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RESEARCH ARTICLE

Trends in hematological cancer in the elderly in Denmark, 1980–2012

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ABSTRACT

Background The number of hematological malignancies is expected to increase as the Danish population ages within the next few decades. Despite this, data on the course of hematological cancers among the oldest patients are sparse with many intervention studies focusing on younger age groups. The aim of this study is to present Danish incidence and mortality rates among older patients with non-Hodgkin lymphomas (NHL), multiple myeloma (MM), chronic lymphocytic leukemia (CLL), and acute myeloid leukemia (AML).

Material and methods Nationwide population-based study presenting the incidence, prevalence and mortality rates of NHL, MM, and AML with a focus on the elderly population in Denmark during the last few decades. Data were drawn from the NORDCAN database.

Results Incidence rates of NHL, MM, CLL and AML were 10–50 times higher among the population aged 70 years or more than among the younger population. An increasing incidence with stable or decreased mortality rates was seen mainly among elderly patients with NHL during the last few decades, leading to increased survival and a greater prevalence of patients with NHL. Increased relative survival and prevalence could also be seen among elderly patients with MM and CLL, while the trends of the incidence rates were inconclusive for these diseases. Survival among patients with AML improved most notably in those aged below 70 years leading to an increased prevalence of AML patients predominantly in this age group.

Conclusion Improvements in diagnostics and treatment have led to increased survival and therefore prevalence of elderly patients with NHL, MM, CLL and AML during the past decades.

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The etiology of hematological malignancies remains largely unknown. It has, however, been shown that ionizing radiation and previous chemotherapy predisposes individuals to acute myeloid leukemia (AML) while immunosuppression has been linked to the development of lymphoma. The incidence of the majority of hematological malignancies increases with age, the only exceptions being acute lymphoblastic leukemia and Hodgkin's lymphoma [1]. Like many other populations [2,3], the Danish population is aging and an increasing number of older adults with hematological cancer is to be expected. Despite this, many intervention studies have focused on younger age groups [4] and often pooled the oldest age stratum of patients at 60–65 years or more [5]. Half of the patients with hematological cancer are older than 70 years at diagnosis [1] and thus the data on the course of hematological cancers among the oldest age groups are sparse. Treatment of the elderly is complicated by comorbidity as well as a higher risk of toxicity and mortality from treatment complications [6]. This is reflected in survival rates of hematological malignancies, which during the last decades have shown a substantially lower improvement in patients over the age of 55 compared with the younger population [7,8].

A recent study of 180 000 European patients with hematological lymphoid neoplasms demonstrated that the proportion with an unspecified lymphoma subtype diagnosis increased with age suggesting that the oldest age groups receive a suboptimal diagnostic workup and therefore treatment [9]. This emphasizes the need for data on incidence and prognosis among the oldest patients with hematological cancer. In this study, we report on nationwide Danish incidences and mortality rates among patients with AML, multiple myeloma (MM), non-Hodgkin lymphomas (NHL) and chronic lymphocytic leukemia (CLL) focusing on the elderly and oldest-old population. These four diagnostic groups represent the most incident and most prevalent hematological cancers among the elderly [10] and have been registered in the Danish Cancer Registry (DCR) for a long period of time [11].

Material and methods

The hematological cancer diagnoses are defined by their ICD-10 codes (NHL: C82-85, C96, MM: C90, CLL: C91.1, AML: C92.0 + C93.0 + C94.0 + C94.2 + C94.4-5). A more detailed description of the materials and methods appears elsewhere

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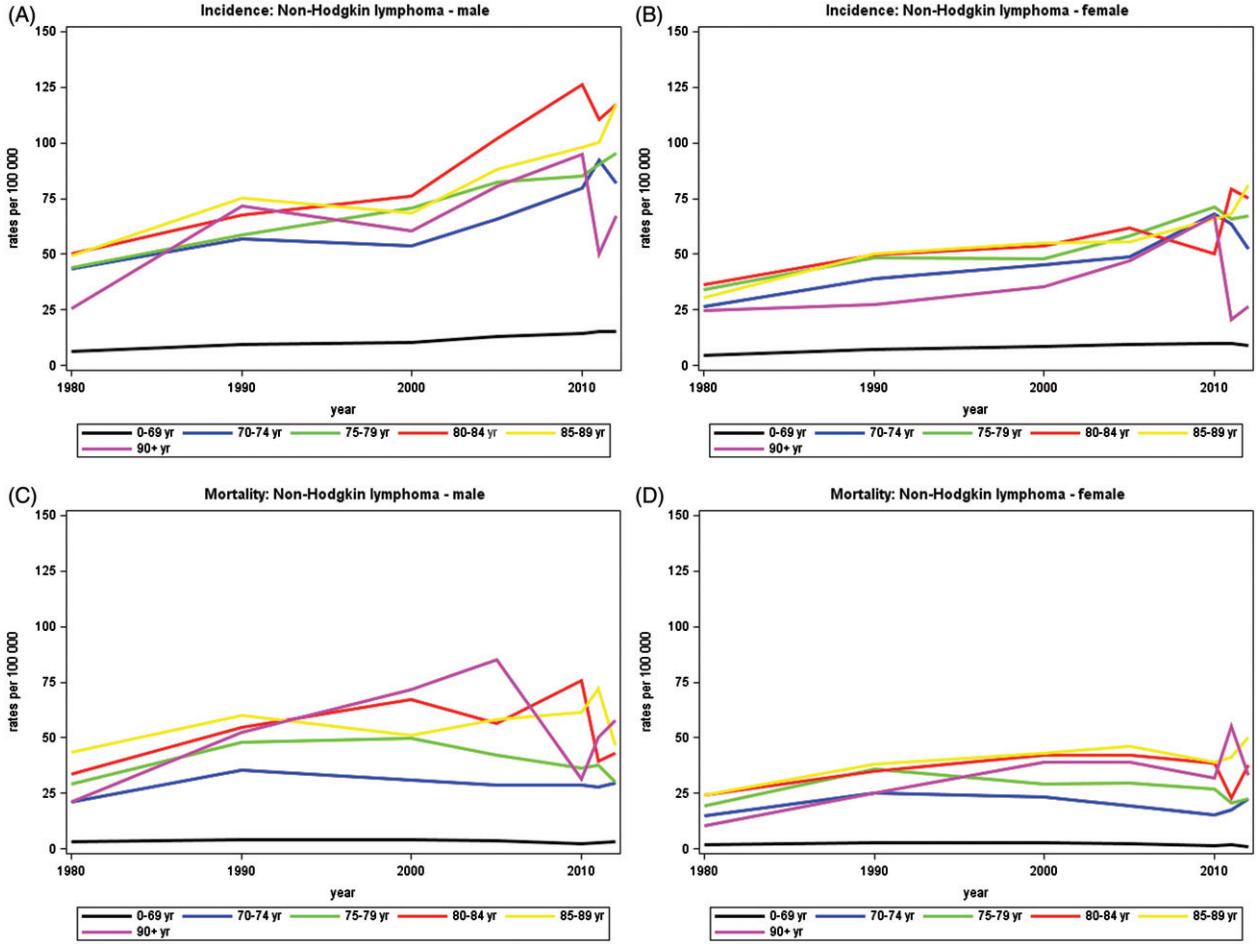

Figure 1. Trends in age- and sex-specific incidence and mortality of non-Hodgkin lymphoma in Denmark 1980–2012. The graphs depict rates per 100 000 person years.

