Patient's age and treatment for haematological malignancy: a report from the Haematological Malignancy Research Network (HMRN)

Haematological Malignancy Research Network
enquiries@hmrn.org
www.hmrn.org

Report prepared on behalf of HMRN by:

Writing group

Russell Patmore[1]
Eve Roman[2]
Alex Smith[2]

Analytical/technical group

Simon Appleton[2]
Tim Bagguley[2]
John Blase[2]

[1]**Queen's Centre for Oncology and Haematology**
Castle Hill Hospital, Hull, HU16 5JQ

[2]**Haematological Malignancy Research Network**
Area 3 Seebohm Rowntree Building, Department of Health Sciences, University of York, YO10 5DD

June 2014

The research presented in this report was jointly supported by funding from Leukaemia and Lymphoma Research (LLR) and The Association of the British Pharmaceutical Industry (ABPI).

Aim

To examine the relationship between age at diagnosis with a haematological malignancy and first-line treatment in a representative UK population.

Summary

Haematological malignancies comprise around 1 in 10 of all new cancer diagnoses in the UK. There are over 60 different subtypes, each differing widely in clinical presentation, treatment options and prognosis. The range of therapies for haematological malignancies continues to expand, and currently includes active monitoring, chemotherapy, radiotherapy, bone marrow transplantation, antibodies and other targeted agents. These therapies can be delivered individually, sequentially, or in combination, either at presentation or following relapse/progression. Hence, unlike many other cancers, for most subtypes there are genuine treatment choices to be made by the patient and physician, both at the time of diagnosis as well as at critical points beyond it. These choices have major implications for patients and their families; with the likelihood of cure or prolonged life-expectancy needing to be balanced against personal costs including length of time in hospital, impact on family members, quality-of-life and emotional well-being. This means that patients and clinicians now face increasingly complex choices regarding therapeutic options that differ in efficacy, toxicity, and cost.

The incidence of the majority of cancers increases markedly with age, and for some malignancies there is emerging evidence that older people may be offered less intensive treatments than their younger counterparts. This report examines the relationship between age at diagnosis and first-line treatment in more than 6,000 patients diagnosed with one of seven haematological malignancies within the UK's population-based Haematological Malignancy Research Network 2004-12. The cancers examined were selected to cover the broad spectrum of haematological malignancies and treatment options; two aggressive (diffuse large B-cell lymphoma and mantle cell lymphoma), four chronic remitting/relapsing (follicular lymphoma, systemic marginal zone lymphoma, extranodal marginal zone lymphoma, and myeloma), and one long-term condition controlled by targeted oral therapy (chronic myeloid leukaemia).

The majority of patients were aged over 70 years when they were diagnosed; the median diagnostic ages ranging from 58 years for chronic myeloid leukaemia, through to 73 years for mantle cell lymphoma, myeloma and systemic marginal zone lymphoma. Whilst patient's age did not determine chemotherapy use per se, older patients were more likely to receive less intensive or attenuated doses. The evidence suggests, however, that chronological age was not the main driver of this choice. For lymphomas, for example, where information on the patient's performance status (ECOG) at diagnosis was available, this measure rather than their age was more important in predicting whether they received chemotherapy or not. This was particularly apparent for the aggressive, but potentially curable, diffuse large B cell lymphoma (DLBCL). For the more chronic incurable follicular and marginal zone lymphomas, disease stage and presence of B-symptoms were strong predictors of whether or not a patient was likely to receive chemotherapy.

Importantly, a positive impact on outcome was generally seen for older patients who received chemotherapy, with the 5-year relative survival estimates of older patients given chemotherapy being markedly higher than the corresponding 5-year overall survival estimated. The exception to this was mantle cell lymphoma where outcomes were generally poor across all ages.

The data outlined in this report highlights the age related dilemma that faces patients and their doctors. Using DLBCL as an example it is clear that even in younger patients, who are almost all treated intensively with chemotherapy, the vast majority of deaths occur in the first few months after diagnosis. The proportion of early deaths increases markedly as performance status declines; this reflects comorbidity and more extensive or aggressive disease, both of which make it more difficult to tolerate therapy. Performance status is generally worse in older patients and their rate of early death is even higher. However if older patients get through therapy their relative survival curves parallel those of younger patients indicating that they benefit just as much.

As the proportion of patients who die early from therapy or disease increases, the decision to embark on potentially curative treatment becomes more difficult for both patients and doctors and it is therefore predictable that fewer older patients will receive intensive therapy. Doctors and patients need better tools to predict an individual's tumour response and their ability to tolerate therapy, as well as less toxic and more effective treatments, for this situation to be improved.

Contents

Tables

Figures

1.0 Background

With a median diagnostic age of 70.6 years (1), the age distribution of most haematological malignancies (leukaemias, lymphomas and myelomas) is similar to that of many other common cancers (Fig 1.1); the incidence rates of the majority of subtypes increasing steadily with increasing age (2,3). Older age at diagnosis also tends to be associated with poorer outcomes; and for this reason traditional international prognostic indices (IPIs) often include age in their scoring algorithms, typically separating those under 60 years from those over 60 years (4–6).

The reasons underpinning the strong prognostic effect of age are complex, and include increased levels of comorbidity and decreased ability to tolerate the side-effects of the toxic chemotherapies given to treat haematological cancers. In this regard, the emergence of novel targeted agents like Rituximab for diffuse large B-cell lymphoma (DLBCL) which was initially trialled in patients over 60 years (7), and tyrosine kinase inhibitors (TKIs) for chronic myeloid leukaemia (8) which are effective at all ages (9), has reduced the impact of age in traditional prognostic scores and drawn attention to the fact that simple dichotomisation is not as informative as it once was (10–13). Nonetheless, there is evidence to suggest that a patient's age still influences treatment choice and clinical-decision making; and there is continued concern that this effect may be independent of the presence of additional comorbidities and other potentially confounding factors (14,15).

With a view to gaining insights into the general nature of the relationship between chronological age and treatment of haematological malignancies in the UK, this project was established to investigate the relationship between age and the propensity to receive treatment using data collected by the UK's Haematological Malignancy Research Network (www.hmrn.org) (1,16). This largely descriptive exercise focuses on seven haematological malignancy sub-types:

- two aggressive mature B-cell lymphomas - diffuse large B-cell lymphoma (DLBCL) and mantle cell lymphoma (MCL);
- four chronic haematological malignancies that are characterized by the remitting/relapsing nature of their pathways – follicular lymphoma (FL), systemic marginal zone lymphoma (sMZL), extranodal marginal zone lymphoma (eMZL) and myeloma;
- chronic myeloid leukaemia (CML) which, following the introduction of TKIs at the turn of the century now has the profile of a long-term condition with a near normal life-span.

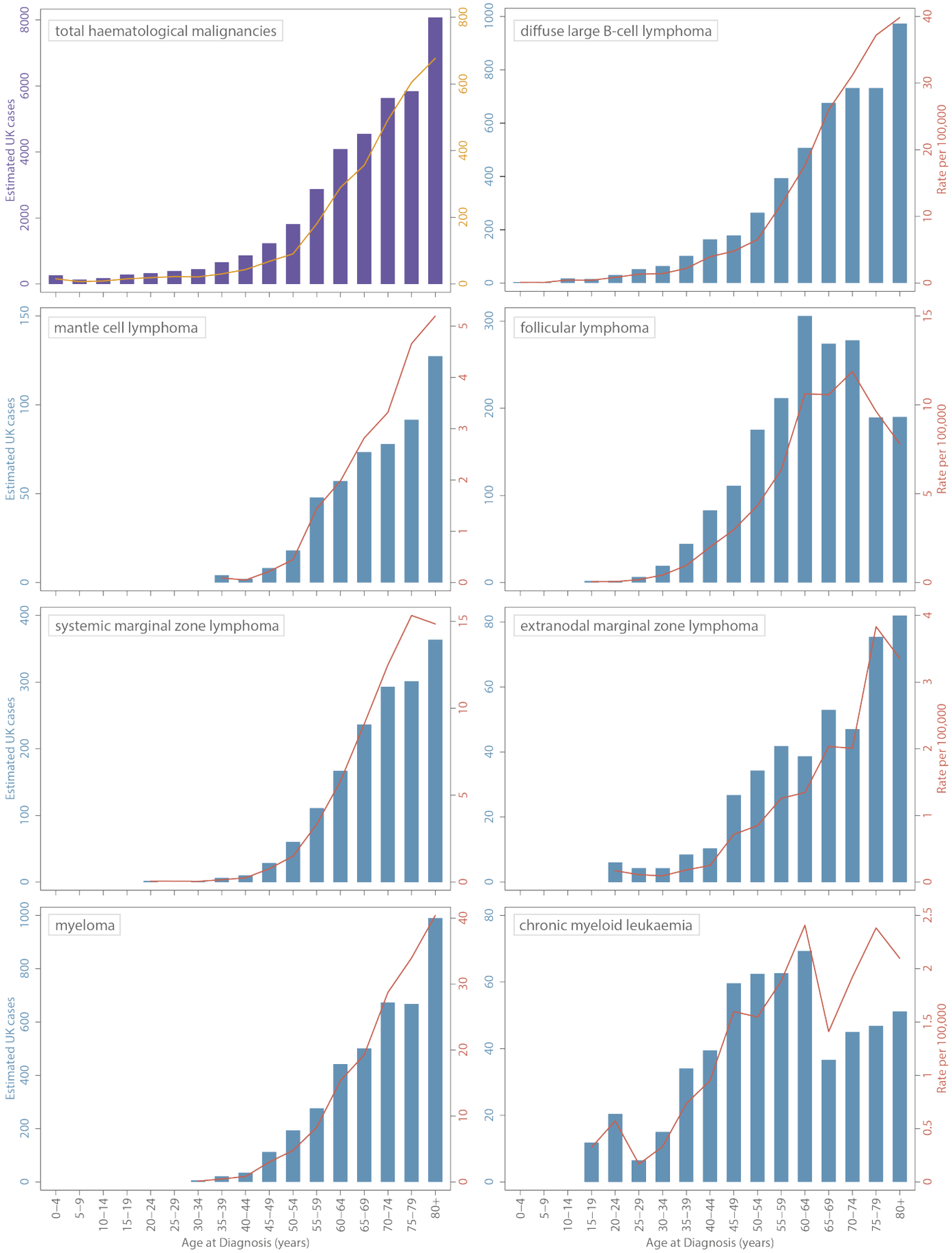
The basic descriptive details of these cancers, as derived from HMRN, are presented in Table 1.1.

In general all seven of these cancers occur more frequently in men than women – MCL being almost twice as common; and with median diagnostic ages ranging from 58.4 years (CML) through to 73.5 years (MCL) their incidence increases markedly with age, as can be seen more clearly in Figure 1.1.

