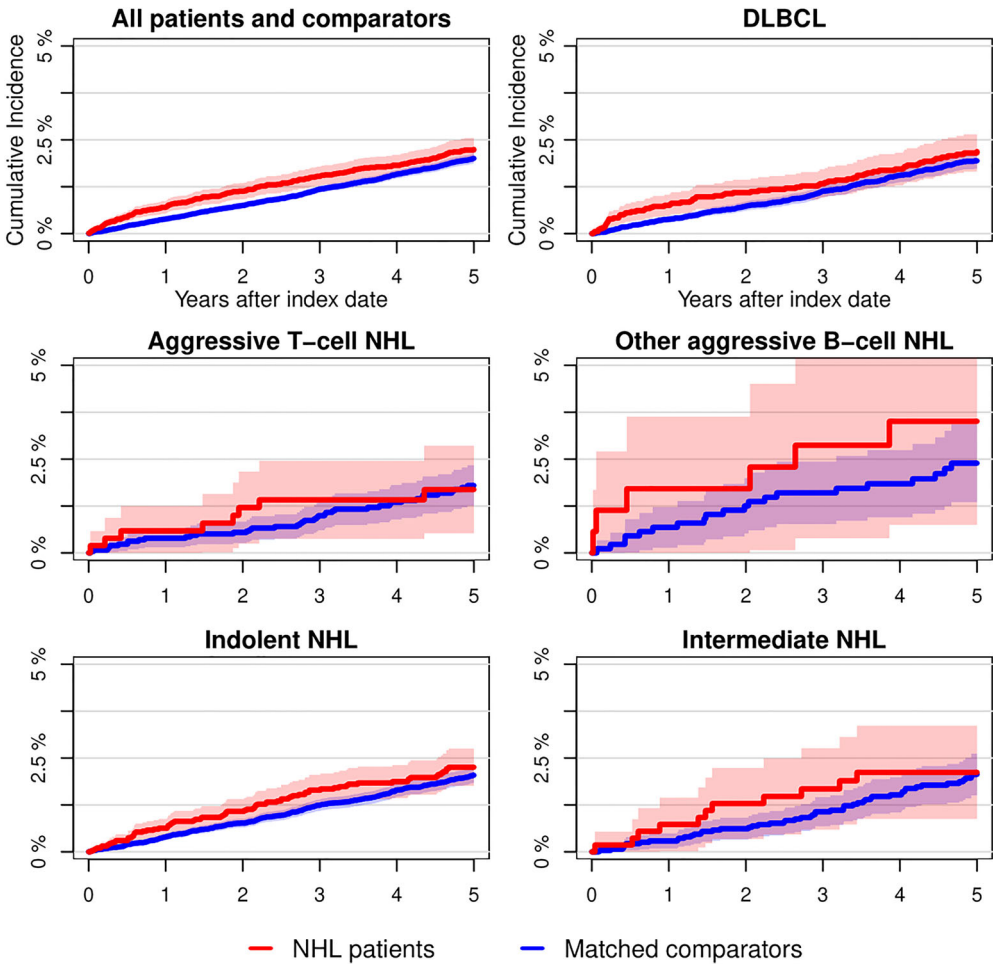

FIGURE 3 Cumulative incidence plots of time to first hospitalization/out-patient visit at a Danish psychiatric hospital stratified by non-Hodgkin lymphoma (NHL) patients and the matched cohort. Gray's test was used to investigate difference between cumulated incidences for NHL patients and the background population. The cumulative incidence of time to first PD prescription was not significantly different for any NHL patient type as compared to the matched comparators [Color figure can be viewed at wileyonlinelibrary.com]