[12]. In brief, data were derived from the NORDCAN database with comparable data on cancer incidence, mortality, prevalence and relative survival in the Nordic countries, where the Danish data are delivered from the DCR and the Danish Cause of Death Registry with follow-up for death or emigration until the end of 2013. This study focuses on the elderly population with age categorized as 0–69, 70–79, 80–89 and 90 + years.

For incidence and mortality, age group specific numbers and rates per 100 000 person years are shown in tables and graphs with calendar periods for time of diagnosis 1978–1982, 1988–1992, 1998–2002, 2003–2007, 2010, 2011 and 2012. Prevalence is defined as the number of cancer patients (including cured patients as well) with that specific diagnosis still alive and is shown in tables by the end of 1980, 1990, 2000, 2010, and 2012.

Sex- and age-specific one- and five-year relative survival proportion ratios were calculated for each of the diagnostic groups for the age groups 0–69, 70–79, 80–89 and 90 + years and for the five-year periods of diagnosis 1968–1972, 1973–1977, . . ., 2003–2007 and 2008–2012.

Relative survival for a group of cancer patients is calculated as the observed survival (where all causes of death are considered events) divided by the expected survival for a group from the Danish population with the same age and year of birth composition. Actuarial method is used for observed survival and Ederer II method for expected survival [13]. Relative survival can be interpreted as the survival if the cancer was the only cause of death. For the most recent period, 2008–2012, not all patients can be followed up for death in five years and we used hybrid methods where we supplement with survival experience from cancer patients diagnosed earlier years. Survival was not calculated for cancer groups with less than five patients [indicated by (-) in tables and blank in the graphs]. If all patients die in the follow-up period resulting in zero survival this is indicated as 0 (-) and if calculation for a cell results in a relative survival higher than 100% the result is shown in tables, but restricted to 100% in graphs.

Results

Non-Hodgkin lymphoma

NHLs constitute the most common hematological cancers and consist of a large group of diagnostic entities including both aggressive and indolent/chronic types of lymphoma. The incidence rates in 1980 were approximately 30–50 per 100 000 person years among the older population compared to 5 per 100 000 person years among the younger. A stable increase since 1980 that is slightly higher among men than women has been observed (Figure 1). From this figure it can be seen that the largest increase in incidence can be attributed mostly to patients above 69 years, where incidences increase at

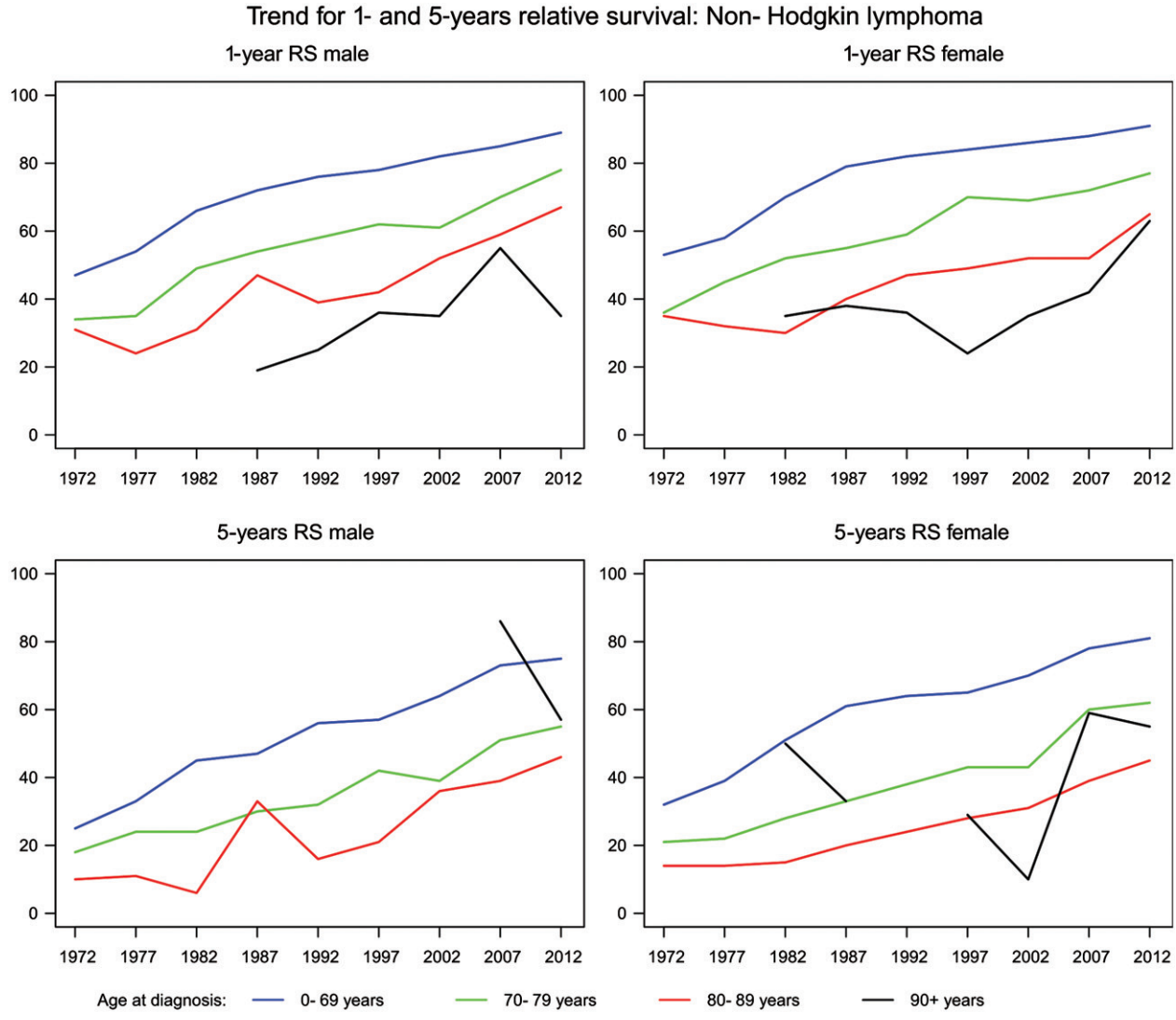

Figure 2. Trends in 1-year and 5-year age-specific relative survival in percent after non-Hodgkin lymphoma (NHL) in Denmark.

similar rates in the five age groups (Figure 1). In parallel, population mortality rates among lymphoma patients increased in the period up to 1990. After this time point mortality rates have been stable or decreased for most age groups, resulting in a widened gap between incidence and mortality rates (Figure 1).

The age-specific one- and five-year relative survival for NHL patients has increased in the same manner by 30–50 percent points across the 0–69, 70–79, 80–89 year age groups and in both sexes (Figure 2). The increasing incidence and improved survival has resulted in an increase in prevalent NHL patients by approximately a factor six from 1980 to 2012 (Table I).

