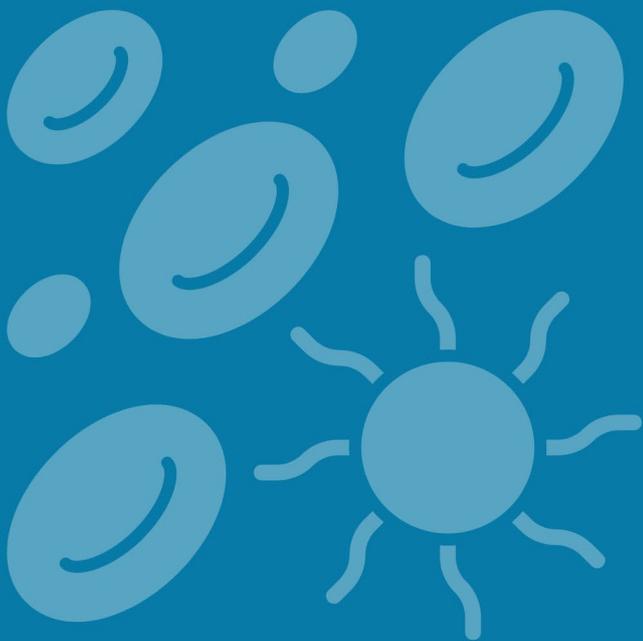




National
Cancer
Registry
Ireland

HAEMATOLOGICAL MALIGNANCIES

Cancer Trends Report 2024



THE NATIONAL CANCER REGISTRY



www.ncri.ie

ABBREVIATIONS

95%CI: 95% confidence interval
95%PI: 95% prediction interval
AAPC: average annual percentage change
APC: annual percentage change
AL: acute leukaemia
AML: acute myeloid leukaemia
CLL: chronic lymphocytic leukaemia
CML: chronic myeloid leukaemia
CR: crude incidence rate
EASR: age-standardized incidence rate according to 2013 European Standard Population
HDCN: Histiocytic and dendritic cell neoplasm
HL: Hodgkin lymphoma
HM / HMs: haematological malignancy / haematological malignancies
ICD-O: International Classification of Diseases for Oncology
IQR: interquartile range
MDS: myelodysplastic syndromes
MPN: myeloproliferative neoplasms
NHL: non-Hodgkin lymphoma
NOS: not otherwise specified

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INTRODUCTION

Haematological malignancies (HMs) are the fourth most frequently diagnosed cancers worldwide [1]. The average annual incidence for HMs in Ireland was 2,392 cases per year during 2019-2021, or about 10% of all invasive cancers (excl. NMSC) which is in the same range as colorectal cancer (2,560 cases/year) and lung cancer (2,586 cases/year) [2].

Haematological malignancies (HMs) originate in the cells of the immune system or in blood-forming tissue, such as the bone marrow. The broadest categories of HMs are lymphoma, myeloma, and leukaemia. Lymphomas start in the lymphatic system, the part of the immune system that fights infection. Because lymphoid tissue is found throughout the body, lymphoma can originate in many locations. The two main types are Hodgkin lymphoma and non-Hodgkin lymphoma. Myeloma is a cancer of the plasma cells (mature B-cells), the white blood cells that secrete immunoglobulins (antibodies). Leukaemia is a cancer of the blood cells and bone marrow. There are several types of leukaemia, grouped by whether it grows faster (acute) or slower (chronic) and whether it originates in lymphoid cells or myeloid cells, i.e., red blood cell or platelet stem cells in the bone marrow.

Our understanding of how and what causes these cancers to occur has improved greatly in recent decades. As a result, the way these cancers are classified has changed resulting in multiple classification updates. Currently, the World Health Organization (WHO) classification provides a consensus classification for clinical and pathologic use [3]. The WHO classification of HMs was collated and refined for population-based cancer registries through the HAEMACARE working group to present complete and accurate data for the full spectrum of HMs [4].

The aim of this report is to provide a similar summary of incidence, incidence trends (1994-2021) and compare survival for 26 subsets of HMs diagnosed in adults and children in Ireland during two consecutive periods (1994-2007 and 2008-2021) using population-based cancer registry data from the Republic of Ireland in order to inform public health, policy, and identify gaps for future research.

1. REPORT AT A GLANCE

What are haematological malignancies (HMs)?

Haematological malignancies (or '*blood cancers*') originate in the cells of the immune system or in blood-forming tissue in the bone marrow.

What causes haematological malignancies?

HMs develop due to a combination of genetic and environmental factors. Ultimately, blood cancers are caused by changes (mutations) in DNA within blood cells which start behaving abnormally.

What are the main types of HMs?

There are several ways of classifying HM. We used the WHO classification. Below are the different categories in order of the most to the least common.

1. Non-Hodgkin lymphoma
2. Leukaemia
3. Immunoproliferative and other/unspecified neoplasms
4. Multiple myeloma
5. Hodgkin lymphoma

How many blood cancers are diagnosed in Ireland?

HMs comprised 10% of all invasive cancers (excl. non-melanoma skin cancer), or 2,392 HM cases per year during 2019-2021. On a case basis, male cases outnumbered female cases by 35%.

Broad types of haematological malignancies	average annual* cases diagnosed 2019-2021	% of all blood cancers
All haematological malignancies	2,392	100%
Non-Hodgkin lymphoma	832	34.8%
Leukaemia	542	22.7%
Immunoproliferative & other/unspecified neoplasms	469	19.6%
Multiple myeloma	392	16.4%
Hodgkin lymphoma	156	6.5%

*Annual average cases are subject to rounding

How many deaths due to blood cancers occur in Ireland?

Deaths due to haematological malignancies (HMs) accounted for 8.5% of all cancer deaths during 2019-2021, or 833 deaths per year. Male deaths outnumbered female deaths by 44%, or 149 more deaths per year during 2019-2021

Broad types of haematological malignancies	average annual* deaths 2019-2021	% of all blood cancers
All HMs	833	100%
Non-Hodgkin lymphoma	287	34.5%
Leukaemia	276	33.1%
Multiple myeloma	190	22.8%
Immunoproliferative & other/unspecified neoplasms	57	6.9%
Hodgkin lymphoma	22	2.7%

*Annual average cases are subject to rounding

What is the chance of being diagnosed with a blood cancer in Ireland?

Broad types of haematological malignancies	Risk of diagnosis before 75th birthday (2019-2021) [2]	
	males	females
Any haematological malignancy	1 in 32	1 in 42
Non-Hodgkin lymphoma	1 in 88	1 in 119
Leukaemia	1 in 132	1 in 194
Multiple myeloma	1 in 190	1 in 269
Immunoproliferative and other/unspecified haematological neoplasms	1 in 196	1 in 234
Hodgkin lymphoma	1 in 439	1 in 491

At what age do blood cancers occur?

Blood cancers can occur at any age but occur mostly in older persons (>60). The typical age at diagnosis (or death) for any cancer is referred to as the '*median age*', and the typical range ('*interquartile range*') is the range of ages between which 50% of incident cases (or deaths) occur.

Type of HM	Median age (2019-2021)			
	...at diagnosis		...at death	
	age	range	age	range
All haematological malignancies	68	[55-77]	78	[70-84]
Multiple myeloma	70	[61-78]	77	[70-84]
Immunoproliferative & other/unspecified neoplasms	71	[61-79]	82	[76-87]
Non-Hodgkin lymphoma	67	[57-76]	78	[70-83]
Leukaemia	67	[52-77]	77	[68-84]
Hodgkin lymphoma	39	[25-61]	77	[71-84]

During the 10-year period 2012-2021, 696 cases of blood cancer were diagnosed in children (0 to <15 years) which comprised 3% of all blood cancer diagnosed during that period.

Are blood cancers increasing in Ireland?

Trends in incidence and mortality rates of blood cancers adjusted for population size and age: 1994-2021

The number of blood cancers has increased as might be expected, corresponding with the increase in population and average age over the last three decades. Rather than just look at numbers of blood cancer cases (or deaths) over time, a better way to understand trends is to look at rates (i.e. the number of new cases of HM or deaths for every 100,000 people). This adjusts for population increase and the upshift in age profile in the population over time.

For blood cancers overall, in males, the incidence rate was stable during 2005-2019 (APC=+0.1%). In females, the incidence rate increased during 1994-2019 (+0.9%). The mortality rate declined significantly from year 1999 in males (-1.3%) and from year 2000 in females (-1.5%).

Incidence rates for Hodgkin lymphoma increased in males (+1.9%) and females (+1.7%) during 1994-2019. Whereas rates for non-Hodgkin lymphoma stabilised after year 2014 in males (-1.3%), and after year 2013 in females (-2.1%).

Incidence rates for leukaemia declined significantly from year 2004 in males (-1.5%) and from year 2009 in females (-2.4%).

Incidence rates for multiple myeloma increased in males (+0.7%) and stabilised in females during 1994-2019 (+0.6%).

For the broad subtypes of blood cancer, mortality rates in males declined for Hodgkin lymphoma (-2.2%) and multiple myeloma (-1.2%) and were stable for non-Hodgkin lymphoma (-0.4%) and leukaemia (-1.0%).

Mortality rates in females declined for non-Hodgkin lymphoma (-1.5%), multiple myeloma (-1.2%) and leukaemia (-2.5%) and was stable for Hodgkin lymphoma (-0.5%).

Deaths attributable to immunoproliferative and other/unspecified blood cancers comprised <7% of all blood cancer deaths during 2019-2021. Yet mortality increased for this subtype possibly due to refinements in death cert coding practice where deaths previously attributed to 'leukaemia' or 'lymphoma' in the 1990s and early 2000s were assigned to immunoproliferative and other/unspecified blood cancers from the late 2000s.