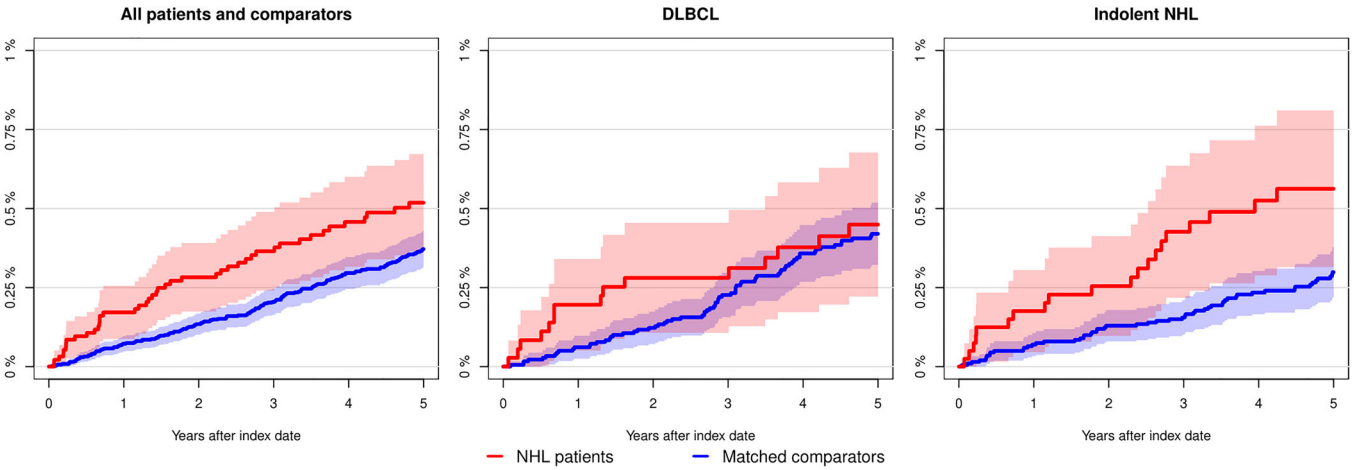

FIGURE 4 Cumulative incidence plots of time to first incident of intentional self-harm or completed suicide stratified by non-Hodgkin lymphoma (NHL) patients and the matched cohort. Gray's test was used to investigate difference between cumulated incidences for NHL patients and the background population. The cumulative incidence of time to first PD prescription were not significantly different for any NHL patient type as compared to the matched comparators [Color figure can be viewed at wileyonlinelibrary.com]

Conte et al. investigated the incidence of depression and anxiety using an approach similar to that of the present study with incident use of PDs as measures for depression and anxiety.[13] In total, 745 NHL patients (mean age 65.1 years, male:female ratio 1.4) were included, and incident PD use was estimated during first 8 months after diagnosis. In total, 31.5% of the NHL patients had at

least one prescription of PDs during follow-up most frequently anxiolytics and hypnotics and 20.8% received at least two prescriptions of any PD at the end of follow-up. While the results resembled those of the present study, type of NHL was only grouped aggregated into follicular lymphoma (FL) and non-FL, rendering subtype comparison between studies difficult. Several other studies have investigated the incidence of depression and anxiety in lymphoma patients in general or in NHL patients as a group, mainly through questionnaires.[6,28–31] All studies demonstrated a high risk of depression (range 17%–47%) and anxiety (range 16%–47%), which were comparable to our findings.

Cancer-related stress and mental health complications may consequently result in attempting suicide for some patients. This has been reported more prevalent in cancer patients with more aggressive and severe types of cancers (e.g., lymphoma, lung, and head and neck).[32] Mohammadi et al. investigated the risk of suicide attempts in 30 705 Swedish patients with NHL, Hodgkin lymphoma, and chronic lymphocytic leukemia.[33] In total, 105 lymphoma patients attempted suicide of which 43 patients completed suicide corresponding to incidences of 6.49 and 2.65/10 000 person years respectively, significantly higher than what was observed in cancer-free comparators (1.25 and 1.44/10 000 person years, respectively). Even though completed suicide is a rare cause of death, our results demonstrate a significantly higher risk of intentional self-harm and completed suicide among NHL patients using the DK algorithm.[21,22] Our findings suggest that the risk of suicide was higher in indolent NHL patients as compared to DLBCL patients using the DK algorithm. The algorithm has previously been validated by Gasse et al.,[21] in which, the positive predictive value of a register based approach compared to review of individual patient records as goal standard was 51.5% (95% CI 46.4%–56.7%). This is an important shortcoming in data when interpreting the results regarding suicide.