Multiple myeloma

MM is a bone marrow malignancy with expansion of abnormal clonal plasma cells in the bone marrow. It is the second most common hematological malignancy in Denmark with 350 newly diagnosed patients every year. MM is an incurable disease with current treatment possibilities. During the study period incidence rates were approximately 20–30 per 100 000 person years among the older population compared to 2–3 per 100 000 person years among the younger (Figure 3). Due to the small number in each age group the incidence and the mortality rates fluctuated in the five oldest age groups revealing no clear sign of change since 1980 (Figure 3). Despite this, the one-year relative survival has shown a steady increase since 1968 and a more pronounced increase is seen in the five-year relative survival from 1993 for patients younger than 70 years (Figure 4). From 2003 the relative five-year survival improves both among the younger and older age groups (Figure 4). These survival improvements are reflected in the prevalence of patients with MM, which has increased from 1980 to 2012 by a factor 3–4 in almost all age groups (Table I).

Chronic lymphocytic leukemia

CLL is a chronic lymphoproliferative neoplasm with accumulation of functionally incompetent monoclonal mature B-cells. It is the most frequent leukemia with 250 new CLL patients diagnosed per year in Denmark. During the study period incidence rates were approximately 20–40 per 100 000 person years among the older population compared to 2–3 per 100 000 person years among the younger (Figure 5).

Table I. Trends in age- and sex-specific prevalences among patients with non-Hodgkin lymphoma, multiple myeloma, chronic lymphocytic leukemia and acute myeloid leukemia in Denmark 1980–2012. Numbers are persons alive with the respective diagnosis by 31 December in the listed calendar years, as well as percentages within each age group this year.

	Men – age groups below							Women – age groups below						
	0–69	70–74	75–79	80–84	85–89	90+	All ages	0–69	70–74	75–79	80–84	85–89	90+	All ages
Non-Hodgkin lymphoma														
1980	576 (68.3)	119 (14.1)	86 (10.2)	47 (5.6)	11 (1.3)	4 (0.5)	843 (100)	469 (61.7)	104 (13.7)	95 (12.5)	54 (7.1)	30 (3.9)	8 (1.1)	760 (100)
1990	1051 (68.2)	194 (12.6)	145 (9.4)	97 (6.3)	43 (2.8)	10 (0.6)	1540 (100)	844 (59.7)	198 (14.0)	181 (12.8)	118 (8.4)	56 (4.0)	16 (1.1)	1413 (100)
2000	1684 (68.2)	278 (11.3)	238 (9.6)	174 (7.0)	73 (3.0)	22 (0.9)	2469 (100)	1425 (60.9)	264 (11.3)	301 (12.9)	188 (8.0)	112 (4.8)	48 (2.1)	2338 (100)
2010	2819 (66.0)	545 (12.8)	403 (9.4)	310 (7.3)	137 (3.2)	56 (1.3)	4270 (100)	2098 (56.1)	528 (14.1)	456 (12.2)	306 (8.2)	246 (6.6)	105 (2.8)	3739 (100)
2012	3020 (63.0)	671 (14.0)	526 (11.0)	334 (7.0)	177 (3.7)	66 (1.4)	4794 (100)	2216 (54.0)	600 (14.6)	516 (12.6)	374 (9.1)	266 (6.5)	133 (3.2)	4105 (100)
Multiple myeloma														
1980	113 (53.1)	39 (18.3)	36 (16.9)	17 (8.0)	8 (3.8)	-	213 (100)	124 (53.9)	41 (17.8)	33 (14.3)	23 (10.0)	7 (3.0)	2 (0.9)	230 (100)
1990	164 (55.2)	54 (18.2)	49 (16.5)	16 (5.4)	14 (4.7)	-	297 (100)	144 (49.3)	47 (16.1)	48 (16.4)	32 (11.0)	18 (6.2)	3 (1.0)	292 (100)
2000	240 (58.4)	69 (16.8)	55 (13.4)	31 (7.5)	10 (2.4)	6 (1.5)	411 (100)	205 (48.6)	66 (15.6)	62 (14.7)	57 (13.5)	24 (5.7)	8 (1.9)	422 (100)
2010	445 (57.1)	135 (17.3)	81 (10.4)	72 (9.2)	40 (5.1)	6 (0.8)	779 (100)	359 (54.8)	100 (15.3)	81 (12.4)	69 (10.5)	35 (5.3)	11 (1.7)	655 (100)
2012	477 (56.1)	170 (20.0)	108 (12.7)	62 (7.3)	29 (3.4)	5 (0.6)	851 (100)	338 (50.0)	126 (18.6)	89 (13.2)	71 (10.5)	40 (5.9)	12 (1.8)	676 (100)
Chronic lymphocytic leukemia														
1980	220 (50.1)	93 (21.2)	62 (14.1)	43 (9.8)	16 (3.6)	5 (1.1)	439 (100)	154 (41.5)	68 (18.3)	83 (22.4)	39 (10.5)	21 (5.7)	6 (1.6)	371 (100)
1990	314 (44.0)	142 (19.9)	127 (17.8)	85 (11.9)	33 (4.6)	13 (1.8)	714 (100)	179 (32.3)	106 (19.1)	101 (18.2)	97 (17.5)	52 (9.4)	19 (3.4)	554 (100)
2000	476 (46.2)	177 (17.2)	171 (16.6)	131 (12.7)	55 (5.3)	20 (1.9)	1030 (100)	280 (33.0)	128 (15.1)	167 (19.7)	134 (15.8)	86 (10.1)	53 (6.3)	848 (100)
2010	656 (46.0)	259 (18.2)	220 (15.4)	171 (12.0)	87 (6.1)	32 (2.2)	1425 (100)	425 (37.1)	171 (14.9)	189 (16.5)	182 (15.9)	128 (11.2)	51 (4.5)	1146 (100)
2012	651 (44.0)	262 (17.7)	252 (17.0)	174 (11.8)	101 (6.8)	40 (2.7)	1480 (100)	421 (36.5)	172 (14.9)	199 (17.2)	175 (15.2)	132 (11.4)	55 (4.8)	1154 (100)
Acute myeloid leukemia														
1980	60 (78.9)	8 (10.5)	4 (5.3)	3 (3.9)	1 (1.3)	-	76 (100)	54 (67.5)	11 (13.8)	9 (11.3)	5 (6.3)	1 (1.3)	–	80 (100)
1990	119 (85.6)	15 (10.8)	2 (1.4)	3 (2.2)	-	-	139 (100)	118 (78.7)	11 (7.3)	10 (6.7)	8 (5.3)	3 (2.0)	–	150 (100)
2000	198 (84.3)	20 (8.5)	12 (5.1)	5 (2.1)	-	-	235 (100)	203 (80.9)	15 (6.0)	20 (8.0)	8 (3.2)	3 (1.2)	2 (0.8)	251 (100)
2010	301 (78.6)	33 (8.6)	27 (7.0)	16 (4.2)	4 (1.0)	2 (0.5)	383 (100)	305 (81.6)	20 (5.3)	28 (7.5)	13 (3.5)	7 (1.9)	1 (0.3)	374 (100)
2012	315 (78.6)	47 (11.7)	19 (4.7)	14 (3.5)	6 (1.5)	-	401 (100)	317 (80.7)	32 (8.1)	19 (4.8)	22 (5.6)	3 (0.8)	-	393 (100)