Table 1.1: Descriptive characteristics of haematological cancers investigated in this report: HMRN, 2004 -12

Diagnosis	HMRN 2004-12				Estimated UK cases per year
	Annual rate (100,000)	Sex-rate ratio (m/f)	Median age at diagnosis (yrs)	5-year relative survival (%)	
Diffuse large B-cell lymphoma	8.4	1.3	69.9	56.7	4910
Mantle cell lymphoma	0.8	1.9	73.5	30.2	510
Follicular lymphoma	3.2	0.9	64.9	86.5	1890
Systemic marginal zone lymphoma	2.7	1.4	72.9	72.8	1580
Extranodal marginal zone lymphoma	0.7	1.0	68.8	86.4	430
Myeloma	6.7	1.5	73.0	42.7	3920
Chronic myeloid leukaemia	1.0	1.1	58.4	86.6	560

Fig. 1.1: Age distribution of all haematological neoplasms and the seven subtypes examined in this report. HMRN, 2004-12



2.0 Data and methods

This project is predicated on the established expertise and infrastructure of the Haematological Malignancy Research Network (www.hmrn.org); which was successfully initiated in 2004, with the aim of providing robust generalizable data to inform research and clinical practice – both locally and nationally (16). Detailed information about HMRN's configuration, data collection methods and ethical approvals has been published (1,16). Briefly, set within the former adjacent Cancer Networks of Yorkshire and the Humber & Yorkshire Coast, HMRN's catchment population (>3.6 million) has a similar socio-demographic profile to the country as a whole, and patient care is provided by a unified clinical network operating across 14 hospitals organised into five multi-disciplinary teams (MDTs) that work to common guidelines. Importantly, all diagnoses (>2,200 new patients a year), including disease progressions and transformations, are coded to the latest WHO classifications (5,17,18) by clinical staff at a single integrated haematopathology laboratory that houses all of the relevant technology and expertise required for diagnosis and on-going monitoring (www.hmds.info); and was cited in the UK's Cancer Reform Strategy as 'the model for delivery of complex diagnostic services'(19). Within HMRN, all patients have full treatment, response and prognostic data collected to clinical trial standards; and the study operates with Section 251 support under the NHS Act 2006, enabling the Health and Social Care Information Centre (HSCIC) to provide nationwide information on deaths, cancer registrations (preceding and succeeding), and Hospital Episode Statistics (HES).

Patients (≥18 years) included in the analysis presented here were newly diagnosed within the HMRN region between September 2004 and August 2012, and followed-up until March 2014. The numbers of patients and deaths is shown in Table 2.1.

Table 2.1: HMRN patients diagnosed September 2004 to August 2012 and followed until March 2014

	No. of patients	Males	Females	No. of deaths (%)
Diffuse large B-cell lymphoma (DLBCL)	2,137	1,117	1,020	1,112 (52.0)
Mantle cell lymphoma (MCL)	235	150	85	162 (68.9)
Follicular lymphoma (FL)	849	381	468	213 (25.1)
Systemic marginal zone lymphoma (SMZL)	682	385	297	280 (41.1)
Extranodal marginal zone lymphoma (EMZL)	196	91	105	51 (26.0)
Myeloma	1,745	991	754	1,113 (63.8)
Chronic myeloid leukaemia (CML)	273	164	109	55 (20.1)

For the purposes of analysis, area-based population counts are routinely sourced from UK national data (20) and sex-specific background mortality rates obtained from national life-tables (21). All analyses presented in this report were conducted within the statistical package Stata V.12; overall survival using standard time to event analysis, and relative survival using the program strel (V1.2.7). First line treatment was examined by age at diagnosis and, for the lymphomas, presence of B-symptoms, stage of disease and performance status (ECOG). These terms, along with the individual agents that comprise the chemotherapy regimens, are defined in section 6.0.

3.0 Results and commentary

The findings for each of the seven haematological malignancies are described in turn below. The figures and tables referred to are in Section 4, and the clinical and treatment definitions are in Section 6.

3.1 Diffuse large B-cell lymphoma

- Of the 2,137 patients diagnosed with DLBCL, 750 (35.1%) were aged over 75 years and 768 (35.9%) were under 65 years (Table 4.1.1). Overall, around 45% of patients presented with at least one B-symptom, and no differences were evident by age. Similarly, no differences with age were evident amongst those whose cancer was fully staged (Table 4.1.1). However, the proportion of patients who did not have all staging investigations (CT scans and/or bone marrow) was higher in those over 75 years (22.8%) than in those at younger ages; only 6% of patients aged 65-74 years and 5.5% of those under 65 years were not staged. The fall in staging investigations continued as age increased, with 40% of those aged 85 years or more not having enough data to assign a stage (Figure 4.1.1).

- Overall, with an ECOG score of 0, just over a quarter (26.9%) of patients were still able to carry out their normal activities when they were diagnosed. The achieved level of activity decreased slightly, however, with increasing age; those with an ECOG score of 0 falling from 35.1% in those under 65 years, to 27.8% in those aged 65-74, reaching 17.6% in those over 75 (Table 4.1.1).

- Around 8 out of 10 (82.9%) of patients newly diagnosed with DLBCL received first-line chemotherapy. This proportion varied with age, falling slightly from 94.1% in those under 65 years to 88.2% in those aged between 65-74 years, reaching 66.9% in those aged 75 years or more (Table 4.1.1).

- As expected only a small proportion of patients received radiotherapy alone (34; 1.6%) or tumour resection with no further treatment (19; 0.9%) (Table 4.1.2). These 53 patients, who predominantly had stage I disease or were not fully staged, tended to be older than those who had chemotherapy; the median ages for chemotherapy, radiotherapy alone and resections alone being 68.1, 86.8 and 83.4 years respectively. With an average age of 79.5 years, the remaining 313 (14.6%) patients treated with a supportive/palliative approach also tended to be older than patients receiving chemotherapy, were less likely to be staged (38.3%) and have higher ECOG scores (70.6%, ≥2).

- ECOG status is a major predictor of chemotherapy treatment at all ages, as can be seen from Figure 4.1.2. Amongst those with an ECOG score of 0, for example, 88% of patients diagnosed over 75 years received chemotherapy, nearly all with curative intent. Indeed, the majority of DLBCL patients who received first-line chemotherapy were given intensive regimens with curative intent (Table 4.1.3), most commonly R-CHOP (79.9%) followed by R-CVP (4.4%). Around 3% of patients with central nervous system (CNS) involvement or with disease considered particularly aggressive were treated with more intensive regimens, including IdaRAM or CODOX-M/R-IVAC; but this was predominantly restricted to those under the age of 65 years, with no patients over the age of 75 receiving either regimen. Less intensive chemotherapies, such as vincristine and chlorambucil, were given to 5% of patients treated with chemotherapy, and this was more likely to be prescribed for patients over the age of 75 years (13.9%) than for those under 65 years (0.6%). Likewise the proportion receiving intensive regimens fell as age increased from 99.4% in those under 65 years to 86.1% in those over 75 years; and the proportion receiving R-CVP increased from 1.2% in those under 65 years to 10.0% in those over 75 years. This latter observation most probably reflects the fact that the anthracycline doxorubicin, included in R-CHOP but not R-CVP, is contraindicated in patients with decreased cardiac function or with pre-existing cardiac disease.

- With respect to outcome following a diagnosis of DLBCL, 5-year overall survival was 45.8%, ranging from 66.4% in patients under the age of 65 years to 26.7% in those over the age of 75. The corresponding 5-year relative survival figures were 68.6% (< 65 years) and 40.2% (≥75 years) (Table 4.1.4). The disparity between overall and relative survival became more marked as age increased, reflecting the greater impact of competing causes of death in older age groups. As can be seen more clearly from Figure 4.1.3, however, much of the difference between the age categories is driven by events in the first year following diagnosis, after which time the relative survival curves run in parallel.

- When the analysis was restricted to the 82.9% of patients who were treated with chemotherapy, 5-year overall survival increased to 56.4% (from 45.8%) and the 5-year relative survival to 65.2% (from 54.5%). The largest difference between overall and relative survival was seen in older patients particularly those over the age of 75 years (Table 4.1.4 & Figure 4.1.4a). At all ages, outcomes were considerably better for patients with lower ECOG scores; for patients with a score of 0 relative survival was 87%, and across the three age groups a score of 0 remained prognostically favourable at 88%, 87% and 76% for those <65, 65-74, ≥75 years respectively (Figure 4.1.4).

3.2 Mantle cell lymphoma

- Of the 235 patients with mantle cell lymphoma, 37.4% presented with B-symptoms and, as expected, the majority of patients had stage IV disease (87.9%) (Table 4.2.1). There were no associations with age for these prognostic factors except for the fact that, as with diffuse large B-cell lymphoma, patients over the age of 75 years were less likely to be fully staged (19; 18.4%). Overall, around 40% of patients had ECOG scores of 0 at the time of diagnosis, and this proportion decreased with increasing age. Around three-quarters (73.2%) of the 235 patients were treated with first-line chemotherapy, the proportion varying with age; falling from 84.1% in those under 65 years to 65% in those who were 75 years or more at the time of diagnosis (Table 4.2.1).

- For 42 patients (17.9%) the initial treatment decision was active monitoring, and these patients tended to have lower ECOG scores and no B-symptoms (Table 4.2.2). By contrast, the ECOG status of patients who were treated with a supportive/palliative approach tended to be higher; ECOG scores ≥2 for 18.0% and 61.9% of those treated with chemotherapy and supportive/palliative approach respectively.

- The overall median age of patients receiving chemotherapy as a first-line treatment was 71.8 years, compared to 76.0 years for those who were actively monitored and 82.2 years for those treated with a supportive/palliative approach (Table 4.2.2). Whilst nearly all patients under the age of 65 years were treated with intensive regimens, such as FC, R-CHOP and Hyper-CVAD, nearly 50% of older patients (≥75 years) were treated with oral chemotherapy alone, predominantly chlorambucil.

- At around 25%, 5-year overall survival was poor ranging from 36.0% among patients under the age of 65 years to 4.6% among patients over the age of 75 years (Figure 4.2.1, Table 4.2.3). The estimates for relative survival were not dissimilar at 37.0% and 6.3% respectively, indicating that nearly all deaths in this patient group could be attributed to mantle cell lymphoma. Findings were similar when the analyses were restricted to the 73.2% of patients who were treated with chemotherapy (Table 4.2.3).

3.3 Follicular lymphoma

- Around a quarter (25.9%) of patients with follicular lymphoma reported B-symptoms at the time of diagnosis, and this varied little with age (Table 4.3.1). By contrast, ECOG score increased with increasing age, with around 20% of patients over the age of 75 years having a score ≥2, compared with around 5% of those under the age of 65 years. As with DLBCL, the proportion of patients who did not have a staging bone marrow and/or CT scan was increased at older ages, reaching about 40% in those over 85 years (Figure 4.3.1). No associations with age were, however, evident among those whose disease was fully staged, the proportion with stage IV disease remaining fairly constant at around 50% in each age group (Table 4.3.1).

- As expected stage of disease and presence of B-symptoms were strong predictors of first-line treatment; patients being more likely to have chemotherapy if they had stage III-IV disease, and radiotherapy alone if they had stage I (Table 4.3.2). Likewise, patients presenting with B-symptoms were more likely to be treated with chemotherapy (38.3%) than to be actively monitored (16.5%). Only a small proportion (1.8%) of patients

were treated with a supportive/palliative approach from the outset (Table 4.3.2), and these patients tended to be older (median age 72.2 years), have advanced disease, and poor performance status. With respect to chemotherapy regime, older patients were more likely to receive chlorambucil and less likely to be treated with the more intensive regimens such as R-CVP and R-CHOP (Table 4.3.3).

- 5-year overall survival was around 75%, and this ranged from 86.9% among patients under the age of 65 years to 49.2% in those over 75 years (Figure 4.3.2, Table 4.3.4). Reflecting the indolent nature of follicular lymphoma there was greater disparity between the estimates for relative and overall survival compared to those seen for the more aggressive diffuse large B-cell (Figure 4.1.3) and mantle cell (Figure 4.2.1) lymphomas. Nonetheless, as with diffuse large B-cell lymphoma, the disparity between overall and relative survival becomes more marked as age increased, reflecting the greater impact of competing causes of death in older age groups (Table 4.3.4, Figure 4.3.2). In contrast to the potentially curable diffuse large B-cell lymphoma, however, the survival estimates for follicular lymphoma (where treatment is triggered by symptoms) were marginally lower when the analysis was restricted to the 397 patients who were initially treated with chemotherapy, and this was most pronounced in patients between the ages of 65-74 years old.