MALE RATES

	<u>Incidence</u>	<u>Mortality</u>
ALL BLOOD CANCERS	2005-2019 ↔	1999-2021 ↓
Rate increasing		
HODGKIN LYMPHOMA	1994-2019 ↑	1994-2021 ↓
MULTIPLE MYELOMA	1994-2019 ↑	1994-2021 ↓
Rate static		
NON-HODGKIN LYMPHOMA	2014-2019 ↔	1994-2021 ↔
IMMUNOPROLIFERATIVE & OTHER/UNSPECIFIED	2005-2019 ↔	1994-2021 ↑
Rate decreasing		
LEUKAEMIA	2004-2019 ↓	2009-2021 ↔

FEMALE RATES

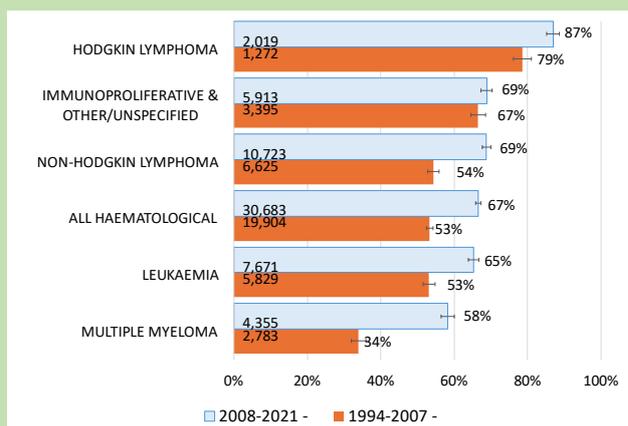
	<u>Incidence</u>	<u>Mortality</u>
ALL BLOOD CANCERS	1994-2019 ↑	2000-2021 ↓
Rate increasing		
HODGKIN LYMPHOMA	1994-2019 ↑	1994-2021 ↔
IMMUNOPROLIFERATIVE & OTHER/UNSPECIFIED	2014-2019 ↑	1994-2021 ↑
Rate static		
NON-HODGKIN LYMPHOMA	2013-2019 ↔	2000-2021 ↓
MULTIPLE MYELOMA	1994-2019 ↔	1994-2021 ↓
Rate decreasing		
LEUKAEMIA	2009-2019 ↓	1999-2021 ↓

Trend: ↑=significant increase, ↓=significant decrease, ↔=no change (static/ stable). Incidence period 1994-2019 (26 years); mortality period 1994-2021 (28 years). The most recent stable trends and the years they span are shown.

Is blood cancer survival improving?

The conventional measure that cancer registries quote is the proportion of cases that survive their cancer up to 5 years after diagnosis ('5-year net survival').

5-year net survival (%) for haematological malignancies: 2008-2021 vs. 1994-2007



Numbers at base of bars represent number of cases

Percentage point improvement in 5-year net survival: 2008-2021 vs. 1994-2007

ALL HAEMATOLOGICAL (all blood cancers)	+14%
MULTIPLE MYELOMA	+24%
NON-HODGKIN LYMPHOMA	+15%
LEUKAEMIA	+12%
HODGKIN LYMPHOMA	+8%
IMMUNOPROLIFERATIVE & OTHER/UNSPECIFIED	+2%

The greatest improvement in 5-year net survival between 1994-2007 and 2008-2021 was seen for multiple myeloma (+24 percentage point (pp) improvement), followed by leukaemia (+12 pp), non-Hodgkin lymphoma (+15 pp) and Hodgkin lymphoma (+8 pp). Survival for immunoproliferative and other/unspecified HMs improved by +2 pp.

For all blood cancers combined, for cases diagnosed during 1994-2007, the proportion that survived their cancer at the five-year mark was 53%. The equivalent figure for those diagnosed during the more recent period (2008-2021) was 67%, a 14-percentage point improvement over the earlier period.

Of the broad subtypes of blood cancers, Hodgkin lymphoma showed the highest 5-year survival during 2008-2021 (87%), followed by immunoproliferative & other unspecified blood cancers (69%), non-Hodgkin lymphoma (69%), leukaemia (65%) and multiple myeloma (58%).

How many persons are living with a blood cancer diagnosis?

The number of persons living with a cancer diagnosis is known as the 'prevalent population'. The NCRI began cancer registration in 1994, and it currently holds 28 years of information on cancer cases up to the end of 2021. At the time of writing, 31/12/2021 was the most recent date for which we know if a cancer case was still alive or not.

Number and percentage of cancer survivors in Ireland diagnosed during 1994-2021

	number alive on 31/12/2021	% of all cancer survivors	% of all survivors of haematological malignancies
All invasive cancers (excl. NMSC)	201,608	100%	
All haematological malignancies	23,010	11.4%	100%
non-Hodgkin lymphoma	8,465	4.2%	36.8%
leukaemia	5,817	2.9%	25.3%
Immunoproliferative and other/unspecified	3,901	1.9%	17.0%
Hodgkin lymphoma	2,525	1.3%	11.0%
Multiple myeloma	2,302	1.1%	10.0%

Of all invasive cancer cases (excl. NMSC) diagnosed since the NCRI was established, 201,608 were still alive at the end of 2021 of which 23,010 (11.4%) were blood cancer survivors.

Of 23,010 blood cancer survivors, 8,465 (36.8%) were survivors of non-Hodgkin lymphoma, 5,817 (25.3%) were survivors of leukaemia, 3,901 (17.0%) were survivors of Immunoproliferative and other/unspecified HMs, 2,525 (11.0%) were survivors of Hodgkin lymphoma and 2,302 (10.0%) were survivors of multiple myeloma.

2. INCIDENCE

Classification of haematological malignancies

The published HAEMACARE classification scheme of HMs has 110 distinct HMs based on ICD-O3 morphology codes [4]. For the purposes of this report we have condensed the published HAEMACARE classification into 26 broad categories by pooling closely related distinct morphologies as described in a recent study conducted by the Belgian cancer registry [5] (Table 2-1).

We also present our findings for the broadest ICD10 classification of HMs in parallel, as these broad HM groupings are often referred to in the literature (i.e., C81 Hodgkin lymphoma, C82-85 NHL, C90 multiple myeloma, C91-95 leukaemia and C88,C96,D47 immunoproliferative & other/unspecified neoplasms).

Table 2-1. Haematological malignancy grouping scheme overview

HM subtype	Topography	Morphology	Behaviour	Grade	ICD10
1) HL, Hodgkin lymphoma	Any	9650-9655,9659,9661-9665,9667	3	Any	C81 Hodgkin lymphoma
2) CLL/SLL, B-cell chronic lymphocytic leukaemia/ small lymphocytic lymphoma	Any	9670,9823	3	Any	C91-95 leukaemia
3) HCL, Hairy cell leukaemia	Any	9940	3	Any	C91-95 leukaemia
4) Other MBCL, Other Mature B-cell leukaemia and related lymphoma	Any C420-C421	9833 9591	3 3	Any 6	C82-85 NHL C82-85 NHL
5) IPD, Immunoproliferative disease	Any	9671,9760-9762,9764	3	Any	C88,C96,D47 immunoproliferative & other/unspecified
6) PCN, Plasma cell neoplasm	Any	9731-9734	3	Any	C90 multiple myeloma
7) MZL, Marginal zone lymphoma	Any	9689,9699	3	Any	C82-85 NHL
8) FL, Follicular lymphoma and related lymphoma	Any	9597,9690,9691,9695,9698	3	Any	C82-85 NHL
9) MCL, Mantle cell lymphoma	Any	9673	3	Any	C82-85 NHL
10) DLBCL, Diffuse large B-cell lymphoma and related large B-cell lymphoma	Any	9675,9678-9680,9684,9688,9712, 9735,9737,9738,9766	3	Any	C82-85 NHL
11) BL, Burkitt lymphoma / leukaemia	Any	9687,9826	3	Any	C82-85 NHL
12) pCTCL, Primary cutaneous T-cell lymphoma	Any	9700-9701,9709,9718,9726	3	Any	C82-85 NHL
13) PNK/TCL, Peripheral NK/T-cell lymphoma	Any	9702,9705,9708,9714,9717,9719, 9724,9827, 9831,9834,9948	3	Any	C82-85 NHL
14) ALL/LL, Precursor Lymphoid neoplasm or acute lymphoblastic leukaemia / lymphoma	Any	9811-9819,9727-9729,9835-9837	3	Any	C91-95 leukaemia
15) AML, Acute myeloid leukaemia and related pre-cursor neoplasm (includes acute leukaemia of ambiguous lineage)	Any	9801,9805-9809,9840,9861, 9865-9867, 9869-9874, 9877-9879,9891,9895-9898, 9910-9912,9920, 9930,9931,9984,9987	3	Any	C91-95 leukaemia
16) CML, Chronic myeloid leukaemia	Any	9863,9875	3	Any	C91-95 leukaemia
17) PV, Polycythaemia vera	Any	9950	3	Any	C88,C96,D47 immunoproliferative & other/unspecified
18) ET, Essential thrombocythemia	Any	9962	3	Any	C88,C96,D47 immunoproliferative & other/unspecified
19) PMF, Primary myelofibrosis	Any	9961	3	Any	C88,C96,D47 immunoproliferative & other/unspecified
20) Other MPN, Other myeloproliferative and related neoplasm	Any	9960,9963-9968	3	Any	C88,C96,D47 immunoproliferative & other/unspecified
21) MCN, Mast cell neoplasm	Any Any	9740-9742,9749 9740,9741	3 1	Any Any	C88,C96,D47 immunoproliferative & other/unspecified
22) MDS, Myelodysplastic syndrome	Any	9980,9982,9983,9985,9986, 9989, 9991-9993	3	Any	C88,C96,D47 immunoproliferative & other/unspecified
23) MDS/MPN Myelodysplastic / myeloproliferative neoplasm	Any	9876,9945,9946,9975	3	Any	C91-95 leukaemia
24) HDCN, Histiocytic and dendritic cell neoplasm	Any Any	9750,9751,9754-9759 9751-9753	3 1	Any Any	C88,C96,D47 immunoproliferative & other/unspecified
25) Other leukaemia	Any	9800,9860	3	Any	C91-95 leukaemia
26) Other lymphoid neoplasm	Any C000-C419, C422-C809 C420-C421	9590,9596,9820,9832 9591 9591	3 3 3	Any 1-5 7-9	C82-85 NHL

Incidence of haematological malignancies

Table 2-2.
Haematological malignancies as a proportion of all invasive cancers (excl. NMSC), by diagnosis period and sex

Diagnosis period	males	females	Total
1994-1998	10.4%	9.2%	9.8%
1999-2003	10.9%	9.1%	10.1%
2004-2008	11.0%	9.5%	10.3%
2009-2013	10.7%	9.3%	10.0%
2014-2018	11.2%	9.1%	10.3%
2019-2021	10.5%	9.0%	9.8%

The proportion of HMs relative to all invasive cancers (excl. NMSC) was relatively stable since the establishment of the NCRI in 1994. This proportion ranged from 9.8% during 1994-1998 to 10.3% during 2014-2018, approximately 10% overall, (Table 2-2).