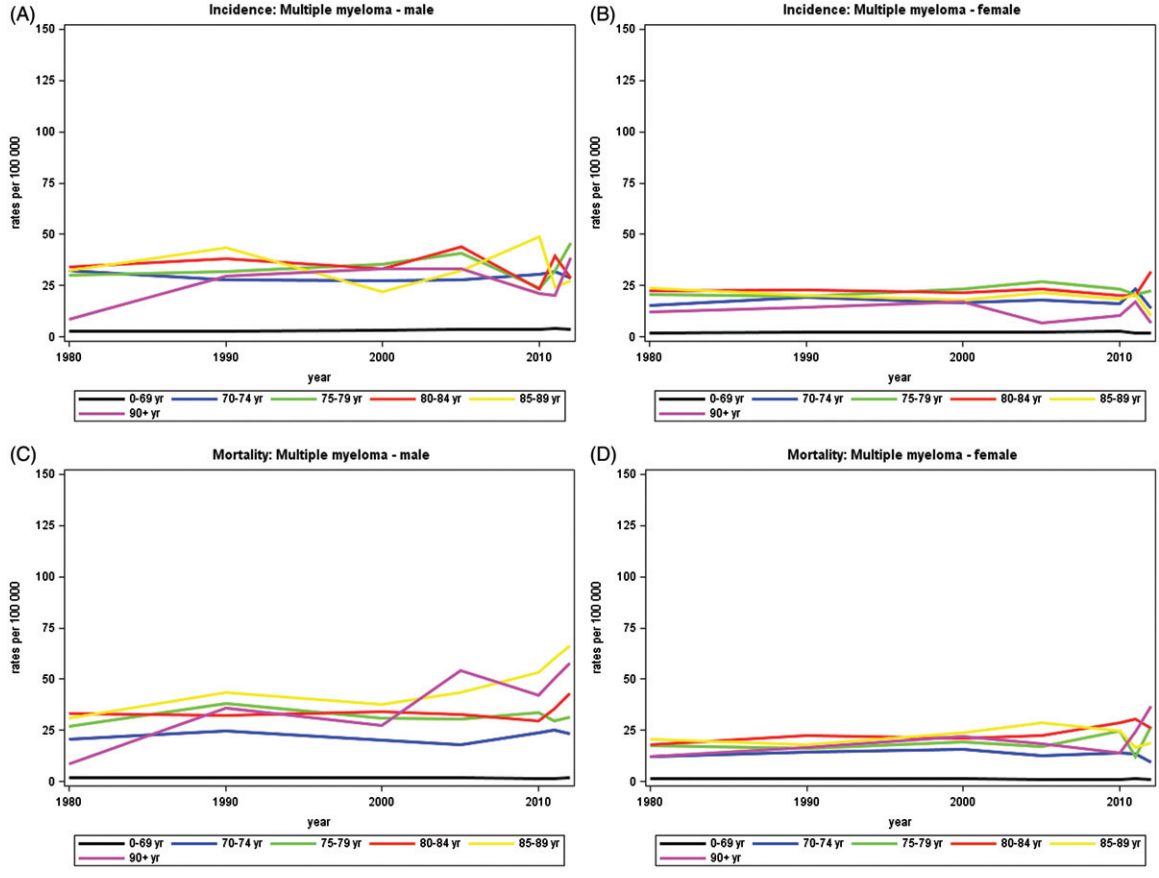

Figure 3. Trends in age- and sex-specific incidence and mortality of multiple myeloma in Denmark 1980–2012. The graphs depict rates per 100 000 person years.

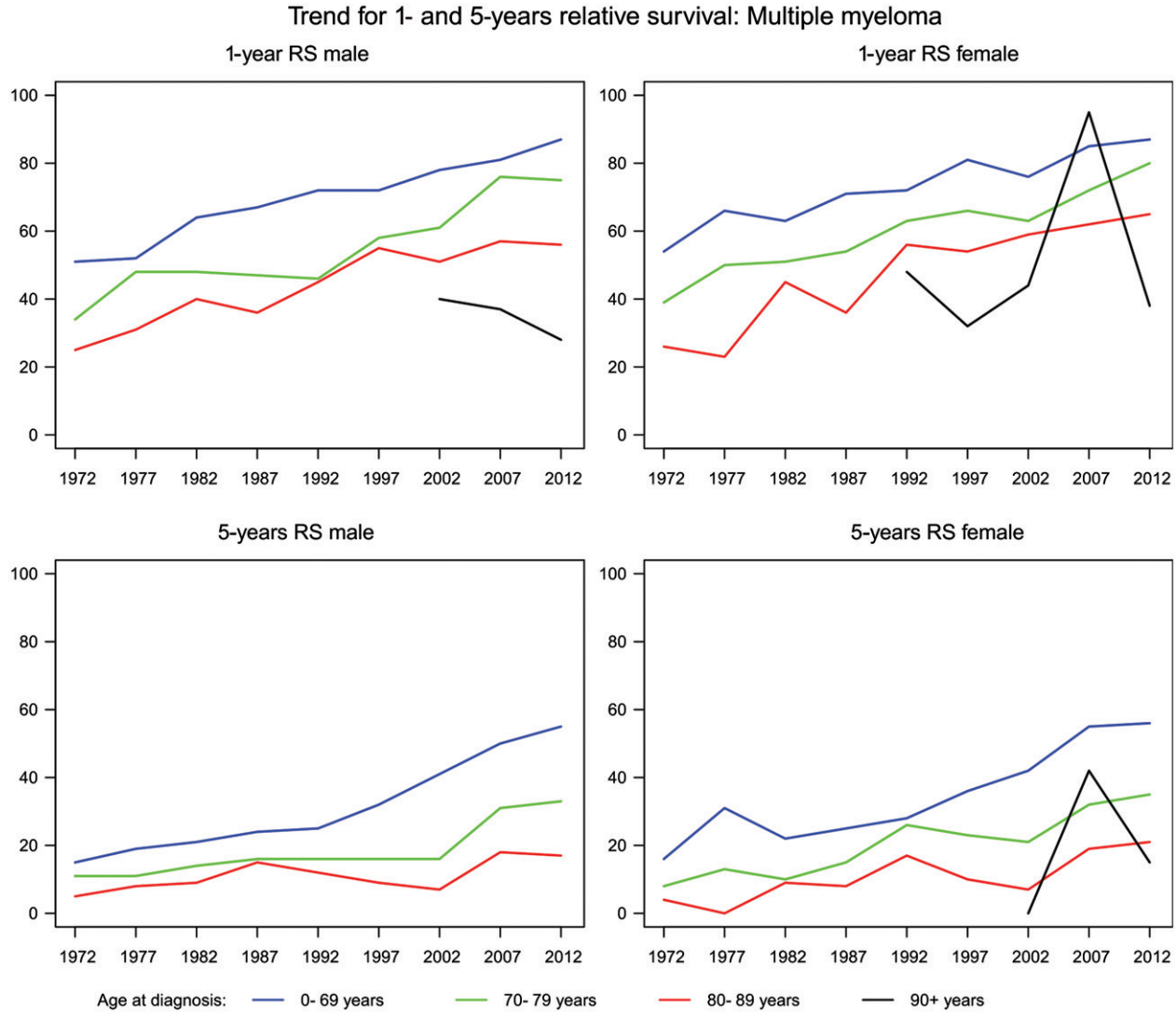

Figure 4. Trends in 1-year and 5-year age-specific relative survival in percent after multiple myeloma (MM) in Denmark.