A major strength of this study is the use of nationwide population-based administrative registries, which have high coverage, completeness, and quality. Data in the registries are collected prospectively independent of this study which eliminates recall bias. An additional strength of this study is the near-to-complete follow-up on all patients. Study limitations include the use of PDs as proxy for mental health complications and not actual diagnosis, but the diagnosis cannot be retrieved from prescription data. Thus, it cannot be excluded that PD therapies could have been initiated against other conditions, such as treatment for chronic pain and other conditions. However, in our clinical experience, neuropathic pain in NHL survivors that require antidepressant is rare. Secondly, in this study, we defined PD use as the first prescription of any PD, but one prescription is typically not enough to treat mental health problems, and the study cannot distinguish between use in these diseases and short-term stress disorders. To account for this limitation, we conducted a sensitivity analysis, in which PD use were defined as having at least two prescriptions of PDs, and results were consistent. Nevertheless, stress disorders may account for a significant proportion of PD use in our cohort, as a cancer diagnosis has a significant impact on life and mental health as shown by occurrence of adjustment disorders being treated with antidepressants.[34] Thirdly, we were not able to capture psychological distress that are not treated with PD, such as the cases managed with psychotherapy alone.[35] Lastly, surveillance bias can be present in this study as the NHL diagnosis would, per se, be associated with more frequent visits to physicians. This could potentially increase the rate of PD prescriptions in the NHL patients more than comparators simply because of more frequent counseling. Finally, not all relapses are captured in LYFO, and therefore, the number of patients with relapsed NHL in the analyses may be too low. However, the capture of relapsed NHL would not be related to PD prescriptions, and therefore, the reported rates would not be affected by underreporting of relapse, especially in indolent NHLs.

In conclusion, the present study shows a significant impact on mental health after diagnosis of NHL, which is likely caused by the distress associated with uncertainties related to a new cancer diagnosis as well as the physical stress associated with subsequent treatment thereof. After some years, patients with aggressive NHLs have similar risk of PD prescription as the background population suggesting that a large fraction of the patients overcome the distress likely because many of these patients either die or are cured from their malignancy. In contrast, patients with indolent NHL remain at higher risk, possibly reflecting the relapsing and remitting nature of these lymphomas. The results underline that focus on mental health in NHL patients is important to maximize quality of life of the patients and address mental health problems that can be treated.

CONFLICT OF INTEREST

AKØ: Covered travel expenses from Pfizer and AbbVie. TCEG: Previous employment by Roche Ltd, Basel, speakers fee Abbvie. KK: Reported speaker's honoraria from Novartis, unrelated to this work. REN: Reported receiving research grants from H. Lundbeck and Otsuka Pharmaceuticals for clinical trials, receiving speaking fees from Bristol-Myers Squibb, Astra Zeneca, Janssen & Cilag, Lundbeck, Servier, Otsuka Pharmaceuticals, Teva A/S, and Eli Lilly and has acted as advisor to Astra Zeneca, Eli Lilly, Lundbeck, Otsuka Pharmaceuticals, Takeda, and Medivir, and being an investigator for Janssen-Cilag, Lundbeck, Boehringer, Compass, and Sage. HF: Received research grants outside this work from Alexion, Gilead, Abbvie, Janssen Pharmaceuticals, and Novartis. PB: Advisor for BMS, Takeda, Roche, Novartis and Incyte. JMJ: Roche, Gilead, Novartis, BMS: Advisory board, not related to this work. RBDS: Travel expenses from Takeda. MRC: Received speaking fee from Janssen, travel grant from Roche and Gilead. Participated in advisory boards for Abbvie and Janssen. All outside this work.

AUTHOR CONTRIBUTIONS

Conception and design: Andreas Kiesbye Øvlisen, Lasse Hjort Jakobsen, Marianne Tang Severinsen, and Tarec Christoffer El-Galaly.

Collection and assembly of data: Andreas Kiesbye Øvlisen, Lasse Hjort Jakobsen, Marianne Tang Severinsen, Tarec Christoffer El-Galaly, Peter de Nully Brown, Rasmus Bo Dahl-Sørensen, Henrik Frederiksen, Pär Lars Josefsson, Ahmed Ludvigsen Al-Mashhadi, Andriette Dessau-Arp, Michael Roost Clausen, Robert Schou Pedersen, and Judit Mészáros Jørgensen. *Data analysis and interpretation*: Andreas Kiesbye Øvlisen, Lasse Hjort Jakobsen, Marianne Tang Severinsen, and Tarec Christoffer El-Galaly. *Interpretation*: All authors. *Manuscript writing, first draft*: AKØ. *Revision of manuscript*: All authors. *Final approval of manuscript*: All authors. *Accountable for all aspects of the work*: All authors.