Table 2-3.
Broad categories of HMs as a percentage of all haematological malignancies: 2019-2021

	Males		Females		Total		MF ratio
	annual average cases	% of all HMs	annual average cases	% of all HMs	annual average cases	% of all HMs	
All haematological malignancies (ICD10, C81-85, C88, C90-96, D47)	1,375	100.0%	1,017	100.0%	2,392	100.0%	1.35
Hodgkin lymphoma (C81)	83	6.0%	73	7.2%	156	6.5%	1.14
Non-Hodgkin lymphoma (C82-85)	479	34.9%	353	34.7%	832	34.8%	1.36
Multiple myeloma (C90)	229	16.6%	163	16.1%	392	16.4%	1.40
Leukaemia (C92-95)	330	24.0%	213	20.9%	542	22.7%	1.55
Immunoproliferative and other/unspecified neoplasms (C88, C96, D47)	255	18.5%	214	21.0%	469	19.6%	1.19

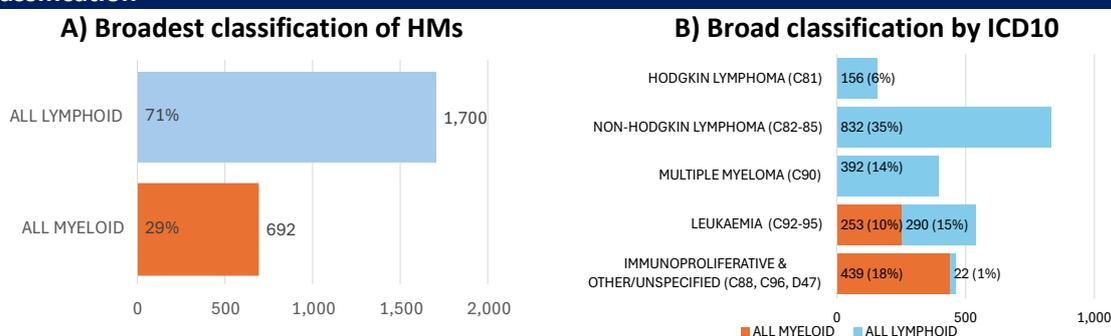
Annual average case counts are subject to rounding

The annual average number of all invasive cancer cases (excl. NMSC) diagnosed during 2019-2021 was 24,424. Haematological malignancies accounted for 9.8% (2,392 cases) of all invasive cancers (excl. NMSC) diagnosed during the same period. Non-Hodgkin lymphoma comprised 34.8% of all HMs, followed by leukaemia (22.7%), immunoproliferative and other/ unspecified (19.6%) and Hodgkin lymphoma (6.5%), (Table 2-3).

As for cancer in general, there were more males than female HM cases, with a male to female case ratio of 1.35 for all HMs combined. Leukaemia had the highest M:F ratio (1.55), or there were 55% more male cases of leukaemia than female cases.

Distribution of haematological malignancies

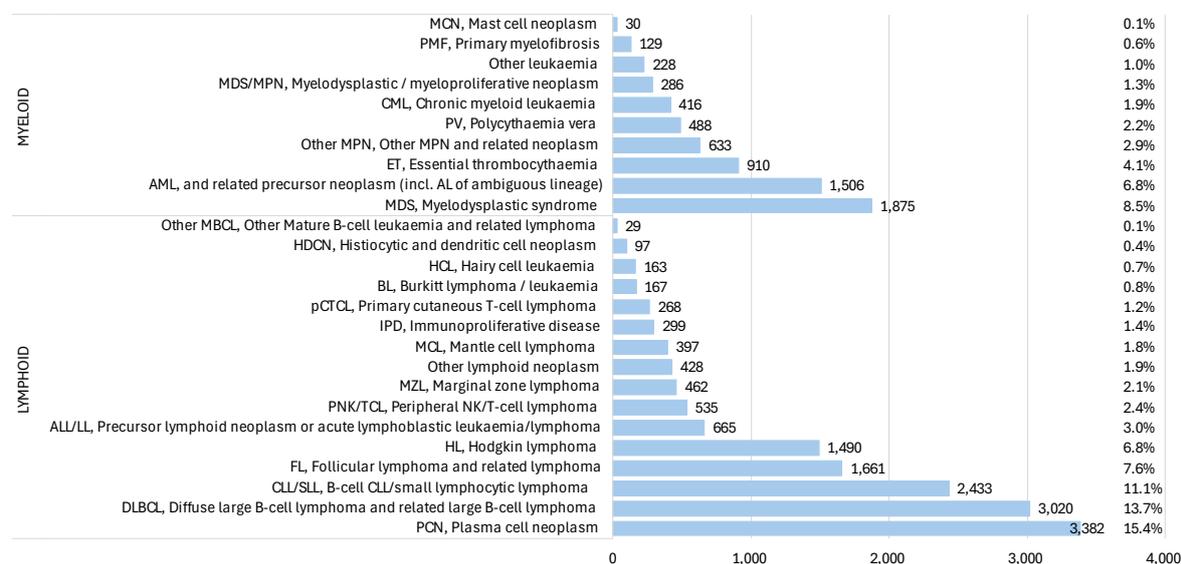
Figure 2-1.
Annual average cases (%) of haematological malignancies diagnosed during 2019-2021, by sub-classification



During 2019-2021, myeloid neoplasms comprised 29% of all HMs, or an annual average of 692 cases per year. Lymphoid neoplasms comprised 71% of all HMs, or an annual average of 1,700 cases per year (Figure 2-1 A).

Looking at incidence of HMs by ICD10 classification, Hodgkin lymphoma, Non-Hodgkin, and Multiple myeloma all originate in lymphoid tissue, whereas leukaemia is almost equally split between lymphoid and myeloid tissue in their origin (Figure 2-1 B).

Figure 2-2.
Incident cases of haematological malignancies by HAEMACARE classification: number, rank and percentage of all HMs diagnosed during 2012-2021



During the most recent 10-year period (2012-2021) for which the NCRI has complete incidence data, *plasma cell neoplasm (multiple myeloma)* was the most common HM diagnosed and comprised 15.4% of all HMs diagnosed, followed by *diffuse large cell lymphoma* (13.7%), *B-cell CLL/small cell lymphocytic lymphoma* (11.1%), *myelodysplastic syndrome* (8.5%) and *follicular lymphoma* (7.6%), (Figure 2-2).

The top 10 (of 26) incident HMs according to a condensed HAEMACARE classification [5] accounted for 77% of all HMs diagnosed during 2012-2021 (Figure 2-2, Table 2-4).

Table 2-4.
Top 10 most common HM subsets:
case numbers and % of all HMs diagnosed during 2012-2021

rank	HAEMACARE classification	No. (%)
	All haematological malignancies	22,952 (100%)
1	PCN, Plasma cell neoplasm (multiple myeloma)	3,382 (14.7%)
2	DLBCL, Diffuse large B-cell lymphoma and related large B-cell lymphoma	3,020 (13.2%)
3	CLL/SLL, B-cell CLL/small lymphocytic lymphoma	2,433 (10.6%)
4	MDS, Myelodysplastic syndrome	1,875 (8.2%)
5	FL, Follicular lymphoma and related lymphoma	1,661 (7.2%)
6	AML, and related precursor neoplasm (incl. acute leukaemia (AL) of ambiguous lineage)	1,506 (6.6%)
7	HL, Hodgkin lymphoma	1,490 (6.5%)
8	ET, Essential thrombocythemia	910 (4.0%)
9	ALL/LL, Precursor lymphoid neoplasm or acute lymphoblastic leukaemia/lymphoma	665 (2.9%)
10	Other MPN, Other MPN and related neoplasm	633 (2.8%)

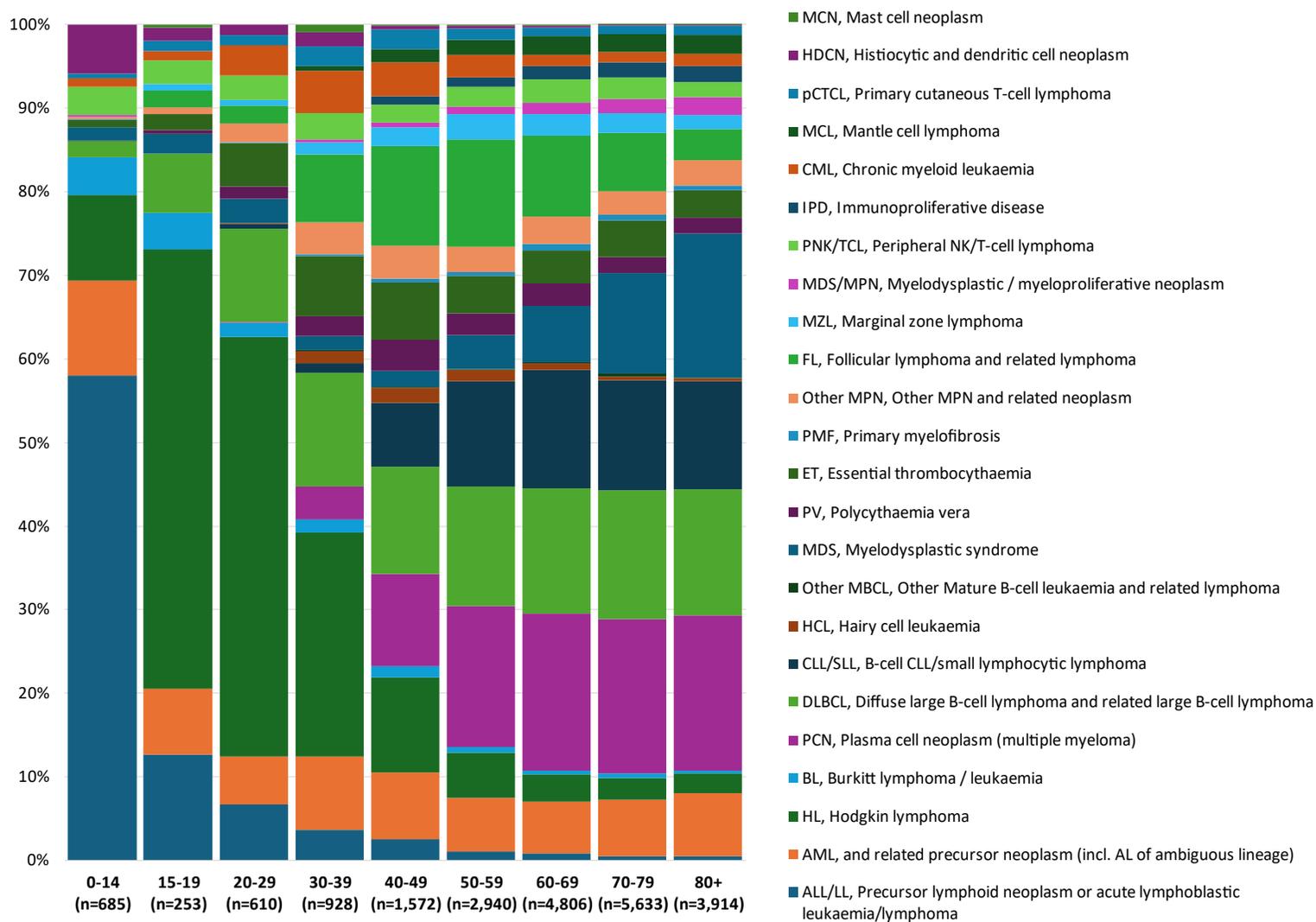
During 2012-2021, 696 HMs were diagnosed in children (<15 years old) which accounted for 12.7% of all HMs diagnosed during that period.