From Figure 5 it can be seen that the incidence rates fluctuated in the five oldest age groups again reflecting small numbers in each group. Thus this figure reveals no clear evidence of changing incidence rates since 1980 (Figure 5). Similarly, mortality rates have remained constant throughout the study period (Figure 5).

The age-standardized one- and five-year relative survival for CLL patients has increased 30–50% percent points since 1968. The largest relative increase is observed in the age groups 70–79 and 80–89 years (Figure 6). In the most recent study period the one-year relative survival of patients aged 70–79 or 80–89 has reached the one-year relative survival level of patients below 70 years (Figure 6). These tendencies results in increasing CLL prevalence in the population which overall has increased by a factor 3 from 1980 to 2012

Acute myeloid leukemia

AML is a highly proliferative cancer derived from myeloid hematopoietic stem cells. Although among the most frequent types of leukemia only 200 new AML patients are diagnosed per year in Denmark. During the study period incidence rates were approximately 15–20 per 100 000 person years among the older population compared to 2–3 per 100 000 person years among the younger (Figure 7). Due to the small numbers in each age group incidence rates fluctuated in the five oldest groups with no evidence of changing incidence rates since 1980 (Figure 7). Likewise, this figure reveals no trend in mortality rates during the study period (Figure 7).

The age-standardized one-year relative survival for AML patients has increased approximately 40 percent points since 1968 among patients below 70 years (Figure 8), whereas among AML patients above 70 years the one-year relative survival has only increased 10% since 1968 (Figure 8). When examining the five-year relative survival, improvements over the past decades are observed only in patients below 70 years (Figure 8). In line with this, the prevalence of AML patients has increased by a factor 5 among patients below 70 years and a factor 2–5 for patients above this age (Table I).

Discussion

In this study we found that incidences of NHL, MM, CLL, or AML were at least 10 times higher among patients above 70 years

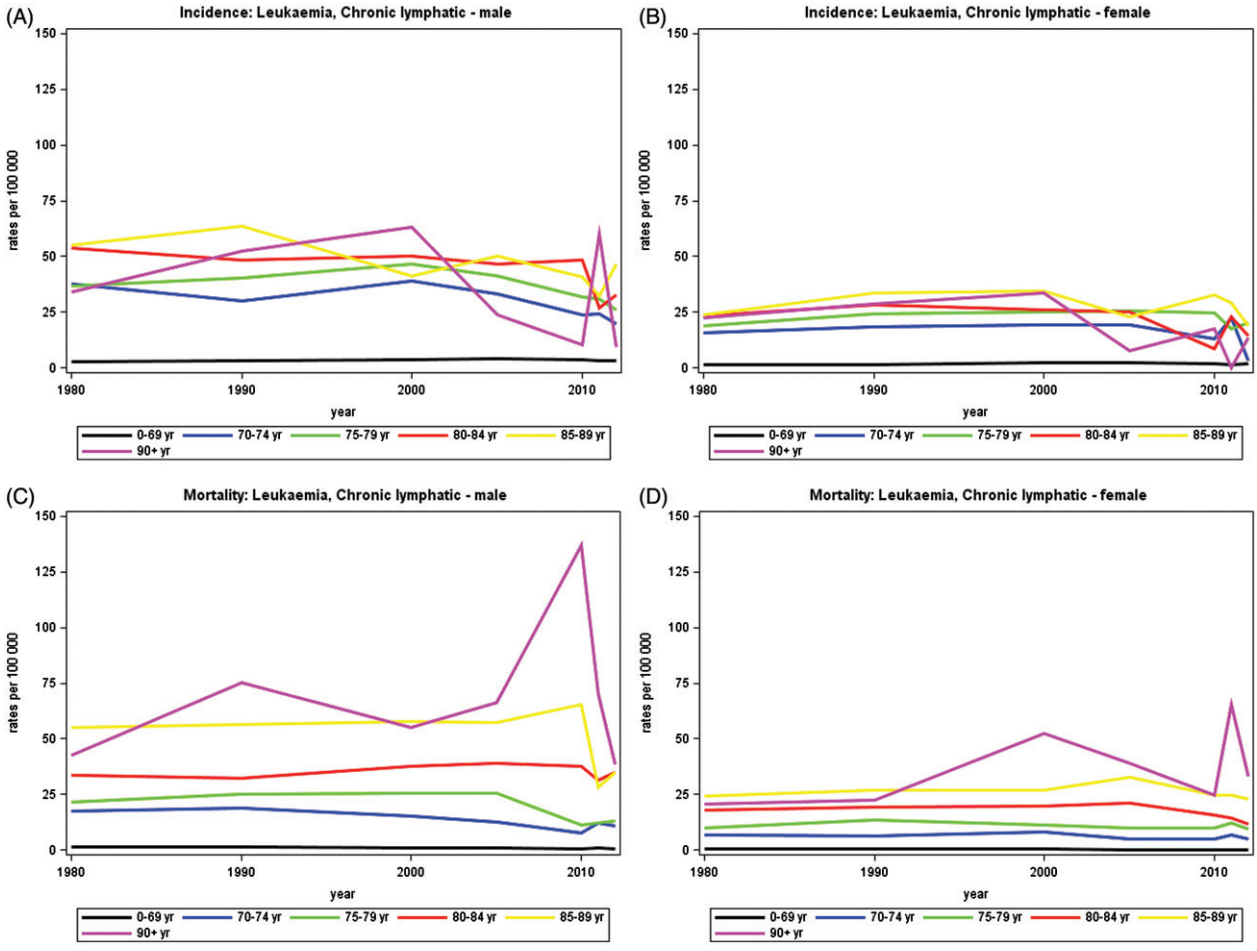

Figure 5. Trends in age- and sex-specific incidence and mortality of chronic lymphocytic leukemia in Denmark 1980–2012. The graphs depict rates per 100 000 person years.

compared to patients below this age. Advances in therapy, diagnostics and classification of hematological neoplasms during the past decades have led to improved prognosis in patients with NHL, MM, CLL, and AML. However, the improvements have evolved differently across the four hematological cancer diagnoses and age groups. For NHL both an increase in incidence and an improvement of prognosis has led to a large increase in the prevalence of patients with this diagnosis. This tendency is observed both among younger and older patients. Due to the nature of the different NHL subtypes this increase most likely affects both cured and chronically affected patients. Also, among patients with MM and CLL an improved prognosis has led to a factor 3–4 increase in the number of patients alive with these chronic diagnoses in recent periods involving both younger and older patients. Yet, among patients with AML the observed survival improvements involve mainly the younger patients although one-year survival in older patients also has improved for this diagnosis.

Few studies have addressed incidence and prognosis among the older population with hematological cancer [10,14]. Generally, previous incidence studies have focused on the younger patient population with the oldest age groups, usually including all patients older than 74 years, being pooled into one group, and no previous studies have provided incidence levels or trends for patients older than 75 years. The prevalence of a disease is dependent on the number of newly diagnosed patients, which again is affected by the extent of diagnostic workup and possibilities of correct disease classification, in parallel with therapeutic options. As these three latter factors have changed substantially during our study period, any trend in both the incidence rate and the prevalence is likely to be affected by this. We observed a steady increase in the incidence of NHL across all age groups in line with previous reports [14,15]. However, the small number of patients in most age groups precluded us from making conclusions regarding trends in incidence rate among older patients with MM, CLL, and AML.