3.4 Systemic marginal zone lymphoma

- Of the 682 patients with systemic MZL, the majority had stage IV disease (93.4%) and 30.5% had B-symptoms. As with the other lymphomas, the ECOG score tended to increase with age, the proportion with an ECOG of 0 falling from 55.8% in those <65 years to 28.6% in those aged 75 years or more (Table 4.4.1).

- With respect to first-line treatment (Table 4.4.2), 55.4% of systemic MZL patients were actively monitored and 38.3% had chemotherapy. Compared to the former those treated with chemotherapy were more likely to present with B-symptoms (19.8% *versus* 46.7%) and have an ECOG score >0 (48.9% *versus* 64.4%). A further 6.3% of patients were initially treated either with radiotherapy alone (2.2%) or with a palliative approach (4.1%); the latter group of patients generally being older (median age 72.2 years) and having an ECOG >0 (96.4%). Overall, whilst age at diagnosis does not appear to influence whether a patient is actively monitored (median age 65.3 years) or treated with chemotherapy (median age 63.7 years), amongst those who were treated, older patients are less likely to receive fludarabine and are more likely to be treated with chlorambucil (Table 4.4.3).

- For systemic MZL, 5-year overall survival was 57.4% and this ranged from 80.7% in patients under the age of 65 years to 39.5% in those over the age of 75 years (Table 4.4.4, Figure 4.4.1). 5-year relative survival was 73.2%, with those under the age of 65 years having similar estimates for overall and relative survival (80.7% *versus* 83.9%). By contrast, for those over the age of 75 years, the 5-year overall and relative survival estimates were 39.5% and 60.9% respectively. As with follicular lymphoma , survival was poorer in those patients who received chemotherapy, reflecting the fact that these patients had more advanced disease (Table 4.4.4).

3.5 Extranodal marginal zone lymphoma

- Of the 196 patients diagnosed with extranodal MZL, 27.6% had B-symptoms at the time of diagnosis, 47.0% had stage I disease (the predominant site of disease being stomach) and 45.1% of patients had an ECOG score of 0. As with all other lymphomas, ECOG tended to increase with age; 69.0% of patients over the age of 75 years having an ECOG score >1 compared to 39.5% of those under 65 years (Table 4.5.1).

- Reflecting the aetiology of the disease, 1 in 5 patients with extranodal MZL were treated with antibiotics for *Helicobacter pylori* eradication (46/196) (Table 4.5.2). For the remaining 150 patients, the most common first-line approach was active monitoring (40.0%), followed by chemotherapy (30.0%), radiotherapy alone

(24.7%), and supportive/palliative care (5.3%). The 45 patients treated with chemotherapy were more likely to have stage IV disease and/or B-symptoms, but there was no trend with age (median age 72.6 years). This latter observation is most likely to be due to the fact that oral chlorambucil is the most commonly prescribed therapy for extranodal MZL (70%).

- Outcomes for extranodal MZL were generally very good with 5-year overall and relative survival estimates of 75.4% and 89.2% respectively (Figure 4.5.1, Table 4.5.3); and, as expected, the 23% patients treated with chemotherapy had slightly poor outcomes, reflecting the fact that their disease tends to be more advanced.

3.6 Myeloma

- Of the 1745 newly diagnosed patients with myeloma, 411 (23.6%) were diagnosed when they were asymptomatic (median age 75.0 years), and their first-line management was by active monitoring. The majority (1104; 63.3%) were treated with first-line chemotherapy and a fifth of these also had an autologous stem cell transplant (ASCT) (Table 4.6.1). With a median age of diagnosis of 58.4 years, this latter group was significantly younger than all other patient groups, the median diagnostic age of patients receiving chemotherapy alone being 73.7 years, for example. No patients over the age of the 70 years received an ASCT. The remaining 230 (13%) patients were treated for symptom control rather than with the intent to modify the disease itself; these patients tended to be older and were mostly treated with a palliative/supportive approach.

- The proportion of patients receiving chemotherapy fell from 77.2% in those under 65 years to 52.2% in those who were 75 years or older at diagnosis (Table 4.6.2). With respect to first-line chemotherapy, CTD/CTDa (45%) was the most commonly prescribed regimen. As expected, patients who received CTDa were, on average, older (median age 74.3 years) than those receiving the full dose (median age 61.2 years). Older patients were also more likely to receive melphalan, which is normally administered orally (Table 4.6.2).

- The 5-year overall survival was 34.0%, ranging from 57.8% in patients under 65 years to 16.4% in those over 75 years (Figure 4.6.1, Table 4.6.3). The 5-year relative survival estimate was 42.6%, and this increase was evident in all age groups, the difference being slightly more marked at older ages. As with the other chronic malignancies, overall and relative survival estimates was slightly poorer in those treated with first-line chemotherapy.

3.7 Chronic myeloid leukaemia

- Of the 265 patients diagnosed with chronic myeloid leukaemia, 96.6% were treated with oral tyrosine kinase inhibitors (TKIs). Overall, the outcome for these patients was generally very good, with 5-year overall and relative survival estimates of 79.8% and 90.4% respectively (Figure 4.7.1, Table 4.7.1). The outcomes were similar for patients of all ages except for those over the age of 75 (17.7%), where 5-year relative survival was only 62.7%. As expected, similar estimates were seen when the 3% of patients who did not receive TKI therapy were excluded.

4.0 Figures & tables

4.1 Diffuse large B-cell lymphoma

Table 4.1.1: Diffuse large B-cell lymphoma: B-symptoms, disease stage, performance status (ECOG) and chemotherapy by age at diagnosis (years); HMRN 2004-12

	Age at diagnosis: N (%)			
	< 65	65 - 74	≥ 75	Total
Total	768 (100.0)	619 (100)	750 (100.0)	2137 (100.0)
B-symptoms				
No	426 (55.5)	331 (53.5)	425 (56.7)	1182 (55.3)
Yes	342 (44.5)	288 (46.5)	325 (43.3)	955 (44.7)
Stage[1]				
I	134 (18.5)	97 (16.7)	107 (18.5)	338 (17.9)
II	155 (21.3)	106 (18.2)	114 (19.7)	375 (19.9)
III	107 (14.7)	102 (17.5)	72 (12.4)	281 (14.9)
IV	330 (45.5)	277 (47.6)	286 (49.4)	893 (47.3)
Not fully staged[2]	42	37	171	250
Performance status (ECOG)[1]				
0	266 (35.1)	168 (27.8)	129 (17.6)	563 (26.9)
1	307 (40.5)	252 (41.7)	302 (41.2)	861 (41.1)
2	131 (17.3)	122 (20.2)	193 (26.3)	446 (21.3)
3	39 (5.1)	46 (7.6)	81 (11.1)	166 (7.9)
4	15 (2.0)	16 (2.6)	28 (3.8)	59 (2.8)
Not known	10	15	17	42
Chemotherapy				
No	45 (5.9)	73 (11.8)	248 (33.1)	366 (17.1)
Yes	723 (94.1)	546 (88.2)	502 (66.9)	1771 (82.9)

[1]Percentages calculated excluding patients with missing information
[2]Either bone marrow and/or CT scan not done

Fig. 4.1.1: Diffuse large B-cell lymphoma: disease stage by age at diagnosis; HMRN 2004-12

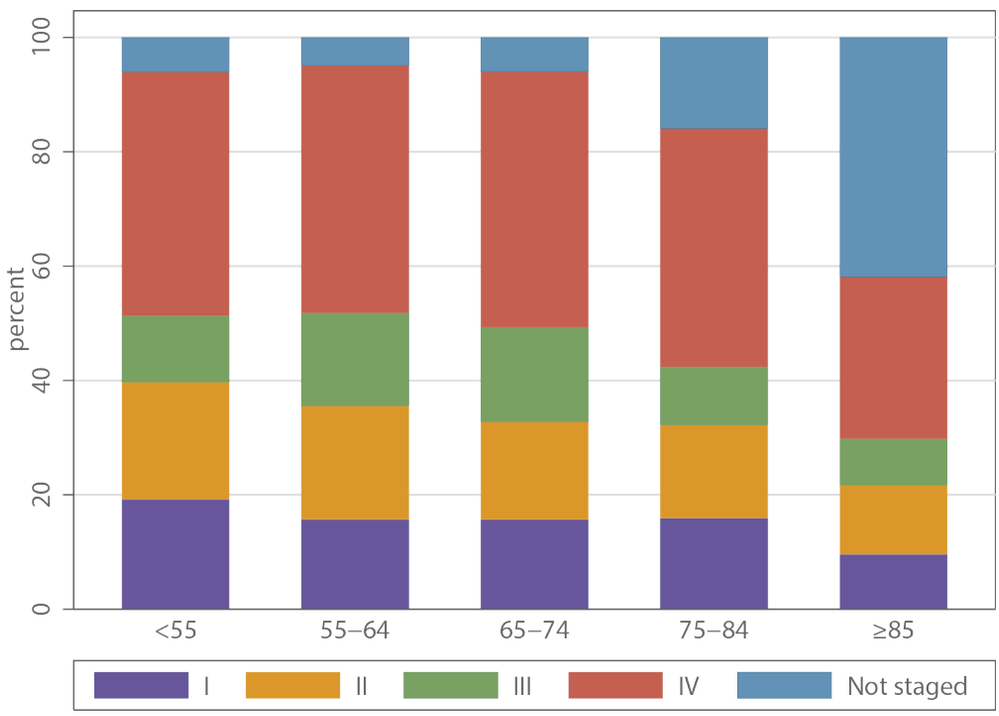


Table 4.1.2: Diffuse large B-cell lymphoma: first line treatment by stage, performance status (ECOG) & age (years); HMRN 2004-12

	First line treatment: N (%)				Total
	Chemotherapy	Radiotherapy[1]	Resection[2]	Supportive/ palliative	
Total	1771 (100.0)	34 (100.0)	19 (100.0)	313 (100.0)	2137 (100.0)
Stage					
I	312 (17.6)	11 (32.4)	8 (42.1)	7 (2.2)	338 (15.8)
II	361 (20.4)	2 (5.9)	0 (0.0)	12 (3.8)	375 (17.5)
III	266 (15.0)	1 (2.9)	0 (0.0)	14 (4.5)	281 (13.1)
IV	729 (41.2)	4 (11.8)	0 (0.0)	160 (51.1)	893 (41.8)
Not fully staged[3]	103 (5.8)	16 (47.1)	11 (57.9)	120 (38.3)	250 (11.7)
Performance status (ECOG)					
0	546 (30.8)	7 (20.6)	4 (21.1)	6 (1.9)	563 (26.3)
1	768 (43.4)	16 (47.1)	7 (36.8)	70 (22.4)	861 (40.3)
2-4	433 (24.4)	9 (26.5)	8 (42.1)	221 (70.6)	671 (31.4)
Not known	24 (1.4)	2 (5.9)	0 (0.0)	16 (5.1)	42 (2.0)
Age at diagnosis					
Median (range)	68.1 (18.3-97.7)	86.8 (37.6-96.3)	83.4 (57.6-97.0)	79.5 (19.2-97.8)	70.2 (18.3-97.8)
< 65	723 (40.8)	1 (2.9)	4 (21.1)	40 (12.8)	768 (35.9)
65 - 74	546 (30.8)	2 (5.9)	1 (5.3)	70 (22.4)	619 (29.0)
≥ 75	502 (28.3)	31 (91.2)	14 (73.7)	203 (64.9)	750 (35.1)

[1]Radiotherapy only [2]Resection only [3]Either bone marrow and/or CT scan not done

Table 4.1.3: Diffuse large B-cell lymphoma: chemotherapy regimen by age (years). HMRN 2004-12.