The top five HMs accounting for 88% of all HMs diagnosed in children were: *ALL/LL, Precursor lymphoid neoplasm or acute lymphoblastic leukaemia/lymphoma* (57% of all HMs in children), *AML, and related precursor neoplasm* (11%), *HL, Hodgkin lymphoma* (10%), *HDCN, Histiocytic and dendritic cell neoplasm* (6%) and *BL, Burkitt lymphoma/leukaemia* (4%), (Table 2-5).

Table 2-5.
Top 5 most common HM subsets in children (0 to <15 years):
case numbers and % of all HMs diagnosed in children (0 to <15 years) during 2012-2021

rank	HAEMACARE classification	No. (%)
	All haematological malignancies in children (0 to <15 years)	696 (100%)
1	ALL/LL, Precursor lymphoid neoplasm or acute lymphoblastic leukaemia/lymphoma	397 (57%)
2	AML, and related precursor neoplasm (incl. AL of ambiguous lineage)	78 (11%)
3	HL, Hodgkin lymphoma	70 (10%)
4	HDCN, Histiocytic and dendritic cell neoplasm	40 (6%)
5	BL, Burkitt lymphoma / leukaemia	31 (4%)

Figure 2-3.
Incidence of HM, by age group: absolute number and percentage of cases diagnosed, 2012-2021 ¹



¹ This graph excludes HM sub-categories with less specific morphologies, i.e. 'other leukaemia' and 'other lymphoid neoplasms' which together comprised <3% of all HMs during 2012-2021

Although almost all HM types can be diagnosed at any age, the majority are diagnosed in adults with incidence increasing with age.

ALL/LL, Precursor lymphoid neoplasm was the most frequently diagnosed HM (57%) in children (<15 years) during 2012-2021, followed by *HL Hodgkin lymphoma*, which is the predominant HM in adolescents (15-19 years) and young adults (20 to 39 years) (53% and 50% of all HM diagnosis, respectively). From the age of 40 upwards, the most common HM types are *PCN, Plasma cell neoplasm (multiple myeloma)* (18%), *DLBCL, Diffuse large B-cell lymphoma* (15%), *CLL/SLL B-cell CLL/small lymphocytic lymphoma* (13%), and *MDS, Myelodysplastic syndrome* (10%), and *FL, Follicular lymphoma and related lymphoma* (8%), (Figure 2-3).

Table 2-6.
Distribution of incident cases, and incidence rates of HMs diagnosed during 2012-2021

ICD10 HM grouping	cases No.	%	CR	95%CI	EASR	95%CI
ALL HAEMATOLOGICAL MALIGNANCIES	22,952	100%	47.9	[45.9-49.9]	62.5	[59.9-65.2]
NON-HODGKIN LYMPHOMA (ICD10, C82-85)	8,069	35.2%	16.8	[15.7-18.0]	22.1	[20.5-23.6]
MULTIPLE MYELOMA (ICD10, C90)	3,382	14.7%	7.05	[6.29-7.79]	9.6	[8.56-10.6]
LEUKAEMIA (ICD10, C91-95)	5,550	24.2%	11.61	[10.6-12.5]	14.9	[13.6-16.1]
IMMUNOPROLIFERATIVE & OTHER/UNSPECIFIED (ICD10, C88, C96, D47)	4,459	19.4%	9.31	[8.4-10.1]	12.6	[11.4-13.8]
HAEMACARE CLASSIFICATION						
PCN, Plasma cell neoplasm	3,382	14.7%	7.05	[6.29-7.79]	9.61	[8.56-10.65]
DLBCL, Diffuse large B-cell lymphoma and related large B-cell lymphoma	3,020	13.2%	6.31	[5.59-7.02]	8.36	[7.39-9.31]
CLL/SLL, B-cell CLL/small lymphocytic lymphoma	2,433	10.6%	5.10	[4.46-5.74]	7.03	[6.13-7.91]
MDS, Myelodysplastic syndrome	1,875	8.2%	3.92	[3.36-4.48]	5.73	[4.90-6.55]
FL, Follicular lymphoma and related lymphoma	1,661	7.2%	3.48	[2.94-4.00]	4.37	[3.69-5.04]
AML, and related precursor neoplasm (incl. AL of ambiguous lineage)	1,506	6.6%	3.14	[2.64-3.64]	4.04	[3.37-4.70]
HL, Hodgkin lymphoma (ICD10, C81)	1,490	6.5%	3.11	[2.61-3.61]	3.33	[2.78-3.88]
ET, Essential thrombocythemia	910	4.0%	1.89	[1.50-2.27]	2.40	[1.90-2.89]
ALL/LL, Precursor lymphoid neoplasm or acute lymphoblastic leukaemia/lymphoma	665	2.9%	1.39	[1.05-1.7]	1.25	[0.93-1.55]
Other MPN, Other MPN and related neoplasm	633	2.8%	1.32	[0.99-1.64]	1.73	[1.29-2.10]
PNK/TCL, Peripheral NK/T-cell lymphoma	535	2.3%	1.12	[0.81-1.41]	1.41	[1.02-1.79]
PV, Polycythaemia vera	488	2.1%	1.02	[0.73-1.29]	1.30	[0.92-1.66]
MZL, Marginal zone lymphoma	462	2.0%	0.97	[0.68-1.24]	1.26	[0.88-1.62]
Other lymphoid neoplasm	428	1.9%	0.89	[0.62-1.14]	1.21	[0.84-1.57]
CML, Chronic myeloid leukaemia	416	1.8%	0.87	[0.60-1.13]	1.04	[0.71-1.36]
MCL, Mantle cell lymphoma	397	1.7%	0.83	[0.57-1.08]	1.13	[0.77-1.48]
IPD, Immunoproliferative disease	299	1.3%	0.62	[0.40-0.84]	0.87	[0.55-1.17]
MDS/MPN, Myelodysplastic / myeloproliferative neoplasm	286	1.2%	0.60	[0.37-0.8]	0.85	[0.53-1.16]
pCTCL, Primary cutaneous T-cell lymphoma	268	1.2%	0.56	[0.34-0.76]	0.70	[0.42-0.96]
Other leukaemia	228	1.0%	0.48	[0.28-0.67]	0.73	[0.42-1.03]
BL, Burkitt lymphoma / leukaemia	167	0.7%	0.35	[0.16-0.5]	0.38	[0.19-0.56]
HCL, Hairy cell leukaemia	163	0.7%	0.34	[0.17-0.50]	0.41	[0.20-0.61]
PMF, Primary myelofibrosis	129	0.6%	0.27	[0.12-0.41]	0.37	[0.17-0.57]
HDCN, Histiocytic and dendritic cell neoplasm	97	0.4%	0.20	[0.07-0.32]	0.19	[0.06-0.31]
MCN, Mast cell neoplasm	30	0.1%	0.06	[0.01-0.13]	0.07	[0.01-0.14]
Other MBCL, Other Mature B-cell leukaemia and related lymphoma	29	0.1%	0.06	[0.01-0.12]	0.08	[0.01-0.16]

95%CI: 95% confidence interval; CR: crude rate; EASR: European age-standardized incidence rate per 100,000 weighted using the European standard population (ESP) 2013.

The crude rate for all HMs during 2012-2021 was 47.9 cases per 100,000 and 62.5 cases per 100,000 for age-standardised rates (Table 2-6). Similar tables are presented for males and females separately in Appendix I.

The NCRI quotes rates, age-weighted by the European standard population (ESP), to allow comparisons over time and between different European countries and registries. When applying 2013 ESP age weights relatively more weight is given to older age groups, which are more prone to developing HMs (the median age at diagnosis for all HMs combined, was 68 in both males and females in Ireland during 2019-2021). This results in an upward shift in age-standardised rates relative to crude rates [6].

Table 2-7. Ranked male/female incidence rate ratio 2012-2021, by HM subset

A) ICD10 broad classification		B) Condensed HAEMACARE classification	
	M:F ratio		M:F ratio
LEUKAEMIA (ICD10, C91-95)	1.86	HCL , Hairy cell leukaemia	5.38
MULTIPLE MYELOMA (ICD10, C90)	1.66	MCL , Mantle cell lymphoma	3.33
ALL HAEMATOLOGICAL	1.56	BL , Burkitt lymphoma / leukaemia	2.65
IMMUNOPROLIFERATIVE & OTHER/ UNSPECIFIED (ICD10, C88, C96, D47)	1.51	MDS/MPN , Myelodysplastic / myeloproliferative neoplasm	2.64
NON-HODGKIN LYMPHOMA (ICD10, C82-85)	1.40	CLL/SLL , B-cell CLL/small lymphocytic lymphoma	2.19
		IPD , Immunoproliferative disease	2.05
		PMF , Primary myelofibrosis	1.99
		MDS , Myelodysplastic syndrome	1.90
		pCTCL , Primary cutaneous T-cell lymphoma	1.81
		CML , Chronic myeloid leukaemia	1.72
		Other MBCL , Other Mature B-cell leukaemia and related lymphoma	1.69
		PCN , Plasma cell neoplasm (multiple myeloma)	1.66
		Other leukaemia	1.60
		AML , and related precursor neoplasm (incl. AL of ambiguous lineage)	1.52
		PNK/TCL , Peripheral NK/T-cell lymphoma	1.49
		DLBCL , Diffuse large B-cell lymphoma and related large B-cell lymphoma	1.44
		Other lymphoid neoplasm	1.42
		PV , Polycythaemia vera	1.38
		HL , Hodgkin lymphoma	1.32
		ALL/LL , Precursor lymphoid neoplasm or acute lymphoblastic leukaemia/lymphoma	1.31
		Other MPN , Other MPN and related neoplasm	1.25
		HDCN , Histiocytic and dendritic cell neoplasm	1.16
		FL , Follicular lymphoma and related lymphoma	1.03
		ET , Essential thrombocythemia	0.91
		MZL , Marginal zone lymphoma	0.87
		MCN , Mast cell neoplasm	0.79

For almost all subsets of HMs, more males were diagnosed than females on a rate basis during 2012-2021. For example, the male to female ratio of all haematological malignancies combined was 1.56, i.e., the male incidence rate for all HMs was 56% greater than that of females. The increased incidence in males was more marked for leukaemia (M:F ratio was 1.86), Table 2-7A.

For the HAEMACARE subsets of HMs, the top five HMs where male cases predominate were: *Hairy cell leukaemia* (5.38) (i.e., the incidence rate in males was 438% greater than females), *Mantle cell lymphoma* (3.33), *Burkitt lymphoma / leukaemia* (2.65), *Myelodysplastic / myeloproliferative neoplasm* (2.64), and *CLL/SLL, B-cell CLL/small lymphocytic lymphoma* (2.19). The categories of HMs where the female rate was higher than males include *Mast cell neoplasm* (0.79), *Marginal zone lymphoma* (0.87) and *Essential thrombocythemia* (0.91), Table 2-7B.