The Danish data is in line with what has been reported from intervention studies during the past decade. The improved survival among elderly patients with NHL, MM, and CLL is likely to be ascribed to improving technology in health care. The increasing understanding of the biology of the diseases defines new possible targets for therapy, and more sophisticated diagnostic methodology makes diagnosis and staging more accurate and therefore therapy more appropriate. As an example – improvement in the prognosis of elderly with the NHL subtype diffuse large B-cell lymphoma (DLBCL) was not seen until the monoclonal CD20 antibody rituximab was combined with the chemotherapy regimen CHOP [16]. Previous attempts to improve DLBCL outcomes in this age group by intensifying chemotherapy regimens had led only to increased toxicity. Similarly, for many years no survival

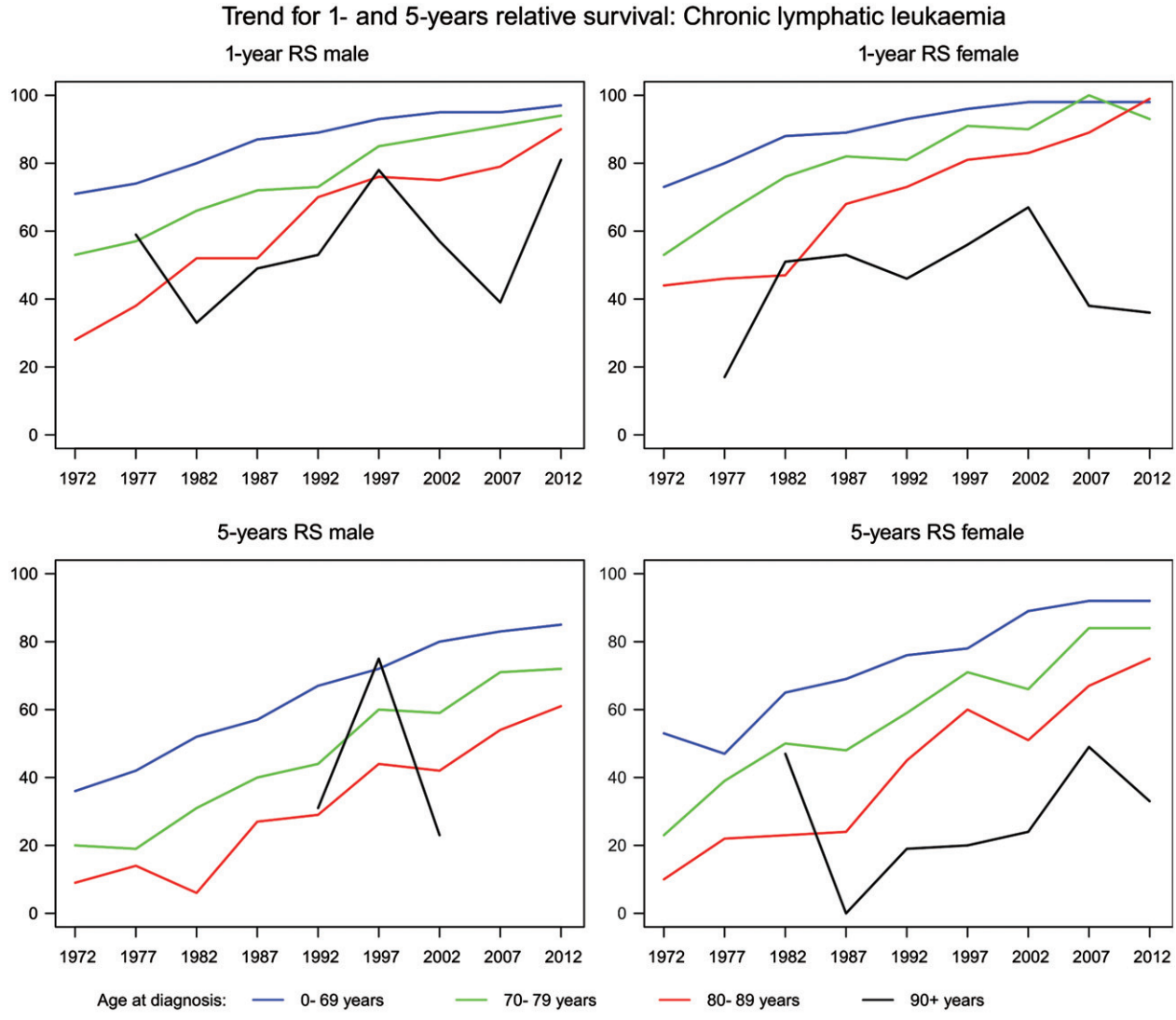

Figure 6. Trends in 1-year and 5-year age-specific relative survival in percent after chronic lymphocytic leukemia (CLL) in Denmark.

benefit had been demonstrated with any treatment for CLL until rituximab was combined with the traditional chemotherapeutic drugs fludarabine and cyclophosphamide [4]. However, this regimen is too toxic for most elderly patients and recently a survival benefit has also been demonstrated by combining a CD20 antibody with chlorambucil which is appropriate in this patient group [17].

Among patients with MM, the introduction of high-dose chemotherapy with stem cell support in the 1990s and more recently of new proteasome inhibiting drugs and immunomodulating and such as bortezomib and lenalidomide has improved prognosis substantially, increasing median survival both among newly diagnosed and relapsed MM patients by more than 12 months [18]. Equivalent improvements in prognosis have also been observed among the elderly patients that are often not eligible for stem cell transplantation [19].

Managing elderly patients with AML is difficult not only due to comorbidity and toxicity issues. Also, the leukemia biology is different as more genetically unstable and hence poor risk AML disease is seen with increasing age [20]. The proportion of elderly AML patients achieving remission after induction therapy seems to be increasing but progress in long-term survival is yet to be seen. The introduction of non-myeloablative allogeneic stem cell transplantation with reduced intensity conditioning regimens may pave the way for progress among elderly AML patients [21].

Although the cancer survival in the elderly has improved, it has not increased to the same extent as that seen in the younger population [6]. This age-related worsening of outcome can be attributed to a greater burden of comorbidity, socioeconomic factors, a greater incidence of treatment-associated complications and maybe also suboptimal treatment [3]. Older patients have an increased risk of prolonged myelosuppression and increased age has been shown to be independently associated with increased mortality from bacteremia in patients with hematological malignancies [3,6]. Also, age-related decay in organ function has a direct impact on pharmacokinetics and pharmacodynamics increasing the risk of both toxicity and suboptimal treatment [22]. Furthermore, older patients have a decreased tolerability of chemotherapy and several studies have shown greater susceptibility in this age group to the toxic effects of such chemotherapeutic agents as anthracyclines and bleomycin [3]. An increasing use of polypharmacy among the elderly has also