	Age: N (%)			Total
	< 65	65 - 74	≥ 75	
Yes	723 (100)	546 (100)	502 (100)	1771 (100)
Intensive[1]	**719 (99.4)**	**529 (96.9)**	**432 (86.1)**	**1680 (94.9)**
R-CHOP	596 (82.5)	459 (84.1)	359 (71.5)	1414 (79.9)
R-CVP	9 (1.2)	18 (3.3)	50 (10.0)	77 (4.4)
Non intensive[2]	**4 (0.6)**	**17 (3.1)**	**70 (13.9)**	**91 (5.1)**

[1]Including R-CHOP, R-CVP, CODOX-M, IdaRAM [2]Including Vincristine, Chlorambucil

Fig. 4.1.2: Diffuse large B-cell lymphoma: first line treatment by performance status (ECOG) and age at diagnosis; HMRN 2004-12

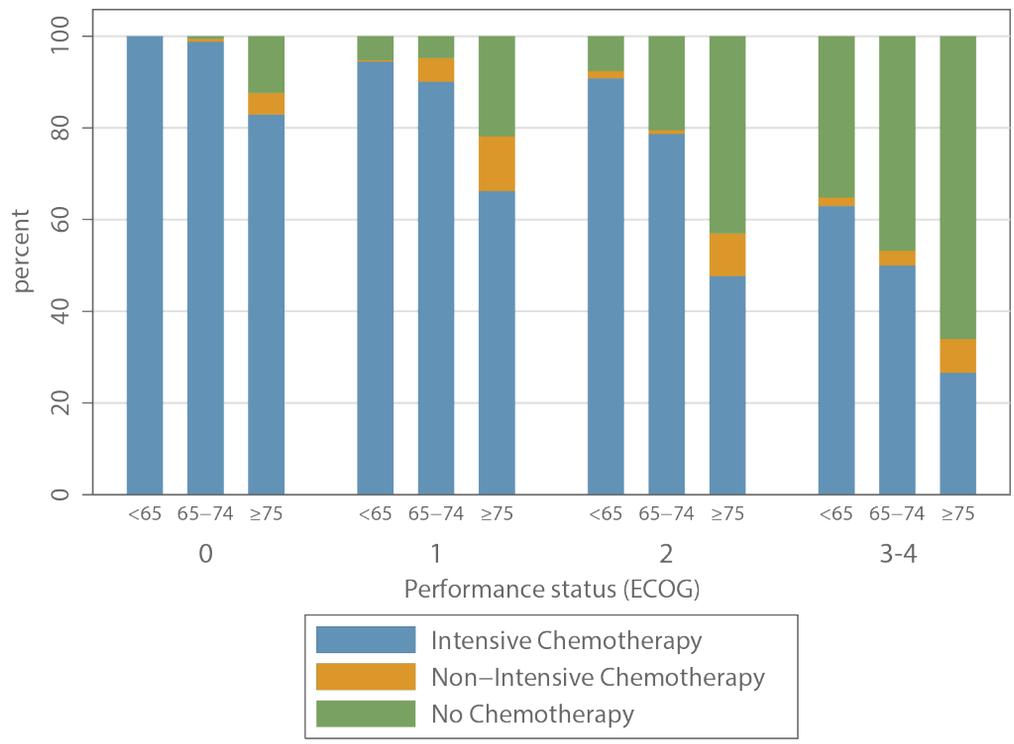


Table 4.1.4: Diffuse large B-cell lymphoma: 5-year overall survival (OS) and relative survival (RS) estimates (95% confidence intervals); HMRN 2004-12

	Total (N = 2137)		Chemotherapy (N = 1771)	
	OS (95% CI)	RS (95% CI)	OS (95% CI)	RS (95% CI)
Total	45.8 (43.5-48.0)	54.5 (51.9-57)	56.4 (53.9-58.8)	65.2 (62.4-67.8)
< 65 years	66.4 (62.7-69.8)	68.6 (64.8-72.1)	69.6 (65.9-73)	72.2 (68.3-75.7)
65 - 74 years	49.1 (44.9-53.2)	55.3 (50.5-59.8)	55.8 (51.3-60.1)	63.3 (58.2-68.1)
≥ 75 years	26.7 (23.4-30.1)	40.2 (35.2-45.1)	37.8 (33.2-42.3)	55.1 (48.4-61.2)

Fig. 4.1.3: Diffuse large B-cell lymphoma: overall and relative survival by age at diagnosis; HMRN 2004-12

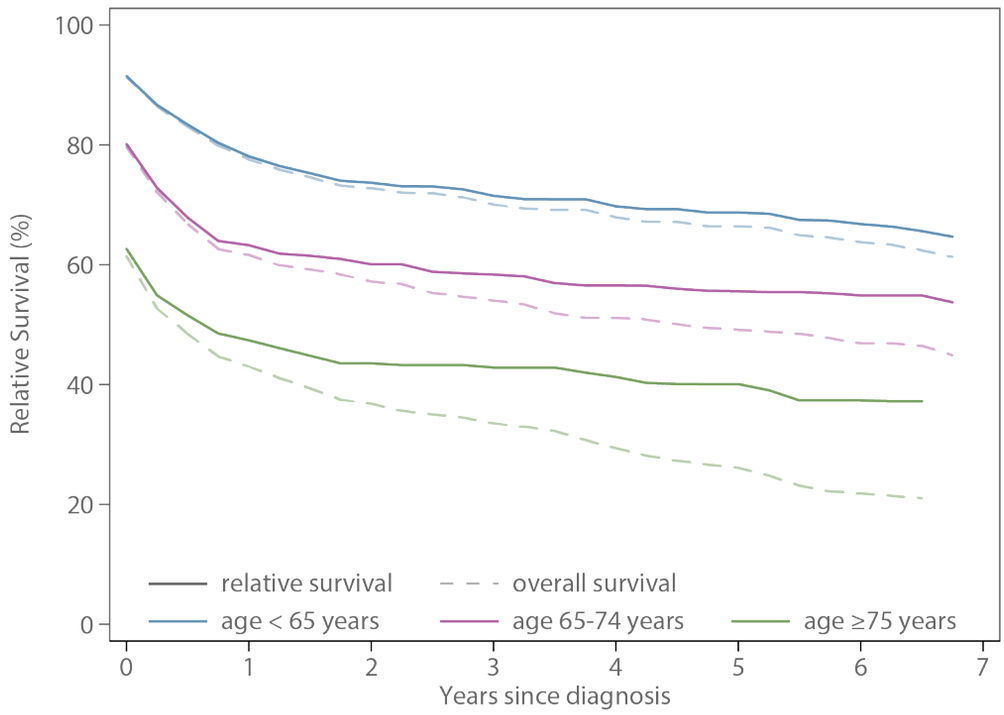
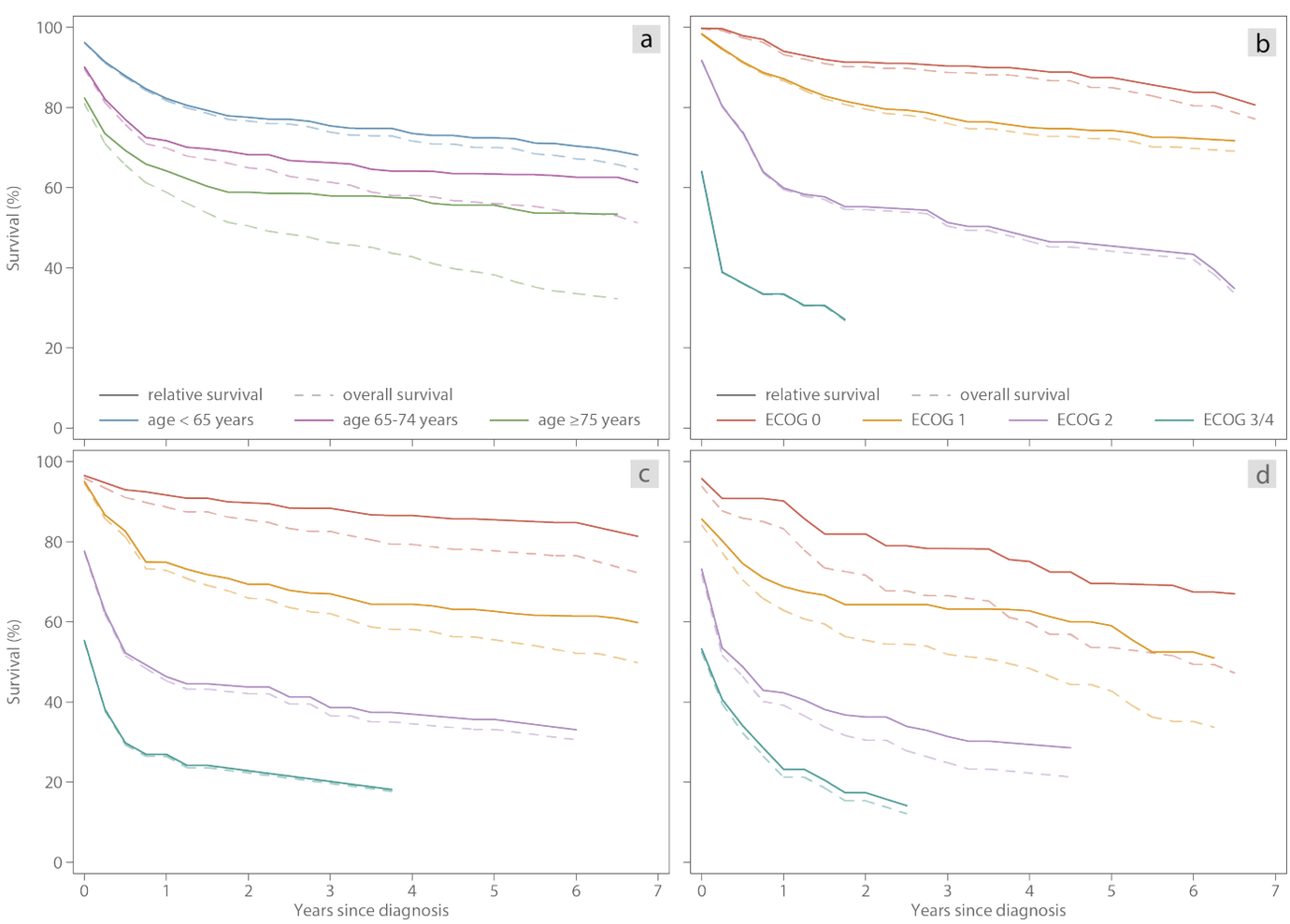


Fig. 4.1.4: Diffuse large B-cell lymphoma: survival by age at diagnosis and performance status
a) chemotherapy only; b) chemotherapy only, age <65; c) chemotherapy only, age 65-74;
d) chemotherapy only, age ≥75; HMRN 2004-12



4.2 Mantle cell lymphoma

Table 4.2.1: Mantle cell lymphoma: B-symptoms, disease stage, performance status (ECOG) and chemotherapy by age at diagnosis (years); HMRN 2004-12

	Age at diagnosis: N (%)			
	< 65	65 - 74	≥ 75	Total
Total	63 (100.0)	69 (100.0)	103 (100.0)	235 (100.0)
Stage[1]				
I-III	2 (3.4)	12 (19.0)	11 (13.1)	25 (12.1)
IV	57 (96.6)	51 (81.0)	73 (86.9)	181 (87.9)
Not fully staged[2]	4	6	19	29
B-symptoms				
No	43 (68.3)	36 (52.2)	68 (66.0)	147 (62.6)
Yes	20 (31.7)	33 (47.8)	35 (34.0)	88 (37.4)
Performance status (ECOG)[1]				
0	29 (46.0)	28 (41.2)	32 (31.1)	89 (38.0)
1	28 (44.4)	30 (44.1)	40 (38.8)	98 (41.9)
2-4	6 (9.5)	10 (14.7)	31 (30.1)	47 (20.1)
Not known	-	1	-	1
Chemotherapy				
No	10 (15.9)	17 (24.6)	36 (35.0)	63 (26.8)
Yes	53 (84.1)	52 (75.4)	67 (65.0)	172 (73.2)