Age at diagnosis for subsets of haematological malignancies

Table 2-8.
Median age at diagnosis of HMs during 2019-2021, by sex and ranked from youngest to oldest

ICD10 broad categories of HMs	males		females		M&F	
	median age	IQR	median age	IQR	median age	IQR
ALL HAEMATOLOGICAL MALIGNANCIES	68	[55,77]	68	[55,78]	68	[55,77]
NON-HODGKIN LYMPHOMA (ICD10, C82-85)	67	[55,76]	68	[58,77]	67	[57,76]
LEUKAEMIA (ICD10, C91-95)	67	[54,77]	67	[49,78]	67	[52,77]
MULTIPLE MYELOMA (ICD10, C90)	70	[61,78]	71	[62,79]	70	[61,78]
IMMUNOPROLIFERATIVE & OTHER/UNSPECIFIED (ICD10, C88, C96, D47)	71	[61,79]	71	[58,80]	71	[60,79]
HAEMACARE categories of HMs						
ALL/LL , Precursor lymphoid neoplasm or acute lymphoblastic leukaemia/lymphoma	11	[4,38]	7	[3,37]	10	[3,38]
HDCN , Histiocytic and dendritic cell neoplasm	18.5	[4,56]	30	[4,46]	23	[4,47]
HL , Hodgkin lymphoma (ICD10, C81)	42	[26,61]	35	[24,60]	39	[25,61]
BL , Burkitt lymphoma / leukaemia	44	[18,63]	62.5	[22.5,73.5]	48	[19,68]
CML , Chronic myeloid leukaemia	58.5	[44,74]	56	[43,70]	57	[44,72]
MCN , Mast cell neoplasm	52	[36,60]	60	[38,65]	57.5	[37,65]
HCL , Hairy cell leukaemia	59	[49,68.5]	60	[46,76]	59	[48,70]
FL , Follicular lymphoma and related lymphoma	62	[51,72]	64	[56,72]	63	[53,72]
pCTCL , Primary cutaneous T-cell lymphoma	64	[47,76]	63	[48,73]	63.5	[48,75]
MZL , Marginal zone lymphoma	67	[56,74]	66	[57,76]	66	[57,75]
PV , Polycythaemia vera	63	[50,72]	68.5	[58,78]	66	[53,75]
ET , Essential thrombocythemia	66.5	[54,75]	65	[48,75]	66	[50,75]
PNK/TCL , Peripheral NK/T-cell lymphoma	65.5	[53,73]	67	[53,75]	67	[53,74]
AML , and related precursor neoplasm (incl. AL of ambiguous lineage)	68	[55,78]	66	[47,77]	67	[52,78]
Other MPN , Other MPN and related neoplasm	66.5	[55,76]	69	[53,78]	67	[54,77]
DLBCL , Diffuse large B-cell lymphoma and related large B-cell lymphoma	68	[57,77]	70	[59,78]	69	[58,77]
PMF , Primary myelofibrosis	69	[61,77]	69.5	[64,79]	69	[62,77]
CLL/SLL , B-cell CLL/small lymphocytic lymphoma	70	[61,77]	70	[62,79]	70	[61,78]
PCN , Plasma cell neoplasm	70	[61,78]	71	[62,79]	70	[61,78]
MCL , Mantle cell lymphoma	70	[61,78]	72	[62,80]	71	[62,79]
Other lymphoid neoplasm	71	[62,79]	72	[59,79]	71	[61,79]
IPD , Immunoproliferative disease	72	[64,80]	72.5	[62.5,80]	72	[64,80]
Other MBCL , Other Mature B-cell leukaemia and related lymphoma	67.5	[59,75]	78	[74,80]	74	[61,78]
MDS/MPN , Myelodysplastic / myeloproliferative neoplasm	74	[67,80]	74	[66,84]	74	[66,82]
MDS , Myelodysplastic syndrome	76	[69,82]	76	[68,83]	76	[68,82]
Other leukaemia	80	[68,87]	81	[74,88]	81	[70,87]

For all haematological malignancies combined the median age at diagnosis was 68 years during 2012-2021 (Males 68 years; Females 68 years). For HMs broadly classified by ICD10, the youngest median age at diagnosis was observed for *Hodgkin lymphoma*, 39 years (Males 42 years; Females 35 years), followed by *leukaemia*, 67 years (Males 67 years; Females 67 years), *non-Hodgkin lymphoma*, 67 years (Males 67 years; Females 68 years), *multiple myeloma* 70 years (Males 70 years; Females 71 years) and *immunoproliferative and other/ unspecified*, 71 years, (Males 71 years; Females 71 years). (Table 2-8).

Of the HAEMACARE classification, the top five with the youngest median age at diagnosis were: *ALL/LL, Precursor lymphoid neoplasm*, 10 years (Males 11 years; Females 7 years), *HDCN, Histiocytic and dendritic cell neoplasm*, 23 years (Males 18.5 years; Females 30 years), *Hodgkin lymphoma* 39 years, (Males 42 years; Females 35 years), *Burkitt lymphoma*, 48 years (Males 44 years; Females 62.5 years) and *Chronic myeloid leukaemia*, 57 years (Males 58.5 years; Females 56 years).

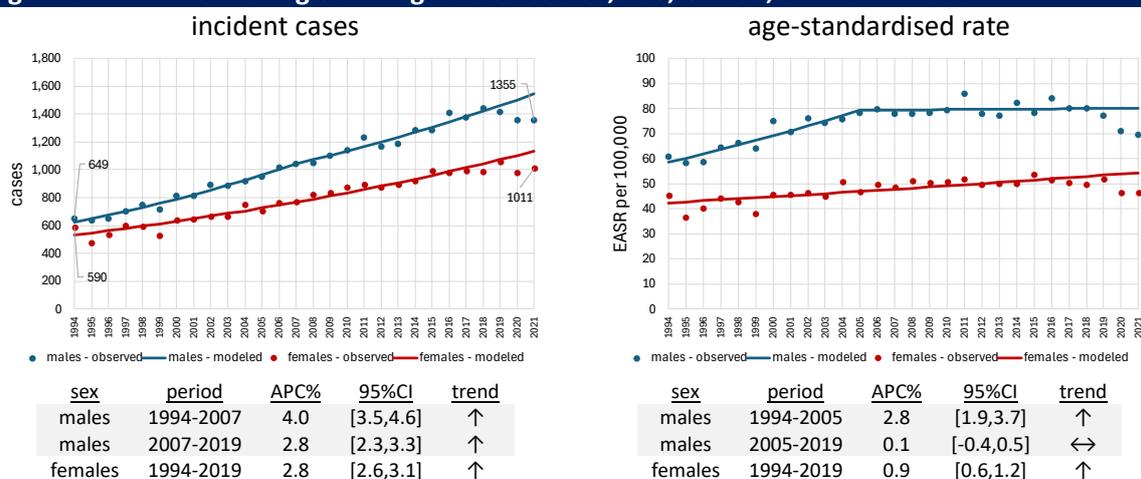
At the other end of the age spectrum, the oldest median age at diagnosis was observed for: *Other leukaemia* 81 years (Males 80 years; Females 81 years), *Myelodysplastic syndrome*, 76 years (Males 76 years; Females 76 years), *Myelodysplastic /myeloproliferative neoplasm* 74 years (Males 74 years; Females 74 years), *other Mature B-cell leukaemia and related lymphoma*, 74 years (Males 67.5 years; Females 78 years) and *Immunoproliferative disease*, 72 years (Males 72 years; Females 72.5 years), (Table 2-8).

Incidence trends of haematological malignancies: 1994-2021

Incidence trends for HMs were calculated for the period 1994-2019 using Joinpoint regression [7]. Even though the registry holds relatively complete incidence data for years 2020 and 2021, at the time of writing, data points for 2020 and 2021 were excluded from trend calculations due to the observed shortfall of diagnoses for leukaemia in 2020 [5], and non-Hodgkin lymphoma and leukaemia in 2021 [2] due to the COVID-19 pandemic, but data points for years 2020 and 2021 are included in the trend graphs below.

We have also summarised overall trends in incidence rates for the HAEMACARE subsets over the full 26-year period using the average annual percentage change (AAPC) metric of Joinpoint regression [7].

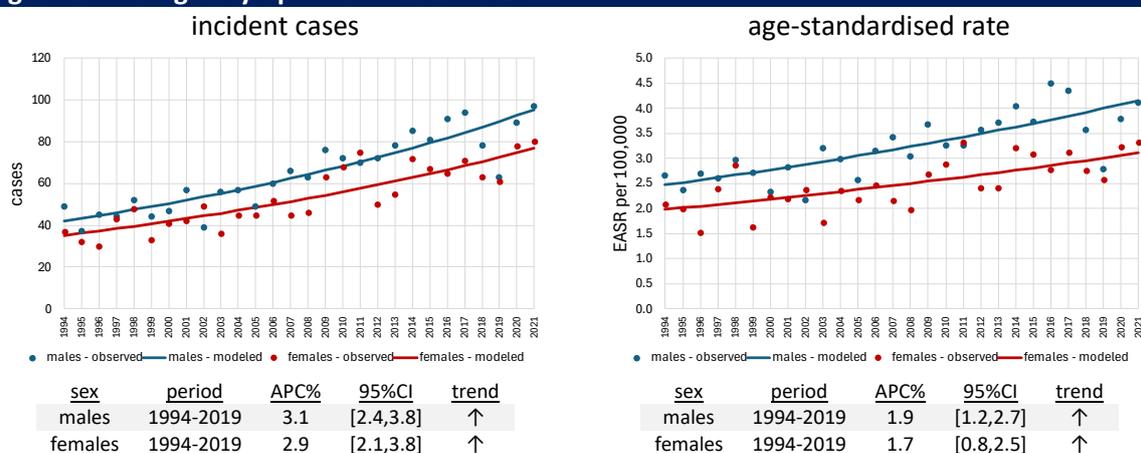
Figure 2-4. All haematological malignancies C81-85, C88, C90-96, D47: 1994-2021



APC%: annual percentage change. Trend: ↑=significant increase, ↓=significant decrease, ↔=no change (static) at the 95% level

Cases of HMs increased at +4.0% annually in males during 1994-2007, moderating to +2.8% annually during 2007-2019. The number of HMs increased consistently in females at +2.8% annually during the whole period (1994-2019). Adjusting for age and population size, rates of HMs in males stabilised during 2005-2019 (+0.1%) after a period of significant increase during 1994-2004, whereas the rate increased consistently and significantly at +0.9% annually in females during the whole period 1994-2019 (Figure 2-4).