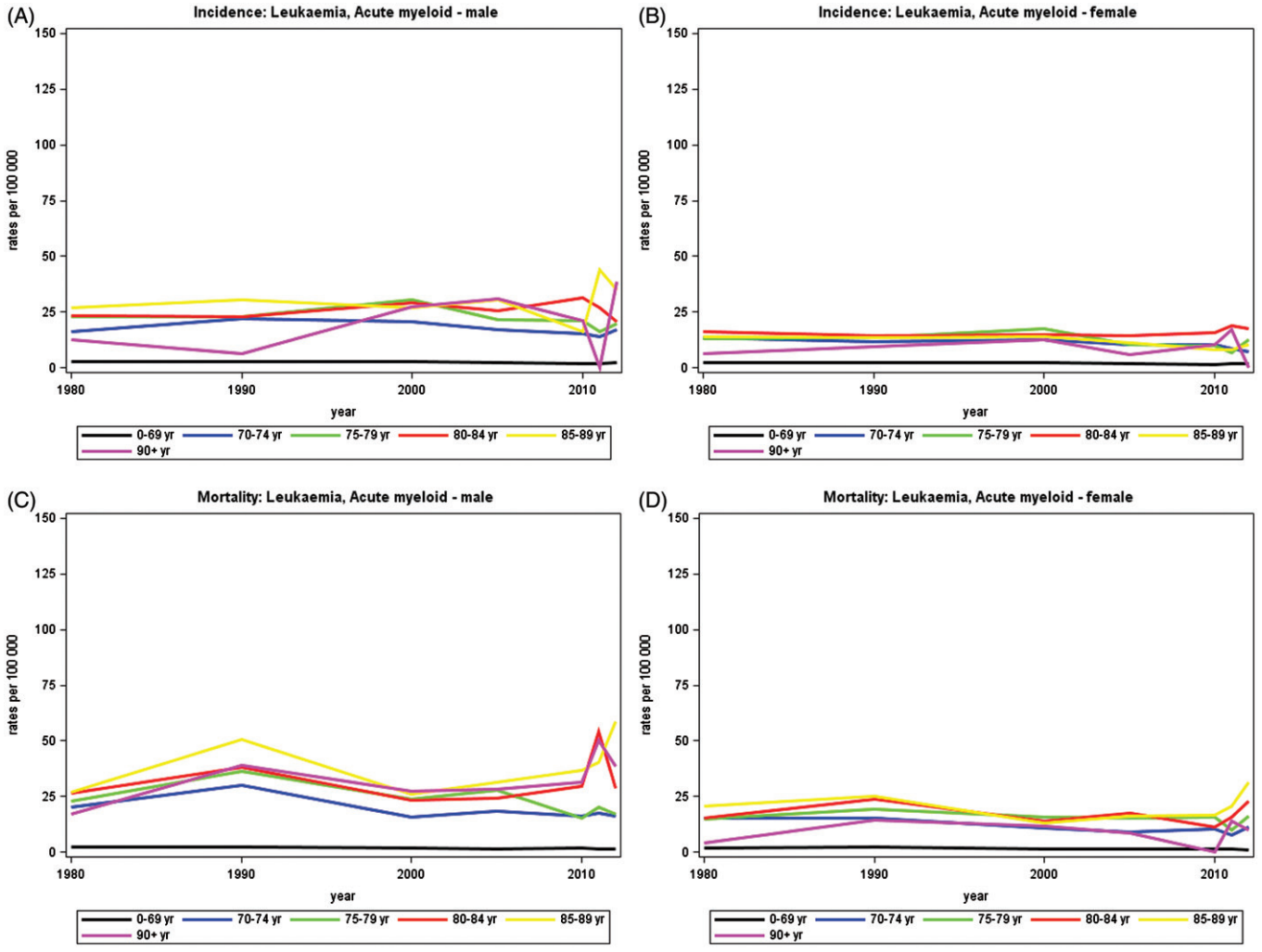

Figure 7. Trends in age- and sex-specific incidence and mortality of acute myeloid leukemia in Denmark 1980–2012. The graphs depict rates per 100 000 person years.

increased the risk of interactions and treatment-related toxicity [22]. These factors have, along with a general lack of data on older patients in clinical trials, raised concerns about the treatment suitability of older patients resulting in less effective treatment of this age group [23]. There have been reported especially low rates of treatment in patients over the age of 85 [2].

There is a great heterogeneity among the elderly in comorbidity, socioeconomic status, coexisting conditions as well as general level of functioning and therefore also heterogeneity in their suitability for receiving chemotherapy [24]. Currently used tools for assessing a patient's suitability for treatment like performance status are insufficient and a more thorough method for stratification must be found [24]. Such a method could consist of a geriatric assessment, which can detect multiple health issues even in people with good performance status, allowing individually tailored treatment options based on a patients general level of functioning [24]. Studies have shown that impairments in geriatric domains are associated with a poorer outcome in elderly patients receiving chemotherapy resulting in higher mortality and treatment-related toxicity [24]. Nevertheless, the optimal way of performing such an evaluation is yet to be found and further research is needed to shed light on how best to handle this age group.

Despite the population-based design with long and complete follow-up our study also has limitations. All hematological cancer diagnoses were based on ICD-10 diagnosis coding in registries. However, both the general validity and completeness of cancer diagnoses in the DCR and specifically the hematological cancers have been reported to be high [11,25] Also, the registry-based design of our study did not provide data on detailed patient- or treatment-specific factors and their influence on prognosis. The rarity of hematological cancer diagnoses resulted in few patients in some age strata resulting in low precision on some of the incidence and mortality estimates.

In conclusion, our study shows that the incidence level of the most common hematological cancers is 10 times higher in the older than in the younger population. The relative survival has improved over the past decades for most groups of patients with these diagnoses. This has led to dramatic increases in the prevalence of patients with hematological cancer. These positive effects can most likely be ascribed to