[1]Percentages calculated excluding patients with missing information
[2]Either bone marrow and/or CT scan not done

Table 4.2.2: Mantle cell lymphoma: first line treatment by stage, performance status (ECOG) and age at diagnosis (years); HMRN 2004-12

	First line treatment: N (%)			
	Chemotherapy	Active monitoring	Supportive/ palliative	Total
Total	172 (100.0)	42 (100.0)	21 (100.0)	235 (100.0)
Performance status (ECOG)				
0	55 (32.0)	31 (73.8)	3 (14.3)	89 (37.9)
1	86 (50.0)	7 (16.7)	5 (23.8)	98 (41.7)
2-4	31 (18.0)	3 (7.1)	13 (61.9)	47 (20.0)
Not known	-	1 (2.4)	-	1 (0.4)
B-symptoms				
No	99 (57.6)	37 (88.1)	11 (52.4)	147 (62.6)
Yes	73 (42.4)	5 (11.9)	10 (47.6)	88 (37.4)
Age at diagnosis				
Median (range)	71.8 (40.0-92.3)	76.0 (57.1-93.0)	82.2 (39.4-96.3)	73.6 (39.4-96.3)
< 65	53 (30.8)	8 (19.0)	2 (9.5)	63 (26.8)
65 - 74	52 (30.2)	12 (28.6)	5 (23.8)	69 (29.4)
≥ 75	67 (39.0)	22 (52.4)	14 (66.7)	103 (43.8)

Fig. 4.2.1: Mantle cell lymphoma: overall and relative survival by age at diagnosis; HMRN 2004-12

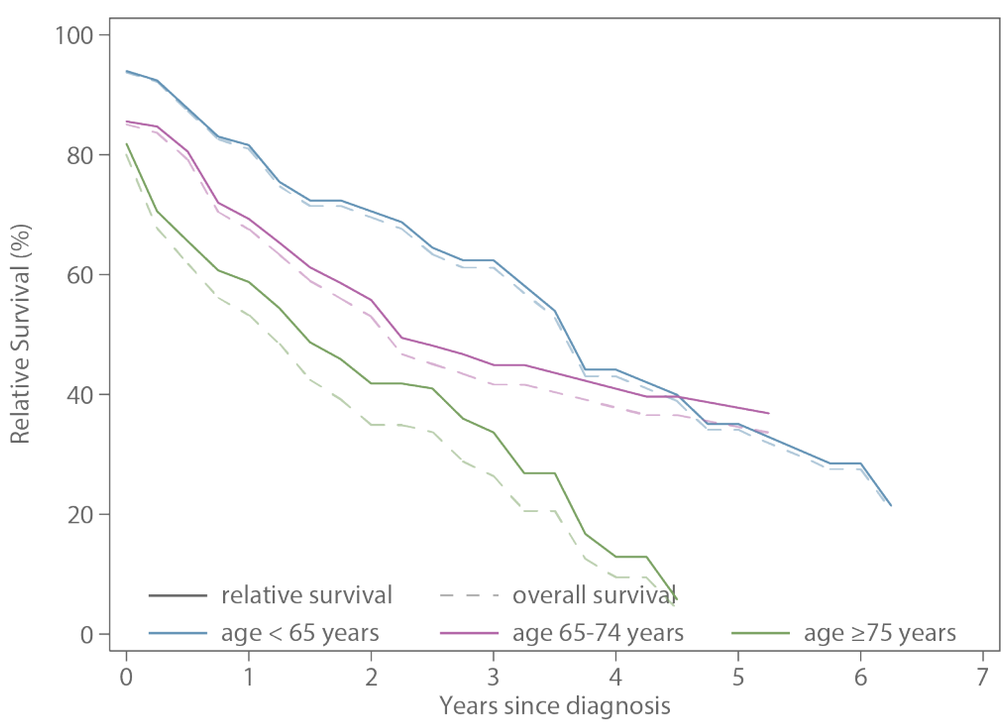


Table 4.2.3: Mantle cell lymphoma: 5-year overall survival (OS) and relative survival (RS) estimates (95% confidence intervals); HMRN 2004-12

	Total (N = 235)		Chemotherapy (N = 172)	
	OS (95% CI)	RS (95% CI)	OS (95% CI)	RS (95% CI)
Total	23.8 (17.6-30.6)	29.9 (22.1-38.2)	24.6 (17.6-32.4)	30.3 (21.5-39.5)
< 65 years	36 (20.6-51.7)	37 (21.1-53.1)	39.2 (23-55.1)	40.7 (23.8-57.1)
65 - 74 years	37.4 (25.3-49.5)	40.6 (27.2-53.5)	35.6 (22.4-49.1)	39.6 (24.6-54.2)
≥ 75 years	4.6 (1-13)	6.3 (1.3-17.5)	3.7 (0.5-12.8)	5.5 (0.7-18.3)

4.3 Follicular lymphoma

Table 4.3.1: Follicular lymphoma: B-symptoms, disease stage, performance status (ECOG) and chemotherapy by age at diagnosis (years); HMRN 2004-12

	Age at diagnosis: N (%)			
	< 65	65 - 74	≥ 75	Total
Total	432 (100.0)	245 (100.0)	172 (100.0)	849 (100.0)
B-symptoms				
No	316 (73.1)	185 (75.5)	128 (74.4)	629 (74.1)
Yes	116 (26.9)	60 (24.5)	44 (25.6)	220 (25.9)
Stage[1]				
I	63 (15.9)	39 (17.3)	21 (15.7)	123 (16.3)
II	59 (14.9)	33 (14.7)	19 (14.2)	111 (14.7)
III	81 (20.5)	35 (15.6)	23 (17.2)	139 (18.4)
IV	192 (48.6)	118 (52.4)	71 (53.0)	381 (50.5)
Not fully staged[2]	37	20	38	95
Performance status (ECOG)[1]				
0	276 (64.3)	131 (54.1)	73 (42.7)	480 (57.0)
1	132 (30.8)	88 (36.4)	65 (38.0)	285 (33.8)
2-4	21 (4.9)	23 (9.5)	33 (19.3)	77 (9.1)
Not known	3	3	1	7
Chemotherapy				
No	223 (51.6)	127 (51.8)	102 (59.3)	452 (53.2)
Yes	209 (48.4)	118 (48.2)	70 (40.7)	397 (46.8)

[1]Percentages calculated excluding patients with missing information
[2]Either bone marrow and/or CT scan not done

Fig. 4.3.1: Follicular lymphoma: disease stage by age at diagnosis; HMRN 2004-12

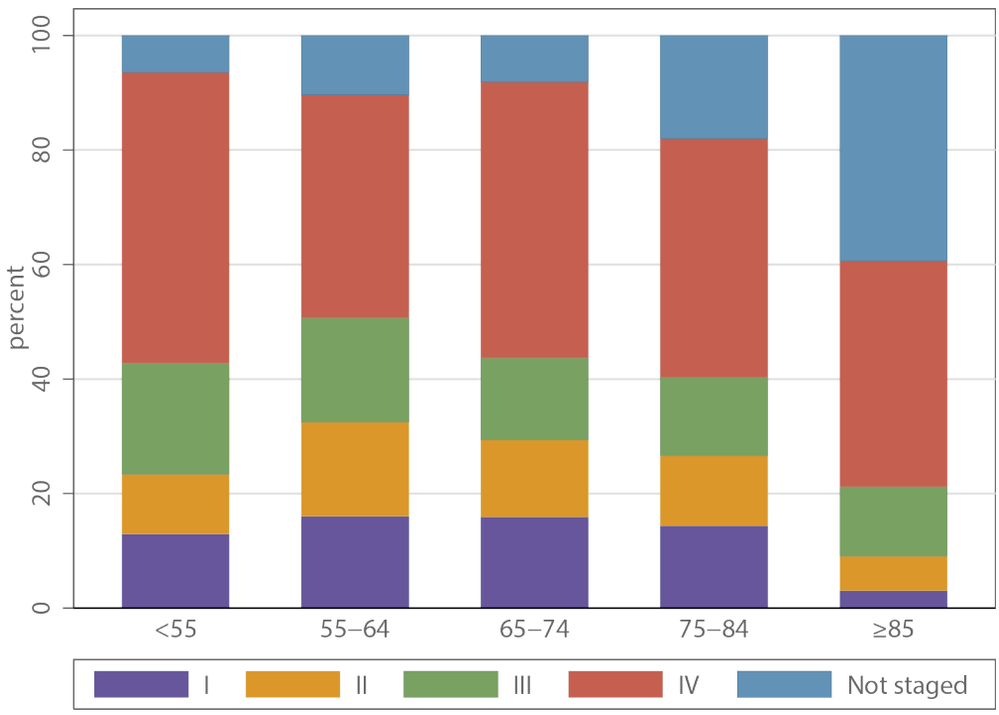


Table 4.3.2: Follicular lymphoma: first line treatment by stage, performance status & age at diagnosis (years): HMRN 2004-12

	First line treatment: N (%)				Total
	Chemotherapy	Radiotherapy[2]	Active monitoring	Supportive/ palliative	
Total	397 (100.0)	110 (100.0)	327 (100.0)	15 (100.0)	849 (100.0)
Stage					
I	13 (3.3)	68 (61.8)	42 (12.8)	0 (0.0)	123 (14.5)
II	51 (12.8)	20 (18.2)	40 (12.2)	0 (0.0)	111 (13.1)
III	66 (16.6)	8 (7.3)	64 (19.6)	1 (6.7)	139 (16.4)
IV	246 (62.0)	7 (6.4)	120 (36.7)	8 (53.3)	381 (44.9)
Not fully staged[1]	21 (5.3)	7 (6.4)	61 (18.7)	6 (40.0)	95 (11.2)
B-symptoms					
No	245 (61.7)	102 (92.7)	273 (83.5)	9 (60.0)	629 (74.1)
Yes	152 (38.3)	8 (7.3)	54 (16.5)	6 (40.0)	220 (25.9)
Performance status (ECOG)					
0	174 (43.8)	87 (79.1)	219 (67.0)	0 (0.0)	480 (56.5)
1	176 (44.3)	17 (15.5)	87 (26.6)	5 (33.3)	285 (33.6)
2-4	43 (10.8)	6 (5.5)	19 (5.8)	9 (60.0)	77 (9.1)
Not known	4 (1.0)	0 (0.0)	2 (0.6)	1 (6.7)	7 (0.8)
Age at diagnosis					
Median (range)	63.7 (19.6-98.3)	63.2 (28.6-89.3)	65.3 (20.6-92.6)	72.2 (47.9-91.8)	64.7 (19.6-98.3)
< 65	209 (52.6)	61 (55.5)	160 (48.9)	2 (13.3)	432 (50.9)
65 - 74	118 (29.7)	32 (29.1)	88 (26.9)	7 (46.7)	245 (28.9)
≥ 75	70 (17.6)	17 (15.5)	79 (24.2)	6 (40.0)	172 (20.3)

[1]Either bone marrow and/or CT scan not done
[2]Radiotherapy only

Table 4.3.3: Follicular lymphoma: chemotherapy regimen by age at diagnosis (years). HMRN 2004-12.