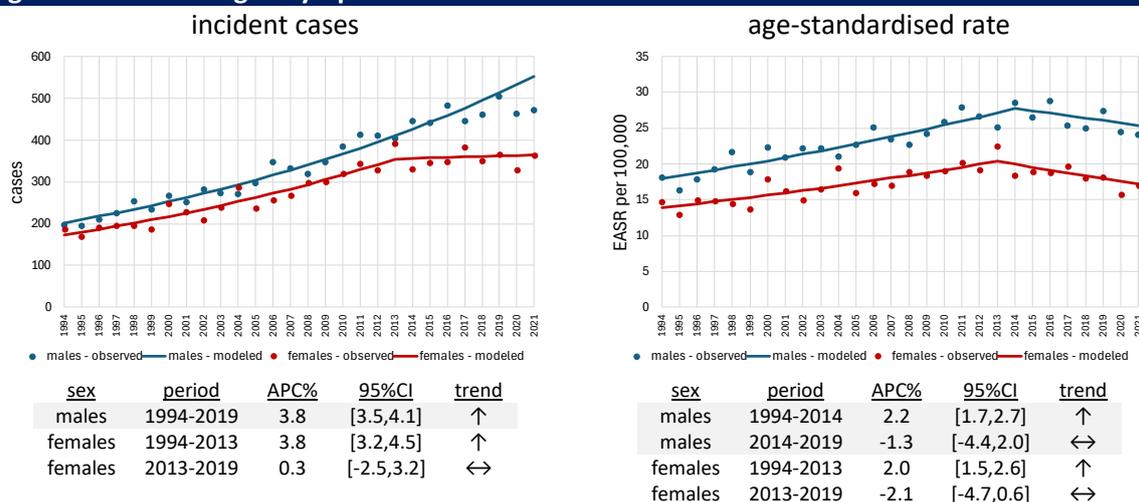
Figure 2-5. Hodgkin lymphoma C81: 1994-2021



Cancer trends No 41. Haematological malignancies

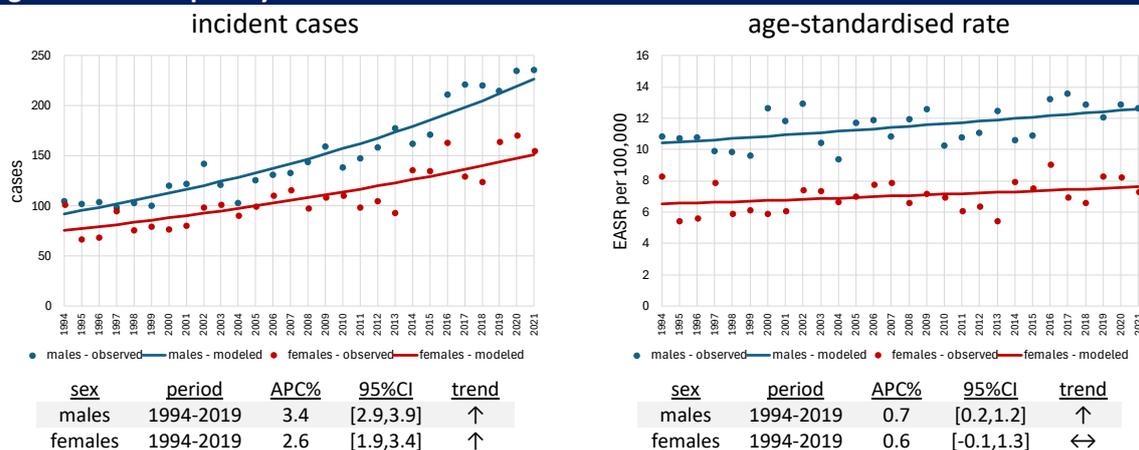
Cases of Hodgkin lymphoma increased at +3.1% annually during 1994-2019 in males and at +2.9% annually in females. After adjusting for age and population the rate increases at +1.9% annually in males and at +1.7% in females (Figure 2-5).

Figure 2-6. Non-Hodgkin lymphoma C82-85: 1994-2021



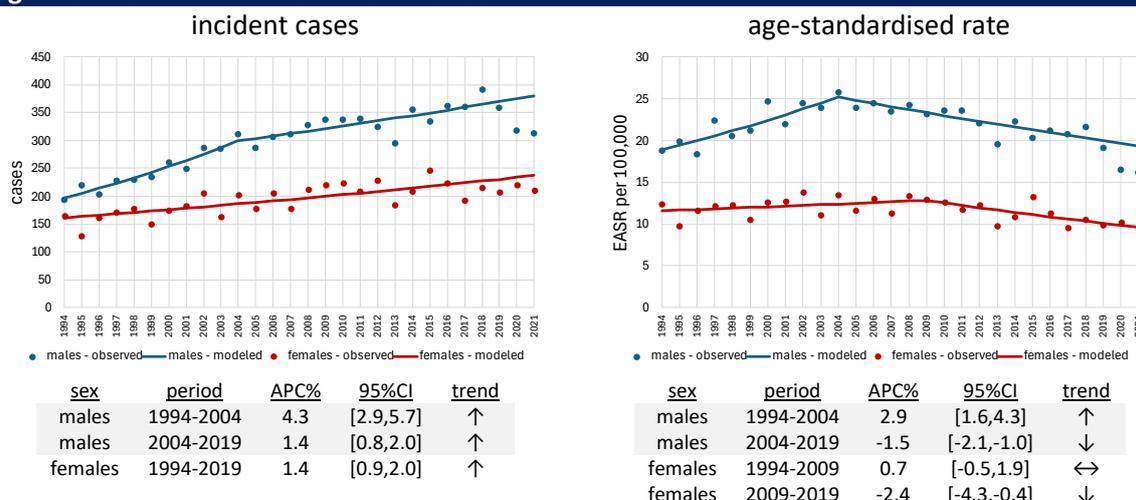
Cases of non-Hodgkin lymphoma increased at +3.8% annually in males over the whole period. Female cases increased at +3.8% annually during 1994-2013 and stabilised thereafter at +0.3% annually. Rates increased at +2.2% annually in males during 1994-2004 and declined marginally or stabilised at -1.3% annually in males. Rates in females increased significantly at +2.0% annually and declined marginally or stabilised at -2.1% annually during 2013-2019 (Figure 2-6).

Figure 2-7. Multiple myeloma C90: 1994-2021



Case numbers of multiple myeloma increased at +3.4% annually in males and +2.6% annually in females during the whole period. Rates increased significantly at +0.7% annually in males and increased marginally but non-significantly at +0.6% in females during the whole period 1994-2019 (Figure 2-7).

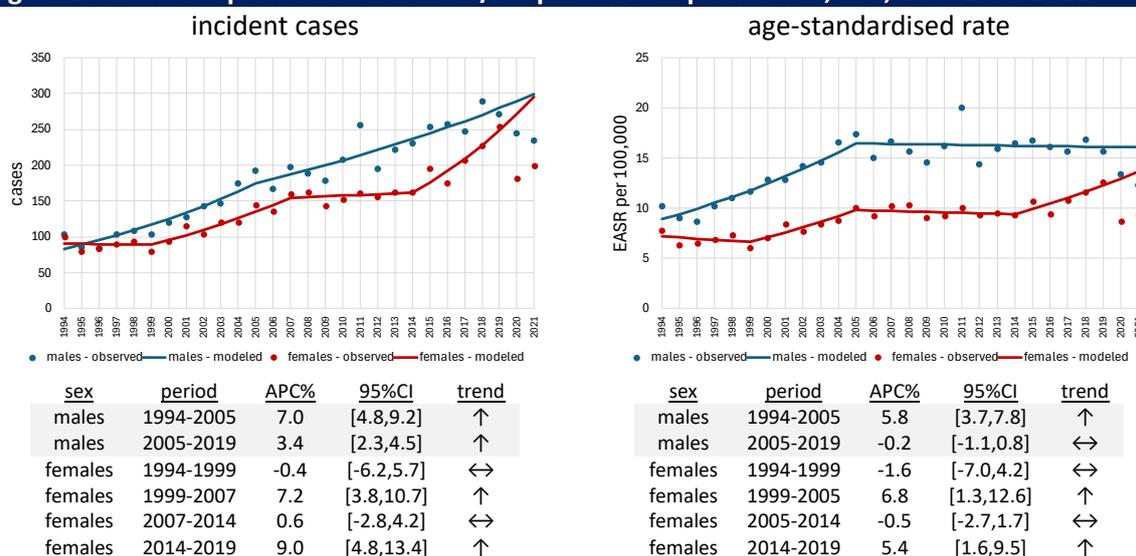
Figure 2-8. Leukaemia C91-95: 1994-2021



Leukaemia cases numbers increased at +4.3% annually in males during 1994-2004, moderating to +1.4% annually thereafter to 2019. Case number in females increased significantly at +1.4% annually over the whole period 1994-2019.

Adjusting for age and population size, leukaemia rates in males increased significantly at +2.9% annually during 1994-2004 and then entered a period of significant decline at -1.5% annually during 2004-2019. Rates in females increased marginally at +0.7% annually during 1994-2009 and then entered a period of significant decline at -2.4% annually during 2009-2019, (Figure 2-8).

Figure 2-9. Immunoproliferative & other/unspecified neoplasms C88, C96, D47: 1994-2021



Cases of immunoproliferative and other/unspecified neoplasms in males increased at +7.0% annually in males during 1994-2005, moderating to +3.4% annually during 2005-2019. Cases numbers in females increased at +7.2% annually during 1999-2007, stabilised during 2007-2014 before increasing significantly at 9.0% annually during 2014-2019. Rates in males increased significantly at +5.8% annually before reaching a stable period during 2005-2019 (-0.2%). Rates in females mirrored the trend in case counts during 1994-2014 before increasing significantly at +5.4% annually during 2014-2019 (Figure 2-9).