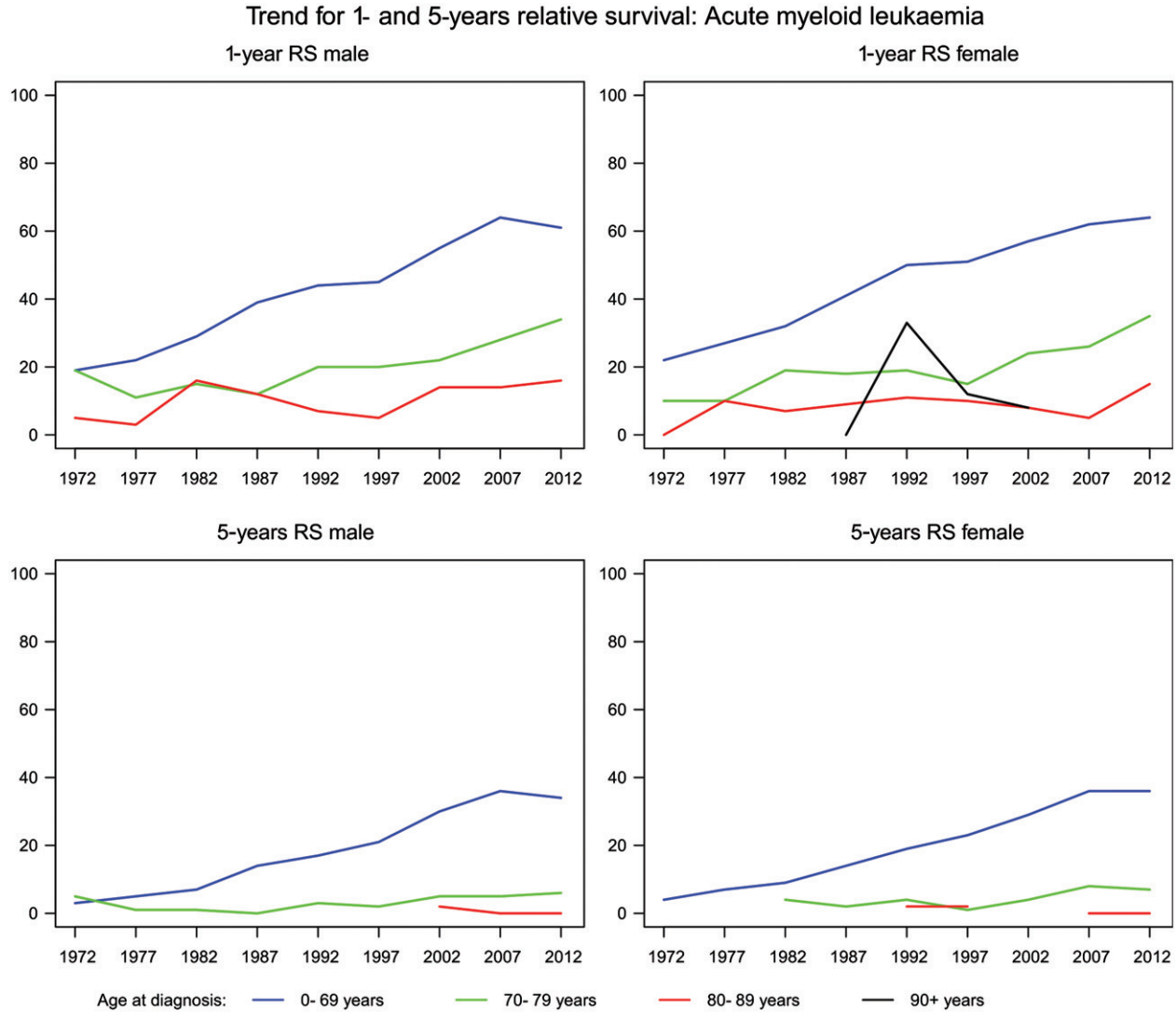

Figure 8. Trends in 1-year and 5-year age-specific relative survival in percent after acute myeloid leukemia (AML) in Denmark.

improvements in diagnostics, as well as therapeutic and supportive treatments.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

References

1. Smith A, Howell D, Patmore R, Jack A, Roman E. Incidence of haematological malignancy by sub-type: a report from the Haematological Malignancy Research Network. Br J Cancer. 2011;105:1684–92.
2. Extermann M, Crane EJ, Boulware D. Cancer in nonagenarians: profile, treatments and outcomes. J Geriatr Oncol 2010;1:27–31.
3. Mora O, Zucca E. Management of elderly patients with hematological neoplasms. Ann. Oncol. 2007;18Suppl1:i49–53.
4. Hallek M, Fischer K, Fingerle-Rowson G, Fink AM, Busch R, Mayer J, et al. Addition of rituximab to fludarabine and cyclophosphamide in patients with chronic lymphocytic leukaemia: a randomised, open-label, phase 3 trial. Lancet. 2010;376:1164–74.
5. Pulte D, Jansen L, Gondos A, Emrich K, Holleczek B, Katalinic A, et al. Improved population level survival in younger Hodgkin lymphoma patients in Germany in the early 21st century. Br J Haematol 2014;164:851–7.
6. Norgaard M, Larsson H, Pedersen G, Schonheyder HC, Rothman KJ, Sorensen HT. Short-term mortality of bacteraemia in elderly patients with haematological malignancies. Br J Haematol. 2006;132:25–31.
7. Westin E. Lymphoma and myeloma in older patients. Sem Oncol 2004;31:198–205.
8. Winton EF, Langston AA. Update in acute leukemia 2003: a risk adapted approach to acute myeloblastic leukemia in adults. Sem Oncol 2004;31:80–6.
9. Marcos-Gragera R, Allemani C, Tereanu C, De Angelis R, Capocaccia R, Maynadie M, et al. Survival of European patients diagnosed with lymphoid neoplasms in 2000-2002: results of the HAEMACARE project. Haematologica 2011;96:720–8.
10. Sant M, Allemani C, Tereanu C, De Angelis R, Capocaccia R, Visser O, et al. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. Blood 2010;116: 3724–34.

11. Gjerstorff ML. The Danish Cancer Registry. Scand J Public Health 2011;39:42–5.
12. Ewertz MCK, Engholm G, Hansen O, Keis AMT, Lund L, et al. Trends in cancer in the elderly population in Denmark, 1980-2012. Acta Oncol 2015;55: doi: 10.3109/0284186X.2015.1114678.
13. Dickman PW, Sloggett A, Hills M, Hakulinen T. Regression models for relative survival. Stat Med 2004;23:51–64.
14. Storm HH, Klint A, Tryggvadottir L, Gislum M, Engholm G, Bray F, et al. Trends in the survival of patients diagnosed with malignant neoplasms of lymphoid, haematopoietic, and related tissue in the Nordic countries 1964-2003 followed up to the end of 2006. Acta Oncol 2010;49:694–712.
15. Cartwright RA, Gilman EA, Gurney KA. Time trends in incidence of haematological malignancies and related conditions. Br J Haematol 1999;106:281–95.
16. Coiffier B, Lepage E, Briere J, Herbrecht R, Tilly H, Bouabdallah R, et al. CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large-B-cell lymphoma. New Eng J Med 2002;346:235–42.
17. Goede V, Fischer K, Busch R, Engelke A, Eichhorst B, Wendtner CM, et al. Obinutuzumab plus chlorambucil in patients with CLL and coexisting conditions. New Eng J Med 2014;370:1101–10.
18. Kumar SK, Rajkumar SV, Dispenzieri A, Lacy MQ, Hayman SR, Buadi FK, et al. Improved survival in multiple myeloma and the impact of novel therapies. Blood 2008;111:2516–20.
19. Kumar SK, Dispenzieri A, Lacy MQ, Gertz MA, Buadi FK, Pandey S, et al. Continued improvement in survival in multiple myeloma: changes in early mortality and outcomes in older patients. Leukemia 2014;28:1122–8.
20. Klepin HD, Rao AV, Pardee TS. Acute myeloid leukemia and myelodysplastic syndromes in older adults. J Clin Oncol 2014;32:2541–52.
21. Hahn T, Mccarthy PL, Jr., Hassebroek A, Bredeson C, Gajewski JL, Hale GA, et al. Significant improvement in survival after allogeneic hematopoietic cell transplantation during a period of significantly increased use, older recipient age, and use of unrelated donors. J Clin Oncol 2013;31:2437–49.
22. Jorgensen TL, Herrstedt J, Friis S, Hallas J. Polypharmacy and drug use in elderly Danish cancer patients during 1996 to 2006. J Geriatr Oncol 2012;3:33–40.
23. Wildes TM, Ruwe AP, Fournier C, Gao F, Carson KR, Piccirillo JF, et al. Geriatric assessment is associated with completion of chemotherapy, toxicity, and survival in older adults with cancer. J Geriatr Oncol 2013;4:227–34.
24. Hamaker ME, Prins MC, Stauder R. The relevance of a geriatric assessment for elderly patients with a haematological malignancy – a systematic review.. Leuk Res 2014;38:275–83.
25. Norgaard M, Skriver MV, Gregersen H, Pedersen G, Schonheyder HC, Sorensen HT. The data quality of haematological malignancy ICD-10 diagnoses in a population-based hospital discharge registry. Eur J Cancer Prev 2005;14:201–6.