	Age: N (%)			Total
	< 65	65 - 74	≥ 75	
Total	209 (100.0)	118 (100.0)	70 (100.0)	397 (100.0)
R-CVP	118 (56.5)	65 (55.1)	34 (48.6)	217 (54.7)
R-CHOP	59 (28.2)	26 (22.0)	10 (14.3)	95 (23.9)
Chlorambucil	12 (5.7)	10 (8.5)	21 (30.0)	43 (10.8)
Other[1]	20 (9.6)	17 (14.4)	5 (7.1)	42 (10.6)

[1]Including Fludarabine, single-agent Rituximab, Vincristine.

Fig. 4.3.2: Follicular lymphoma: overall and relative survival by age at diagnosis; HMRN 2004-12

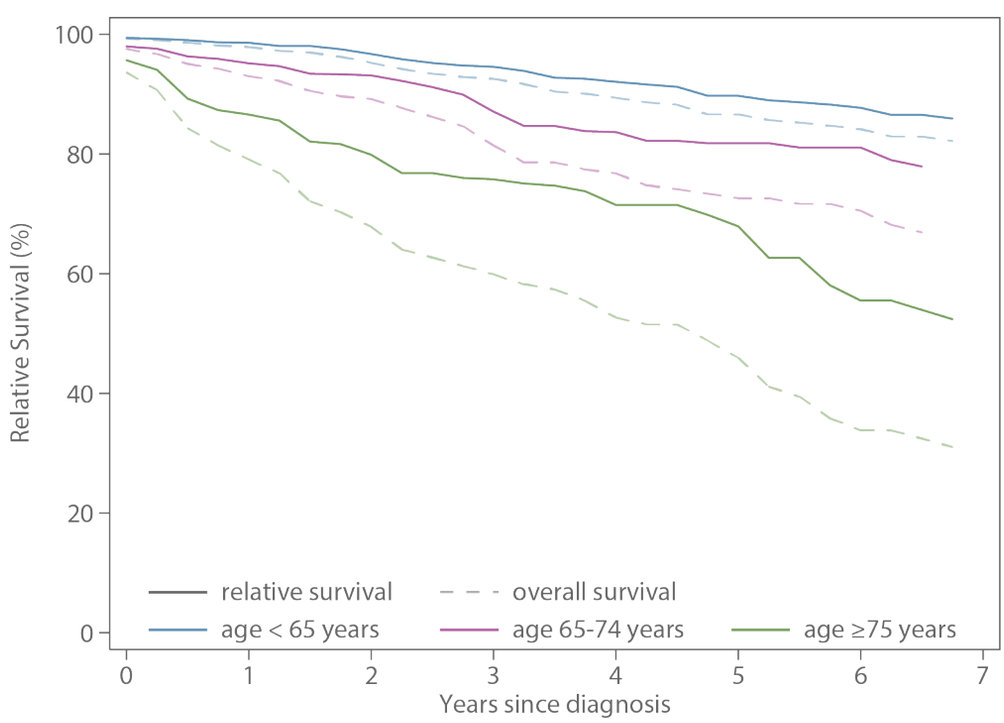


Table 4.3.4: Follicular lymphoma: 5-year overall survival (OS) and relative survival (RS) estimates (95% confidence intervals); HMRN 2004-12

	Total (N = 682)		Chemotherapy (N = 397)	
	OS (95% CI)	RS (95% CI)	OS (95% CI)	RS (95% CI)
Total	75.3 (71.9-78.4)	86.5 (82.7-89.5)	72.8 (67.7-77.3)	83.7 (77.8-88.1)
< 65 years	86.9 (82.8-90.1)	90 (85.6-93.1)	85.2 (79.3-89.6)	88.5 (81.9-92.8)
65 - 74 years	73.1 (66.2-78.8)	81.5 (73.3-87.4)	64.3 (53.5-73.1)	72.7 (59.7-82)
≥ 75 years	49.2 (40.5-57.3)	70.2 (56.6-80.2)	48.3 (34.6-60.6)	73.3 (48.1-87.7)

4.4 Systemic marginal zone lymphoma

Table 4.4.1: Systemic marginal zone lymphoma: B-symptoms, disease stage, performance status (ECOG) and chemotherapy by age at diagnosis (years); HMRN 2004-12

	Age at diagnosis: N (%)			
	< 65	65 - 74	≥ 75	Total
Total	161 (100.0)	231 (100.0)	290 (100.0)	682 (100.0)
B-symptoms				
No	122 (75.8)	157 (68.0)	195 (67.2)	474 (69.5)
Yes	39 (24.2)	74 (32.0)	95 (32.8)	208 (30.5)
Stage[1]				
I-III	19 (12.3)	12 (5.3)	12 (4.4)	43 (6.6)
IV	135 (87.7)	214 (94.7)	263 (95.6)	612 (93.4)
Not fully staged[2]	7	5	15	27
Performance status (ECOG)[1]				
0	87 (55.8)	120 (52.4)	83 (28.6)	290 (43.0)
1-4	69 (44.2)	109 (47.6)	207 (71.4)	385 (57.0)
Not known	5	2	-	7
Chemotherapy				
No	104 (64.6)	142 (61.5)	175 (60.3)	421 (61.7)
Yes	57 (35.4)	89 (38.5)	115 (39.7)	261 (38.3)

[1]Percentages calculated excluding patients with missing information
[2]Either bone marrow and/or CT scan not done

Table 4.4.2: Systemic marginal zone lymphoma: first line treatment by stage, performance status (ECOG) & age at diagnosis (years); HMRN 2004-12

	First line treatment: N (%)				Total
	Chemotherapy	Radiotherapy[2]	Supportive/ palliative	Active monitoring	
Total	261 (100.0)	15 (100.0)	28 (100.0)	378 (100.0)	682 (100.0)
Stage					
I-III	15 (5.7)	7 (46.7)	2 (7.1)	19 (5.0)	43 (6.3)
IV	244 (93.5)	6 (40.0)	22 (78.6)	340 (89.9)	612 (89.7)
Not fully staged[1]	2 (0.8)	2 (13.3)	4 (14.3)	19 (5.0)	27 (4.0)
B-symptoms					
No	139 (53.3)	15 (100.0)	17 (60.7)	303 (80.2)	474 (69.5)
Yes	122 (46.7)	0 (0.0)	11 (39.3)	75 (19.8)	208 (30.5)
Performance status (ECOG)					
0	90 (34.5)	10 (66.7)	0 (0.0)	190 (50.3)	290 (42.5)
1-4	168 (64.4)	5 (33.3)	27 (96.4)	185 (48.9)	385 (56.5)
Not known	3 (1.1)	0 (0.0)	1 (3.6)	3 (0.8)	7 (1.0)
Age at diagnosis					
Median (range)	63.7 (19.6-98.3)	63.2 (28.6-89.3)	72.2 (47.9-91.8)	65.3 (20.6-92.6)	64.7 (19.6-98.3)
< 65	57 (21.8)	4 (26.7)	2 (7.1)	98 (25.9)	161 (23.6)
65 - 74	89 (34.1)	7 (46.7)	7 (25.0)	128 (33.9)	231 (33.9)
≥ 75	115 (44.1)	4 (26.7)	19 (67.9)	152 (40.2)	290 (42.5)

[1]Either bone marrow and/or CT scan not done
[2]Radiotherapy only

Table 4.4.3: Systemic marginal zone lymphoma: chemotherapy regimen by age at diagnosis (years); HMRN 2004-12.

	Age: N (%)			Total
	< 65	65 - 74	≥ 75	
Total	57 (100)	89 (100)	115 (100)	261 (100)
Chlorambucil	25 (43.9)	45 (50.6)	92 (80.0)	162 (62.1)
Fludarabine	27 (47.4)	30 (33.7)	10 (8.7)	67 (25.7)
Other[1]	5 (8.8)	14 (15.7)	13 (11.3)	32 (12.3)

[1]Including R-CVP, single-agent Rituximab, R-CHOP

Fig. 4.4.1: Systemic marginal zone lymphoma: overall and relative survival by age at diagnosis; HMRN 2004-12

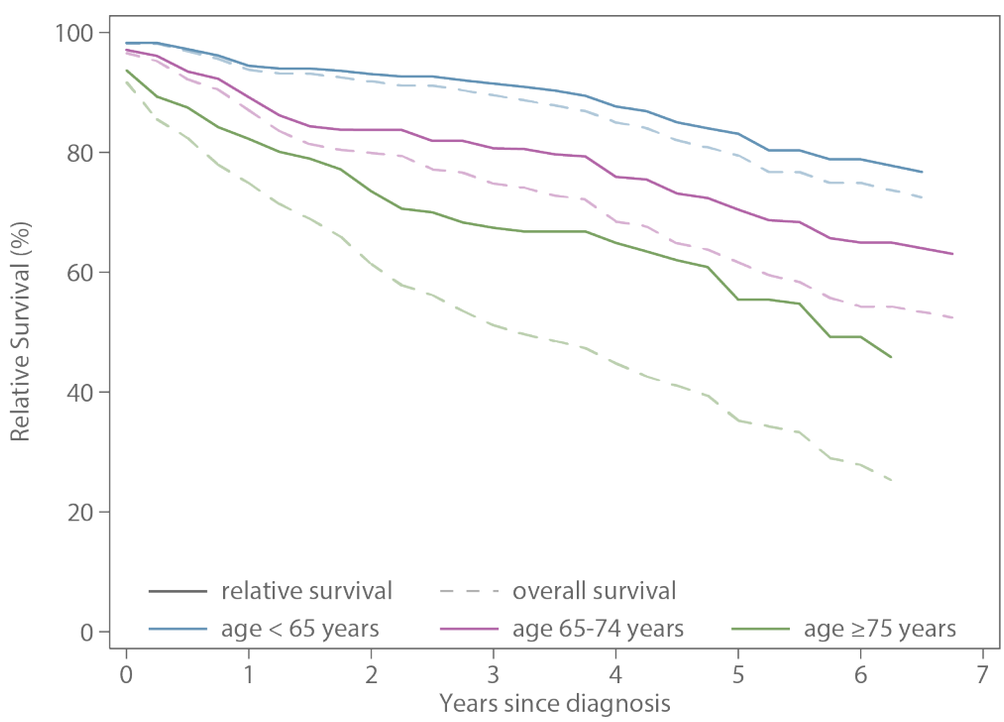


Table 4.4.4: Systemic marginal zone lymphoma: 5-year overall survival (OS) and relative survival (RS) estimates (95% confidence intervals); HMRN 2004-12

	Total (N = 682)		Chemotherapy (N = 261)	
	OS (95% CI)	RS (95% CI)	OS (95% CI)	RS (95% CI)
Total	57.4 (53-61.5)	73.2 (67.7-77.9)	48.3 (41.3-54.9)	62.1 (53.1-69.9)
< 65 years	80.7 (72.6-86.5)	83.9 (75.2-89.7)	80.5 (65.7-89.4)	83.9 (67.2-92.5)
65 - 74 years	64 (56.3-70.7)	72.7 (63.5-79.9)	49.4 (36.5-60.9)	56.2 (41.1-68.9)
≥ 75 years	39.5 (32.9-46.1)	60.9 (50.3-69.9)	31.1 (22-40.6)	48.7 (33.9-62.1)

4.5 Extranodal marginal zone lymphoma

Table 4.5.1: Extranodal marginal zone lymphoma: B-symptoms, disease stage, performance status (ECOG) and chemotherapy by age at diagnosis (years); HMRN 2004-12