Table 2-9.
Annual average percentage change (AAPC%) in HM incidence rates 1994-2019, by sex

Broad ICD10 HM categories	cases diagnosed	MALES			FEMALES			M&F		
		AAPC%	95%CI	trend	AAPC%	95%CI	trend	AAPC%	95%CI	trend
ALL HAEMATOLOGICAL	46,553	1.3	[0.8,1.7]	↑	0.9	[0.6,1.2]	↑	1.2	[0.8,1.6]	↑
IMMUNOPROLIFERATIVE & OTHER/UNSPECIFIED (C88,C96,D47)	8,479	2.5	[1.5,3.4]	↑	2.2	[0.3,4.1]	↑	2.5	[1.6,3.3]	↑
LEUKAEMIA (C91-95)	12,745	0.2	[-0.4,0.8]	↔	-0.5	[-1.6,0.5]	↔	0.1	[-0.5,0.7]	↔
MULTIPLE MYELOMA (C90)	6,466	0.7	[0.2,1.2]	↑	0.6	[-0.1,1.3]	↔	0.7	[0.3,1.2]	↑
NON-HODGKIN LYMPHOMA (C82-85)	15,904	1.5	[0.8,2.2]	↑	1.0	[0.3,1.8]	↑	1.3	[0.9,1.8]	↑
CONDENSED HAEMACARE CATEGORIES										
Other MBCL, Other Mature B-cell leukaemia and related lymphoma	30	26.5	[10.2,45.1]	↑	22.4	[10.1,36]	↑	25.2	[14,37.5]	↑
MCN, Mast cell neoplasm	38	26.8	[15.2,39.7]	↑	22.2	[6.8,39.9]	↑	24.0	[12.8,36.4]	↑
MZL, Marginal zone lymphoma	583	11.5	[4.9,18.5]	↑	9.8	[3,17.1]	↑	12.4	[5.7,19.5]	↑
HDCN, Histiocytic and dendritic cell neoplasm	144	17.6	[8.9,26.9]	↑	16.8	[7.6,26.9]	↑	11.5	[5.8,17.4]	↑
MCL, Mantle cell lymphoma	554	11.7	[7.3,16.3]	↑	7.9	[3.8,12.2]	↑	10.4	[7.4,13.5]	↑
PNK/TCL, Peripheral NK/T-cell lymphoma	715	6.6	[4.4,8.8]	↑	7.2	[4.5,9.9]	↑	7.2	[5.3,9.1]	↑
BL, Burkitt lymphoma / leukaemia	270	6.8	[4.2,9.5]	↑	12.1	[1.6,23.6]	↑	6.2	[3.5,8.9]	↑
MDS/MPN, Myelodysplastic / myeloproliferative neoplasm	417	5.8	[3.6,8.1]	↑	4.7	[2.0,7.5]	↑	6.0	[4.2,7.8]	↑
ET, Essential thrombocythemia	1,451	4.6	[2.9,6.4]	↑	5.2	[0.8,9.7]	↑	5.3	[3.1,7.5]	↑
PMF, Primary myelofibrosis	200	6.4	[0.1,13]	↑	10.2	[0.8,20.4]	↑	4.2	[0.0,8.5]	↑
FL, Follicular lymphoma and related lymphoma	2,868	4.0	[2.8,5.1]	↑	2.0	[-1.6,5.7]	↔	3.6	[2.3,4.9]	↑
DLBCL, Diffuse large B-cell lymphoma and related large B-cell	5,013	4.5	[3.8,5.3]	↑	3.8	[3.1,4.5]	↑	3.5	[2.0,4.9]	↑
MDS, Myelodysplastic syndrome	3,660	2.0	[0.4,3.5]	↑	2.2	[0.9,3.5]	↑	2.0	[0.8,3.3]	↑
HL, Hodgkin lymphoma	2,959	1.9	[1.2,2.7]	↑	1.7	[0.8,2.5]	↑	1.8	[1.2,2.4]	↑
HCL, Hairy cell leukaemia	340	1.5	[0.0,3.0]	↑	5.7	[-1.3,13.3]	↔	1.8	[0.2,3.4]	↑
IPD, Immunoproliferative disease	575	1.4	[-0.1,3.1]	↔	1.8	[-0.5,4.1]	↔	1.7	[0.3,3.2]	↑
PCN, Plasma cell neoplasm (multiple myeloma)	6,466	0.7	[0.2,1.2]	↑	0.6	[-0.1,1.3]	↔	0.7	[0.3,1.2]	↑
pCTCL, Primary cutaneous T-cell lymphoma	622	1.9	[-1.4,5.3]	↔	-1.0	[-3.0,1.1]	↔	0.9	[-1.9,3.9]	↔
Other MPN, Other MPN and related neoplasm	1,147	0.8	[-8.2,10.6]	↔	0.1	[-8.0,1.9]	↔	0.4	[-5.9,7.3]	↔
CLL/SLL, B-cell CLL/small lymphocytic lymphoma	5,907	0.6	[-0.6,1.8]	↔	-0.7	[-2.4,1.1]	↔	0.3	[-1.0,1.5]	↔
CML, Chronic myeloid leukaemia	842	0.8	[-3.3,5.1]	↔	0.9	[-0.8,2.5]	↔	0.3	[-0.6,1.2]	↔
ALL/LL, Precursor lymphoid /acute lymphoblastic leukaemia /lymphoma	1,575	-0.4	[-1.3,0.6]	↔	-0.1	[-1.4,1.2]	↔	0.0	[-0.8,0.8]	↔
AML, and related precursor (incl. AL of ambiguous lineage)	3,340	0.0	[-0.6,0.7]	↔	-0.2	[-1.0,0.6]	↔	0.0	[-0.6,0.5]	↔
PV, Polycythaemia vera	1,076	-0.6	[-1.9,0.8]	↔	-1.2	[-2.5,0.1]	↔	-0.8	[-1.8,0.2]	↔
Other lymphoid neoplasm	2,031	-3.1	[-7.2,1.2]	↓	-6.4	[-8.5,-4.2]	↓	-4.6	[-7.6,-1.4]	↓
Other leukaemia	816	-5.1	[-6.4,-3.9]	↓	-5.5	[-6.8,-4.3]	↓	-5.4	[-6.4,-4.4]	↓

AAPC: Average annual percentage change 1994-2019. Trend: ↑=significant increase, ↓=significant decrease, ↔=no change (static) at the 95% level

Table 2-9 summarises overall trends in incidence rates for the HAEMACARE subsets over a 26-year period using the average annual percentage change (AAPC) metric of Joinpoint regression [7]. The AAPC metric is useful for looking at overall trends in HAEMACARE HM subsets where the APC metric (Figures 2-4 to 2-9) can be difficult to interpret where there are multiple segments of changing trends over almost three decades.

The rates of most HMs increased over 26 years with some exceptions. For all HMs combined the age-standardised rate increased significantly at +1.2% annually during the full period 1994-2019 (i.e. AAPC=+1.2% for both sexes combined, or +1.3% in males and +0.9% in females). However, this masks a stabilisation of overall HM rates in males apparent from 2005-2019 (Figure 2-4).

Of the broad ICD10 HM subsets, leukaemia rates were stable in males (AAPC=+0.2%) and females (-0.5%) over the full 26-year period using the AAPC metric, again this masks a distinct significant increase and decrease in leukaemia rates that occurred on either side of 2004 in males and 2009 in females according to the APC metric (Figure 2-8). Therefore, in the case of leukaemia, despite the stable AAPC trend over the whole period it does appear that leukaemia rates decreased significantly from the mid-2000s up to 2019 (Figure 2-8) during which time various subsets of leukaemia also stabilised including: *CLL/SLL, B-cell CLL/small lymphocytic lymphoma* (+0.3%), *CML, Chronic myeloid leukaemia* (+0.3%), *ALL/LL, Precursor lymphoid neoplasm* (0.0%), *AML, and related precursor neoplasm* (0.0%), or declined significantly (*Other leukaemia*, -5.6%), (Table 2-9).

Some HAEMACARE subsets showing very high increases in rates during 1994-2019 included: *Other MBCL Mature B-cell leukaemia* (AAPC=+25.2%), *MCN, Mast cell neoplasm* (+24.0%), *MZL, Marginal zone lymphoma* (+12.4%) and *HDCN, Histiocytic and dendritic cell neoplasm* (+11.5%), but these are rare HMs where the incidence of such cases was very low in the earliest years (1990s) and increased thereafter, possibly as a result of refinements in diagnostics and coding practices which accentuated the apparent increase in rates for these HMs.

HAEMACARE HMs with relatively high case counts (>1000 during 1994-2019) and showing significantly increasing rates during 1994-2019 included: *ET, Essential thrombocythemia* (AAPC=+5.3% annually), *FL, Follicular lymphoma and related lymphoma* (+3.6%), *DLBCL, Diffuse large B-cell lymphoma* (+3.5%), *MDS, Myelodysplastic syndrome* (+2.0%), *HL, Hodgkin lymphoma* (+1.8%) and *PCN, Plasma cell neoplasm* (+0.7%).

Other HAEMACARE HMs with relatively high case counts (>1000 during 1994-2019) and stable rates during the whole period (i.e., AAPC tending to 0.0% annually) included: *Other MPN and related neoplasm* (+0.4%) and *PV, Polycythaemia vera* (-0.8%).

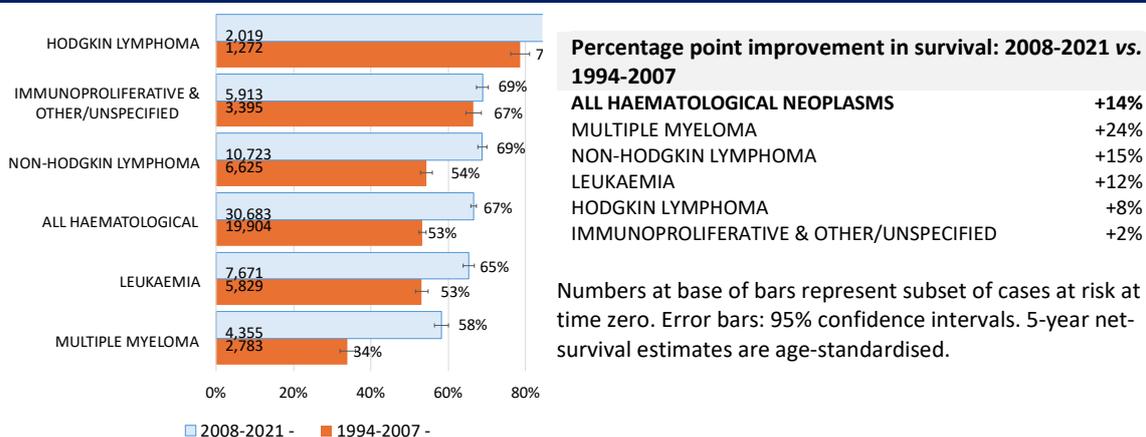
HAEMACARE HMs with significantly declining rates during 1994-2019 included: *other lymphoid neoplasm* (-4.6%) and *other leukaemia* (-5.4%). These subsets with more uncertain morphologies in earlier years (1994-2007) would have been assigned more specific diagnostic codes in more recent years (2008-2019).

3. SURVIVAL

Five-year net survival is a commonly quoted metric by cancer registries to allow comparison between registries. It is the expected survival in the hypothetical situation in which cancer is the only possible cause of death after factoring out other causes of death [8]. Five-year net survival was calculated for the broad classification of HMs and HAEMACARE subsets diagnosed during two consecutive periods, 1994-2007 and 2008-2021.

For cases diagnosed during 2008-2021, 5-year net survival for all HMs combined was 67%, compared with 53% for cases diagnosed during the earlier period 1994-2007, a 14-percentage point (pp) improvement from the earlier period to the later period (Figure 3-1).