DATA AVAILABILITY STATEMENT

Research data are not shared, as export of data from Statistics Denmark is not allowed.

ORCID

Andreas Kiesbye Øvlisen https://orcid.org/0000-0002-4631-9936
Lasse Hjort Jakobsen https://orcid.org/0000-0001-6575-7686
Henrik Frederiksen https://orcid.org/0000-0001-8905-0220
Ahmed Ludvigsen Al-Mashhadi https://orcid.org/0000-0002-8739-0421
Marianne Tang Severinsen https://orcid.org/0000-0003-0996-1812

REFERENCES

1. Herschbach P, Book K, Brandl T, et al. Psychological distress in cancer patients assessed with an expert rating scale. *Br J Cancer*. 2008;99(1):37-43.
2. Herschbach P, Keller M, Knight L, et al. Psychological problems of cancer patients: a cancer distress screening with a cancer-specific questionnaire. *Br J Cancer*. 2004;91(3):504-511.
3. Gonen G, Kaymak SU, Cankurtaran S, Karslioglu H, Ozalp E, Soygur H. The factors contributing to death anxiety in cancer patients. *J Psychosoc Oncol*. 2012;30(3):347-358.
4. Carlson LE, Angen M, Cullum J, et al. High levels of untreated distress and fatigue in cancer patients. *Br J Cancer*. 2004;90(12):2297-2304.
5. Pinquart M, Duberstein PR. Depression and cancer mortality: a meta-analysis. *Psychol Med*. 2010;40(11):1797-1810.
6. Linden W, Vodermaier A, MacKenzie R, Greig D. Anxiety and depression after cancer diagnosis: prevalence rates by cancer type, gender, and age. *J Affect Disord*. 2012;141(2–3):343-351. doi:10.1016/j.jad.2012.03.025
7. Hinz A, Krauss O, Hauss JP, et al. Anxiety and depression in cancer patients compared with the general population. *Eur J Cancer Care (Engl)*. 2010;19(4):522-529.
8. Ng CG, Boks MPM, Zainal NZ, De Wit NJ. The prevalence and pharmacotherapy of depression in cancer patients. *J Affect Disord*. 2011;131(1–3):1-7. doi:10.1016/j.jad.2010.07.034
9. Armitage JO, Gascoyne RD, Lunning MA, Cavalli F. Non-Hodgkin lymphoma. *Lancet*. 2017;390:298-310.
10. Shankland KR, Armitage JO, Hancock BW. Non-Hodgkin lymphoma. *Lancet*. 2012;380:848-857.
11. Jakobsen LH, Bøgsted M, Brown PDN, et al. Minimal loss of lifetime for patients with diffuse large B-cell lymphoma in remission and event free 24 months after treatment: a Danish population-based study. *J Clin Oncol*. 2017;35(7):778-784.
12. Øvlisen AK, Jakobsen LH, Kragholm KH, Nielsen RE, Hutchings M, et al. Depression and anxiety in Hodgkin lymphoma patients: a Danish nationwide cohort study of 945 patients. *Cancer Med*. 2020;9:4395-4404.
13. Conte C, Rueter M, Laurent G, Bourrel R, Lapeyre-Mestre M, Despas F. Psychotropic drug initiation during the first diagnosis and the active treatment phase of B cell non-Hodgkin's lymphoma: a cohort study of the French national health insurance database. *Support Care Cancer*. 2016;24(11):4791-4799.
14. Arboe B, El-Galaly TC, Clausen MR, et al. The Danish National Lymphoma Registry: coverage and data quality. *PLoS One*. 2016;11(6):e0157999.
15. Schmidt M, Pedersen L, Sørensen HT. The Danish Civil Registration System as a tool in epidemiology. *Eur J Epidemiol*. 2014;29(8):541-549.
16. Pedersen CB, Gøtzsche H, Møller JO, Mortensen PB. The Danish Civil Registration System. A cohort of eight million persons. *Dan Med Bull*. 2006;53(4):441-449.
17. Pedersen CB. The Danish civil registration system. *Scand J Public Health*. 2011;39(7):22-25.
18. Schmidt M, Schmidt SAJ, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish National Patient Registry: a review of content, data quality, and research potential. *Clin Epidemiol*. 2015;7:449-490.