	Age at diagnosis: N (%)			
	< 65	65 - 74	≥ 75	Total
Total	77 (100.0)	46 (100.0)	73 (100.0)	196 (100.0)
B-symptoms				
No	57 (74.0)	36 (78.3)	49 (67.1)	142 (72.4)
Yes	20 (26.0)	10 (21.7)	24 (32.9)	54 (27.6)
Stage[1]				
I	31 (48.4)	20 (52.6)	20 (40.8)	71 (47.0)
II-IV	33 (51.6)	18 (47.4)	29 (59.2)	80 (53.0)
Not fully staged[2]	13	8	24	45
Performance status (ECOG)[1]				
0	46 (60.5)	19 (41.3)	22 (31.0)	87 (45.1)
1-4	30 (39.5)	27 (58.7)	49 (69.0)	106 (54.9)
Not known	1	-	2	3
Chemotherapy				
No	63 (81.8)	35 (76.1)	53 (72.6)	151 (77.0)
Yes	14 (18.2)	11 (23.9)	20 (27.4)	45 (23.0)

[1]Percentages calculated excluding patients with missing information
[2]Either bone marrow and/or CT scan not done

Table 4.5.2: Extranodal marginal zone lymphoma: first line treatment by stage, performance status (ECOG) & age at diagnosis (years); HMRN 2004-12

	First line treatment: N (%)					
	Chemotherapy	Radiotherapy[2]	Active monitoring	*H. pylori* eradication	Supportive/ palliative	Total
Total	45 (100.0)	37 (100.0)	60 (100.0)	46 (100.0)	8 (100.0)	196 (100.0)
Stage						
I	9 (20.0)	23 (62.2)	18 (30.0)	21 (45.7)	0 (0.0)	71 (36.2)
II-IV	32 (71.1)	11 (29.7)	27 (45.0)	7 (15.2)	3 (37.5)	80 (40.8)
Not fully staged[1]	4 (8.9)	3 (8.1)	15 (25.0)	18 (39.1)	5 (62.5)	45 (23.0)
B-symptoms						
No	23 (51.1)	33 (89.2)	52 (86.7)	30 (65.2)	4 (50.0)	142 (72.4)
Yes	22 (48.9)	4 (10.8)	8 (13.3)	16 (34.8)	4 (50.0)	54 (27.6)
Performance status (ECOG)						
0	13 (28.9)	21 (56.8)	32 (53.3)	21 (45.7)	0 (0.0)	87 (44.4)
1-4	31 (68.9)	16 (43.2)	27 (45.0)	25 (54.3)	7 (87.5)	106 (54.0)
Not known	1 (2.2)	0 (0.0)	1 (1.7)	0 (0.0)	1 (12.5)	3 (1.5)
Age at diagnosis						
Median (range)	72.6 (48.6-91.1)	67.9 (36.3-87.6)	70.2 (20.4-93.4)	65.3 (24.7-90.6)	78.8 (28.8-96.2)	68.9 (20.4-96.2)
< 65	14 (31.1)	16 (43.2)	24 (40.0)	22 (47.8)	1 (12.5)	77 (39.3)
65 - 74	11 (24.4)	13 (35.1)	11 (18.3)	11 (23.9)	0 (0.0)	46 (23.5)
≥ 75	20 (44.4)	8 (21.6)	25 (41.7)	13 (28.3)	7 (87.5)	73 (37.2)

[1]Either bone marrow and/or CT scan not done
[2]Radiotherapy only

Fig. 4.5.1: Extranodal marginal zone lymphoma: overall and relative survival by age at diagnosis. HMRN 2004-12.

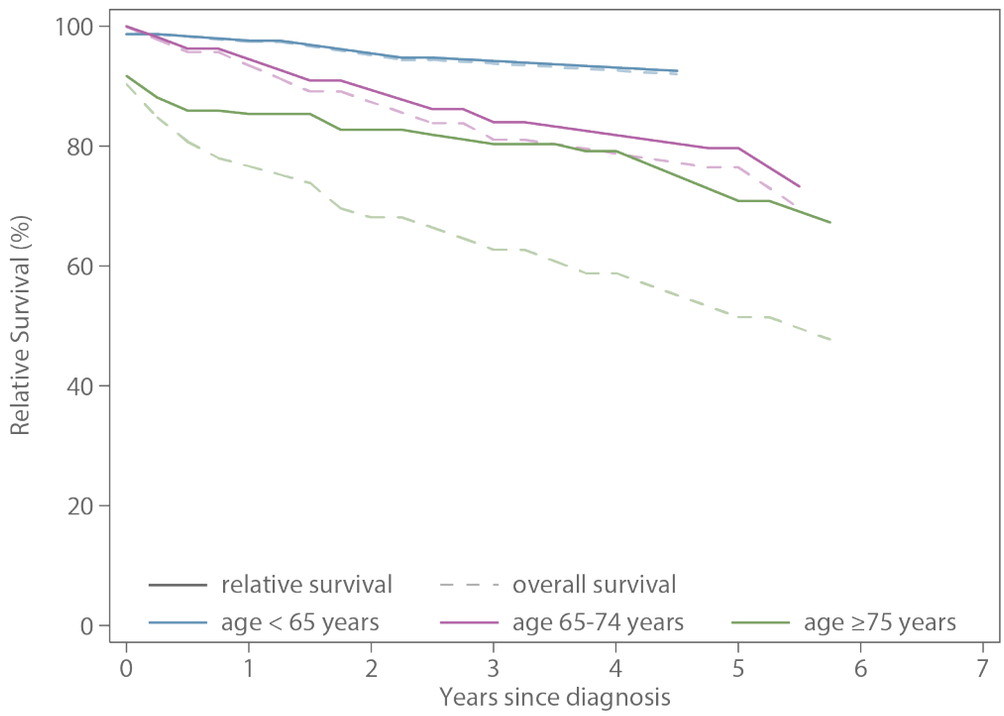


Table 4.5.3: Extranodal marginal zone lymphoma: 5-year overall survival (OS) and relative survival (RS) estimates (95% confidence intervals); HMRN 2004-12

	Total (N = 196)		Chemotherapy (N = 45)	
	OS (95% CI)	RS (95% CI)	OS (95% CI)	RS (95% CI)
Total	75.4 (68.2-81.1)	89.2 (80-94.3)	64.6 (48.1-77.1)	80.7 (55.6-92.5)
< 65 years	90.7 (80.1-95.8)	91.2 (80.2-96.3)	(-)	(-)
65 - 74 years	76.8 (59-87.6)	80 (60.3-90.6)	51.7 (19.2-76.8)	56.1 (19.3-81.7)
≥ 75 years	58 (45.2-68.8)	77.5 (56.7-89.2)	59.3 (34.6-77.3)	85 (22.4-98.2)

4.6 Myeloma

Table 4.6.1: Myeloma: first line treatment by age at diagnosis (years); HMRN 2004-12

	First line treatment N (%)						
	Chemotherapy			Active monitoring	Supportive/ palliative	Radiotherapy	Total
	All	Chemotherapy only	Chemotherapy + ASCT[1]				
Total	1104 (100.0)	875 (100.0)	229 (100.0)	411 (100.0)	201 (100.0)	29 (100.0)	1745 (100.0)
Age							
Median (range)	70.9 (33.4 - 95.5)	73.7 (38.8 - 95.5)	58.4 (33.4 - 70.2)	75.0 (30.6 - 94.1)	80.0 (47.4-94.7)	77.2 (56.8 - 90.4)	73.2 (30.6 - 95.5)
<65	366 (33.2)	171 (19.5)	195 (85.2)	84 (20.4)	18 (9.0)	6 (20.7)	474 (27.2)
65-74	349 (31.6)	315 (36.0)	34 (14.8)	122 (29.7)	47 (23.4)	8 (27.6)	526 (30.1)
75+	389 (35.2)	389 (44.5)	0 (0.0)	205 (49.9)	136 (67.7)	15 (51.7)	745 (42.7)

[1]autologous stem cell transplant

Table 4.6.2: Myeloma: chemotherapy regimen by age at diagnosis (years); HMRN 2004-12

		Age: N (%)			Total
		< 65	65 - 74	≥ 75	
All patients		**474 (100.0)**	**526 (100.0)**	**745 (100.0)**	**1745 (100.0)**
Chemotherapy	**No**	108 (22.8)	177 (33.7)	356 (47.8)	641 (36.7)
	Yes	366 (77.2)	349 (66.3)	389 (52.2)	1104 (63.3)
Chemotherapy treated		366 (100.0)	349 (100.0)	389 (100.0)	1104 (100.0)
	CTD	183 (50.0)	69 (19.8)	3 (0.8)	255 (23.1)
	CTDa	26 (7.1)	110 (31.5)	111 (28.5)	247 (22.4)
	Melphalan +/- steroids	9 (2.5)	83 (23.8)	168 (43.2)	260 (23.6)
	Other[1]	148 (40.4)	87 (24.9)	107 (27.5)	342 (31.0)

[1]Includes CVAD, Cyclophosphamide ± steroids, C-Z-Dex, MPT, PAD, RCD, Thalidomide ± steroids, VAD, VCD, Velcade ± steroids, VMP, Z-DEX

Fig. 4.6.1: Myeloma: overall and relative survival by age at diagnosis; HMRN 2004-12

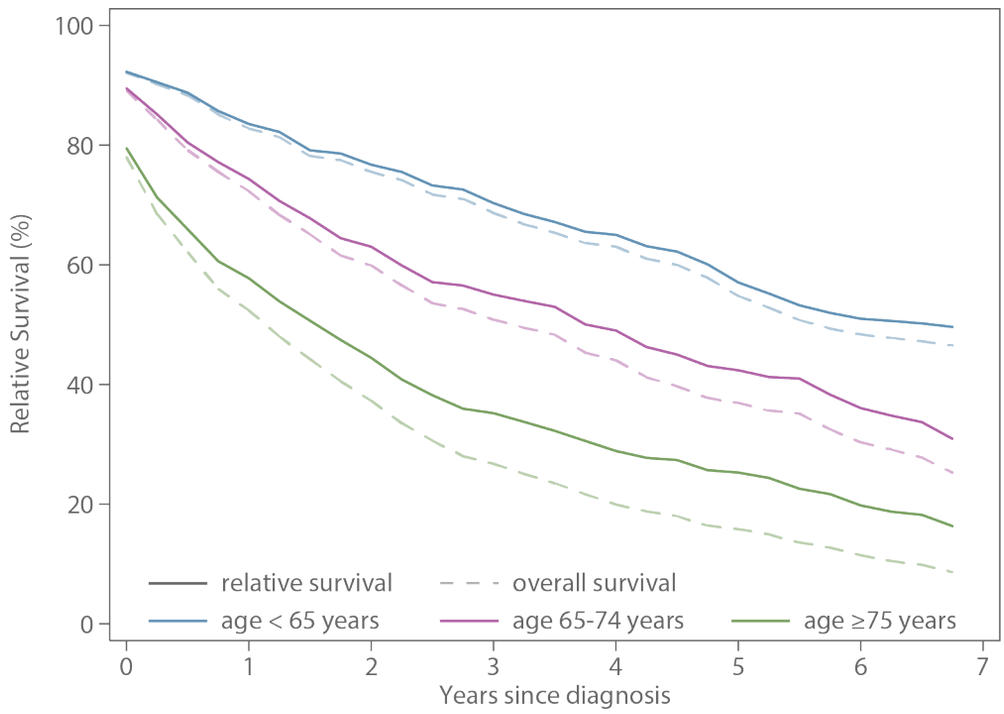


Table 4.6.3: Myeloma: 5-year overall survival (OS) and relative survival (RS) estimates (95% confidence intervals); HMRN 2004-12