19. Thygesen SK, Christiansen CF, Christensen S, Lash TL, Sørensen HT. The predictive value of ICD-10 diagnostic coding used to assess Charlson comorbidity index conditions in the population-based Danish National Registry of Patients. *BMC Med Res Methodol*. 2011;11:83.
20. Quan H, Li B, Couris CM, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. *Am J Epidemiol*. 2011;173(6):676-682.
21. Gasse C, Danielsen AA, Pedersen MG, Pedersen CB, Mors O, Christensen J. Positive predictive value of a register-based algorithm using the Danish National Registries to identify suicidal events. *Pharmacoepidemiol Drug Saf*. 2018;27(10):1131-1138. doi:10.1002/pds.4433
22. Helweg-Larsen K, Kjøller K, Juel M, et al. Markant fald, men stigende antal selvmordsforsøg. Hvorfor? (Suicide in Denmark, significant decrease in suicide, but increasing suicide attempts. Why?); 2006.
23. Mors O, Perto GP, Mortensen PB. The Danish psychiatric central research register. *Scand J Public Health*. 2011;39(7):54-57.
24. Wallach Kildemoes H, Toft Sørensen H, Hallas J. The Danish National Prescription Registry. *Scand J Public Health*. 2011;39(7):38-41.
25. Pottegård A, Schmidt SAJ, Wallach-Kildemoes H, Sørensen HT, Hallas J, Schmidt M. Data resource profile: the Danish national prescription registry. *Int J Epidemiol*. 2017;46(3):798.
26. Jensen VM, Rasmussen AW. Danish education registers. *Scand J Public Health*. 2011;39(7):91-94.
27. Gray RJ. A class of K-sample tests for comparing the cumulative incidence of a competing risk. *Ann Stat*. 1988;16(3):1141-1154.
28. Vargas-Román K, Díaz-Rodríguez CL, Cañadas-De la Fuente GA, Gómez-Urquiza JL, Ariza T, De la Fuente-Solana EI. Anxiety prevalence in lymphoma: a systematic review and meta-analysis. *Health Psychol*. 2020;39(7):580-588.
29. Jensen RE, Arora NK, Bellizzi KM, et al. Health-related quality of life among survivors of aggressive non-Hodgkin lymphoma. *Cancer*. 2013;119(3):672-680.
30. Oerlemans S, Mols F, Nijziel MR, Zijlstra WP, Coebergh JWW, van de Poll-Franse LV. The course of anxiety and depression for patients with Hodgkin's lymphoma or diffuse large B cell lymphoma: a longitudinal study of the PROFILES registry. *J Cancer Surviv*. 2014;8(4):555-564.
31. Wang Y, Zou L, Jiang M, Wei Y, Jiang Y. Measurement of distress in Chinese inpatients with lymphoma. *Psychooncology*. 2013;22(7):1581-1586. doi:10.1002/pon.3170

32. Zaorsky NG, Zhang Y, Tuanquin L, Bluethmann SM, Park HS, Chinchilli VM. Suicide among cancer patients. *Nat Commun*. 2019; 10:207.
33. Mohammadi M, Moradi T, Bottai M, Reutfors J, Cao Y, Smedby KE. Risk and predictors of attempted and completed suicide in patients with hematological malignancies. *Psychooncology*. 2014;23(11):1276-1282. doi:10.1002/pon.3561
34. Mitchell AJ, Chan M, Bhatti H, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol*. 2011;12(2):160-174.
35. Sundhedsstyrelsen. Reference program for unipolar depression hos voksne [Internet]. 2007. Cited March 6, 2019. http://www.sst.dk

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Øvlisen AK, Jakobsen LH, Kragholm KH, et al. Mental health among patients with non-Hodgkin lymphoma: A Danish nationwide study of psychotropic drug use in 8750 patients and 43 750 matched comparators. *Am J Hematol*. 2022;97(6):749-761. doi:10.1002/ajh.26538