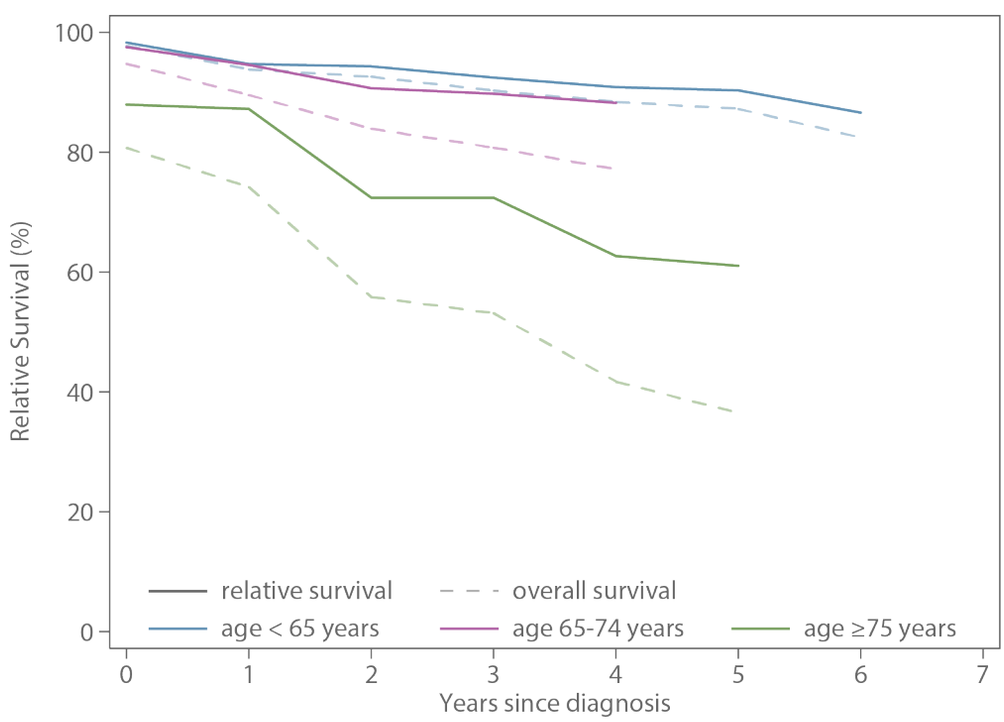
	Total (N = 1745)		Chemotherapy (N = 1104)	
	OS (95% CI)	RS (95% CI)	OS (95% CI)	RS (95% CI)
Total	34 (31.6-36.5)	42.6 (39.6-45.6)	31.6 (28.7-34.6)	38.4 (34.9-41.9)
< 65 years	57.8 (52.8-62.6)	60.1 (54.8-65)	52.7 (47-58)	54.7 (48.8-60.1)
65 - 74 years	37.7 (32.9-42.6)	43.1 (37.5-48.5)	31.9 (26.6-37.3)	36.3 (30.3-42.3)
≥ 75 years	16.4 (13.4-19.6)	25.7 (21-30.6)	12 (8.7-15.8)	18.2 (13.1-23.9)

4.7 Chronic myeloid leukaemia

Table 4.7.1: Chronic myeloid leukaemia: 5-year overall survival (OS) and relative survival (RS) estimates (95% confidence intervals); HMRN 2004-12

	Total			Tyrosine kinase inhibitor		
	N	OS (95% CI)	RS (95% CI)	N	OS (95% CI)	RS (95% CI)
Total	265	79.8 (73.6-84.7)	90.4 (83.5-94.5)	256	78.5 (72.4-83.4)	89.3 (82.5-93.5)
< 65 years	180	88.4 (82-92.6)	90.9 (83.9-94.9)	176	89 (82.5-93.2)	91.5 (84.3-95.5)
65 - 74 years	38	77.2 (59.1-88)	88.2 (58.3-97.1)	36	78.6 (59.9-89.3)	89.8 (55.8-98)
≥ 75 years	47	41.7 (25.5-57.1)	62.7 (34.5-81.5)	44	44.7 (27.4-60.5)	66.6 (35.8-85.1)

Fig. 4.7.1: Chronic myeloid leukaemia: overall and relative survival by age at diagnosis; HMRN 2004-12



5.0 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 Nov 22;105(11):1684–92.

2. De Angelis R, Sant M, Coleman MP, Francisci S, Baili P, Pierannunzio D, et al. Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE–5-a population-based study. The lancet oncology. 2014 Jan;15(1):23–34.

3. Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. CA: a cancer journal for clinicians. 2014;64(1):9–29.

4. Solal-Céligny P, Roy P, Colombat P, White J, Armitage JO, Arranz-Saez R, et al. Follicular lymphoma international prognostic index. Blood. 2004 Sep;104(5):1258–65.

5. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Fourth Edition [Internet]. 4th ed. IARC; 2008. 439 p. Available from: http://apps.who.int/bookorders/anglais/detart1.jsp?codlan=1&codcol=70&codcch=4002

6. Vaidya R, Witzig TE. Prognostic Factors For Diffuse Large B Cell Lymphoma In the R(X)CHOP Era. Ann Oncol. 2014 May 17;(00):1-10.

7. 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. The New England journal of medicine. 2002 Jan;346(4):235–42.

8. Druker BJ, Guilhot F, O'Brien SG, Gathmann I, Kantarjian H, Gattermann N, et al. Five-year follow-up of patients receiving imatinib for chronic myeloid leukemia. N Engl J Med. 2006 Dec 7;355(23):2408–17.

9. Smith AG, Painter D, Howell DA, Evans P, Smith G, Patmore R, et al. Determinants of survival in patients with chronic myeloid leukaemia treated in the new era of oral therapy: findings from a UK population-based patient cohort. BMJ open. 2014 Jan;4(1):e004266.

10. Sehn LH, Berry B, Chhanabhai M, Fitzgerald C, Gill K, Hoskins P, et al. The revised International Prognostic Index (R-IPI) is a better predictor of outcome than the standard IPI for patients with diffuse large B-cell lymphoma treated with R-CHOP. Blood. 2007 Mar 1;109(5):1857–61.

11. Gugliotta G, Castagnetti F, Palandri F, Breccia M, Intermesoli T, Capucci A, et al. Frontline imatinib treatment of chronic myeloid leukemia: no impact of age on outcome, a survey by the GIMEMA CML Working Party. Blood. 2011 May 26;117(21):5591–9.

12. Rousselot P, Cony-Makhoul P, Nicolini F, Mahon FX, Berthou C, Réa D, et al. Long-term safety and efficacy of imatinib mesylate (Gleevec®) in elderly patients with chronic phase chronic myelogenous leukemia: results of the AFR04 study. Am J Hematol. 2013 Jan;88(1):1–4.

13. Barrans SL, Crouch S, Care MA, Worrillow L, Smith A, Patmore R, et al. Whole genome expression profiling based on paraffin embedded tissue can be used to classify diffuse large B-cell lymphoma and predict clinical outcome. Br J Haematol. 2012 Nov;159(4):441–53.

14. National Cancer Equality Initiative in partnership with the ABPI Pharmaceutical Oncology Initiative. The impact of patient age on clinical decision-making in oncology [Internet]. 2012. Report No.: Gateway Reference 17160. Available from: http://www.cancerinfo.nhs.uk/images/stories/docs/ncat_dh_impactageonco_final.pdf

15. National Cancer Equality Initiative in partnership with the ABPI. Are older people receiving cancer drugs? An analysis of patterns in cancer drug delivery according to the age of the patient [Internet]. 2013 Dec. Available from: http://www.england.nhs.uk/wp-content/uploads/2013/12/old-people-rec-cancer-drugs.pdf

16. Smith A, Roman E, Howell D, Jones R, Patmore R, Jack A. The Haematological Malignancy Research Network (HMRN): a new information strategy for population based epidemiology and health service research. Br J Haematol. 2010 Mar;148(5):739–53.

17. Vardiman JW, Thiele J, Arber DA, Brunning RD, Borowitz MJ, Porwit A, et al. The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia: rationale and important changes. [Internet]. 2009. 937–51 p. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19357394

18. Campo E, Swerdlow SH, Harris NL, Pileri S, Stein H, Jaffe ES. The 2008 WHO classification of lymphoid neoplasms and beyond: evolving concepts and practical applications. Blood. 2011 May;117(19):5019–32.

19. Department of Health. Cancer Reform Strategy. 2007.

20. Office for National Satistics. 2001 Census: aggregate data (England and Wales) [computer file]. UK Data Service Census Support Downloaded from : http://casweb.mimas.ac.uk

21. Cancer Research UK Cancer Survival Group. Strel computer program and life tables for cancer survival analysis [Internet]. Available from: http://www.lshtm.ac.uk/ncde/cancersurvival/tools.htm

6.0 Definition of terms

6.1 Ann Arbor lymphoma staging system

Stage	Definition
I	Involvement of a single lymph node region or lymphoid structure (eg, spleen, thymus, Waldeyer's ring)
I_E	Involvement of a single extralymphatic organ or site
II	Involvement of two or more lymph node regions on the same side of the diaphragm. The number of regions involved can be indicated by a subscript (e.g. II_3)
II_E	Involvement of a single extralymphatic site contiguous or proximal to known nodal site plus involvement of one or more lymphoid regions or structures the same side of the diaphragm
III	Involvement of lymphoid regions or structures on both sides of the diaphragm
III_E	Localised involvement of a single extralymphatic site contiguous or proximal to known nodal site plus involvement of lymphoid regions or structures on both sides of the diaphragm
III_S	Localised splenic involvement plus involvement of lymphoid regions or structures on both sides of the diaphragm
III_{SE}	Fulfilling the definitions of both III_E and III_S
IV	Diffuse or disseminated involvement of one or more extralymphatic organs or tissues with or without associated lymph node involvement. Liver involvement is always considered diffuse and therefore stage IV Marrow involvement also dictates elevation to stage IV

6.2 B-symptoms

- fever greater than 38°C
- drenching sweats, especially at night
- unintentional weight loss of >10% of normal body weight over a period of 6 months or less

6.3 Performance status (ECOG) scale

Stage	Definition
0	Able to carry out all normal activity without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out light work.
2	Ambulatory and capable of all self care, but unable to carry out any work; up and about for more than 50% of waking hours.
3	Capable of only limited self care; confined to bed or chair for more than 50% of waking hours.
4	Completely disabled; cannot carry on any self care. Totally confined to bed or chair.

6.4 Chemotherapy regimen agents

CHOP	Cyclophosphamide, Doxorubicin, Vincristine, Prednisolone
CODOX-M/ IVAC-R	Cyclophosphamide, Vincristine, Doxorubicin, Methotrexate (HD) / Ifosfamide, Etoposide, Cytarabine, Rituximab
CTD	Cyclophosphamide, Thalidomide, Dexamethasone
CTDa	CTD attenuated (Cyclophosphamide, Thalidomide, Dexamethasone)
CVAD	Cyclophosphamide, Vincristine, Doxorubicin, Dexamethasone
C-Z-Dex	Cyclophosphamide, Idarubicin, Dexamethasone
FC	Cyclophosphamide, Fludarabine
Hyper CVAD	Cyclophosphamide, Vincristine, Doxorubicin, Dexamethasone, Methotrexate, AraC
IdaRAM	Idarubicin, AraC, Methotrexate, Dexemethasone
MPT	Melphalan, Prednisolone, Thalidomide
PAD	Velcade, Doxorubicin, Dexamethasone
RCD	Revlamid, Cyclophosphamide, Dexamethasone
RCDa	RCD attenutated (Revlamid, Cyclophosphamide, Dexamethasone)
R-CHOP	Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisolone
R-CVP	Rituximab, Cyclophosphamide, Vincristine, Prednisolone
VAD	Vincristine, Doxorubicin, Dexamethasone
VCD	Velcade, Cyclophosphamide, Dexamethasone
VMP	Bortezomib, Melphalan, Prednisolone
Z-DEX	Idarubicin, Dexamethasone

www.hmrn.org