Figure 3-1.
5-year net survival (%) for haematological malignancies: ICD10 classification: 2008-2021 vs. 1994-2007

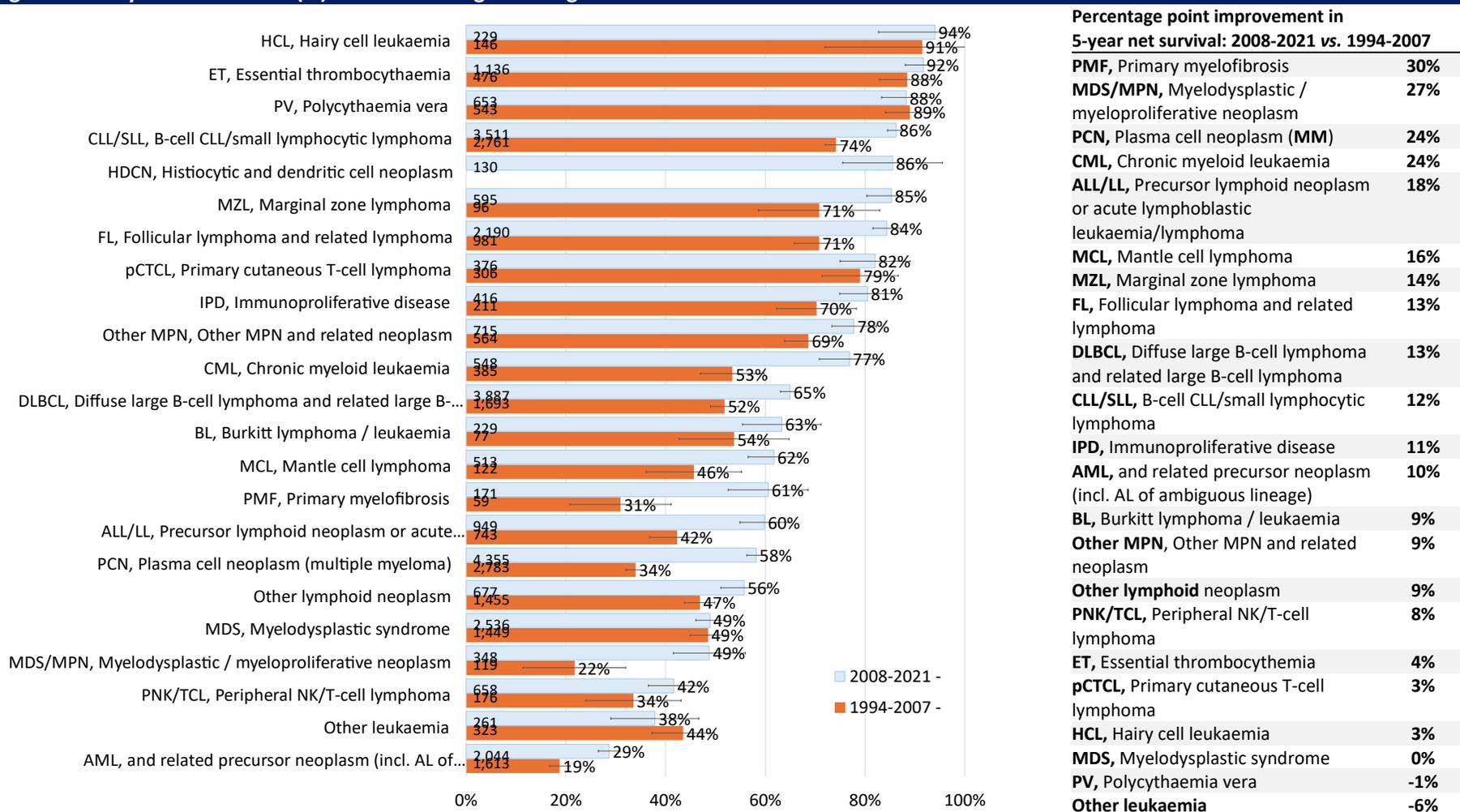


For broad ICD10 classification of HMs, the greatest improvement in 5-year net survival between 1994-2007 and 2008-2021 was seen for multiple myeloma (+24 percentage point (pp) improvement), followed by leukaemia (+12 pp), non-Hodgkin lymphoma (+15 pp) and Hodgkin lymphoma (+8 pp). Survival for immunoproliferative and other/unspecified HMs improved by +2 pp.

For all blood cancers combined, for cases diagnosed during 1994-2007, the proportion that survived their cancer at the five-year mark was 53%. The equivalent figure for those diagnosed during the more recent period (2008-2021) was 67%, a 14-percentage point improvement over the earlier period.

Of the broad subtypes of blood cancers, Hodgkin lymphoma showed the highest 5-year survival during 2008-2021 (87%), followed by immunoproliferative & other unspecified blood cancers (69%), non-Hodgkin lymphoma (69%), leukaemia (65%) and multiple myeloma (58%). (Figure 3-1).

Figure 3-2. 5-year net survival (%) for haematological malignancies: 2008-2021 vs. 1994-2007: HAEMACARE classification



Numbers at base of bars represent the cases in subset at risk at time zero. Error bars: 95% confidence intervals. 5-year net-survival estimates are age-standardised. Age standardised 5-year net survival for *HDCN histiocytic and dendritic cell neoplasm (during 1994-2007)*, *other MBCL mature B-cell leukaemia* and *MCN mast cell neoplasms* were not reliably calculable as the case numbers were too low.

For HAEMACARE classifications of HMs during the recent period 2008-2021, the top five HMs with the highest 5-year net survival were *hairy cell leukaemia* (94%), *essential thrombocythemia* (92%), *polycythaemia vera* (88%), *CLL/SLL, B-cell CLL/small lymphocytic lymphoma* (86%) and *HDCN, histiocytosis* (86%).

At the other end of the spectrum, the five HMs with the lowest 5-year net survival during 2008-2021 were *AML and related precursor neoplasms* (29%), *other leukaemia* (38%), *PNK/TCL, Peripheral NK/T-cell lymphoma* (42%), *MDS/MPN, Myelodysplastic/ myeloproliferative neoplasm* (49%), and *MDS, Myelodysplastic syndrome* (49%) (Figure 3-2).

The top five HMs with the greatest improvement in 5-year net survival between 1994-2007 and 2008-2021 were *primary myelofibrosis* (+30 percentage point (PP) improvement), *MDS/MPN, Myelodysplastic / myeloproliferative neoplasm* (+27 pp), *PCN, Plasma cell neoplasms* (+24 percentage points), *CML, chronic myelomonocytic leukaemia* (+24 pp) and *ALL/LL, Precursor lymphoid neoplasm or acute lymphoblastic leukaemia/lymphoma* (+18 pp).

At the other end of the spectrum, the five HAEMACARE HMs with the lowest improvement in 5-year net survival were *other leukaemia* (-6 pp), *PV, Polycythaemia vera* (-1 pp), *MDS, Myelodysplastic syndrome* (0 pp), *HCL, Hairy cell leukaemia* (+3 pp) and *pCTCL, Primary cutaneous T-cell lymphoma abnormalities* (+3 pp), (Figure 3-2).

While AML had the poorest survival prospects of all the HM subsets during 2008-2021 (29%), survival improved by +10 pp since the earlier diagnosis period 1994-2007 (19%).

Prevalence of haematological malignancies

Complete cancer prevalence is defined as the number of persons surviving with, or following a diagnosis of, cancer in a given population at a particular point in time. For a cancer registry, *fixed-duration prevalence* is the number of cancer survivors calculated directly from observed data collected by the cancer registry since it was established. The NCRI began national collation of cancer registration in 1994, and it currently holds 28 years of complete incidence and follow-up information on cancer cases, up to the end of 2021. At the time of writing, 31/12/2021 was the most recent date for which vital status was ascertained.

Table 3-1.
Number and proportion of cancer cases diagnosed during 1994-2021 alive on 31/12/2021

	number alive on 31/12/2021	% of all cancer survivors	% of all survivors of haematological malignancies
All invasive cancers (excl. NMSC) C00-43, C45-96	201,608	100%	
All haematological malignancies C81-85, C88, C90-96	23,010	11.4%	100%
non-Hodgkin lymphoma C82-85	8,465	4.2%	36.8%
leukaemia C91-95	5,817	2.9%	25.3%
Immunoproliferative and other/ unspecified C88, C96	3,901	1.9%	17.0%
Hodgkin lymphoma C81	2,525	1.3%	11.0%
Multiple myeloma C90	2,302	1.1%	10.0%

Of all invasive cancer cases (excl. NMSC) diagnosed since the NCRI was established, 201,608 were still alive at the end of 2021 (Table 3-1).

Of all 201,608 cancer survivors, 23,010 (11.4%) were survivors of HMs.

Of 23,010 HM survivors, 8,465 (36.8%) were survivors of non-Hodgkin lymphoma, 5,817 (25.3%) were survivors of leukaemia, 3,901 (17.0%) were survivors of Immunoproliferative and other/ unspecified HMs, 2,525 (11.0%) were survivors of Hodgkin lymphoma and 2,302 (10.0%) were survivors of multiple myeloma (Table 3-1).

4. MORTALITY

All HM related deaths are captured within the following broad ICD10 classification: all haematological malignancies combined (ICD10 C81-85, C88, C91-96, D47), immunoproliferative and other/unspecified neoplasms (C88, C96, D47), multiple myeloma (C90), non-Hodgkin lymphoma (C82-85), leukaemia (C91-95) and Hodgkin lymphoma (C81). Using ICD10 classification, trends in mortality during 1994-2021 and median age at death are presented. Cause of death derived from death certificates is available the CSO up to year 2021 (www.cso.ie) and were coded using the broader ICD10 classification. It is not possible to classify HM deaths at the discrete levels of the HAEMACARE classification as this level of detail is not available in death certificates.

Deaths due to haematological malignancies

Table 4-1.
Deaths due to haematological malignancies as a proportion of all deaths attributable to cancer, by diagnosis period and sex

Diagnosis period	males	females	total
1994-1998	8.3%	7.8%	8.1%
1999-2003	9.3%	8.6%	9.0%
2004-2008	9.2%	7.9%	8.6%
2009-2013	8.8%	7.9%	8.4%
2014-2018	9.2%	7.5%	8.4%
2019-2021	9.2%	7.5%	8.4%

The numbers of deaths due to HMs as a proportion of all deaths from any cancer increased marginally from 8.1% during 1994-1998 to 8.4% during 2019-2021 (Table 4-1).

Table 4-2.
Deaths due to specific haematological malignancies (HMs) as a proportion of all deaths due to HMs: 2019-2021

	males		females		total		M: F ratio
	annual average deaths	% of all HM deaths	annual average deaths	% of all HM deaths	annual average deaths	% of all HM deaths	
All haematological malignancies (C81-85, C88, C90-96, D47)	491	100%	342	100	833	100	1.44
Hodgkin lymphoma (C81)	11	2.3%	11	3.2%	22	2.7%	1.03
Non-Hodgkin lymphoma (C82-85)	160	32.6%	127	37.3%	287	34.5%	1.26
Multiple myeloma (C90)	110	22.4%	80	23.4%	190	22.8%	1.38
Leukaemia (C92-95)	176	35.9%	99	29.1%	276	33.1%	1.78
Immunoproliferative and other/unspecified neoplasms (C88, C96, D47)	33	6.8%	24	7.0%	57	6.9%	1.39

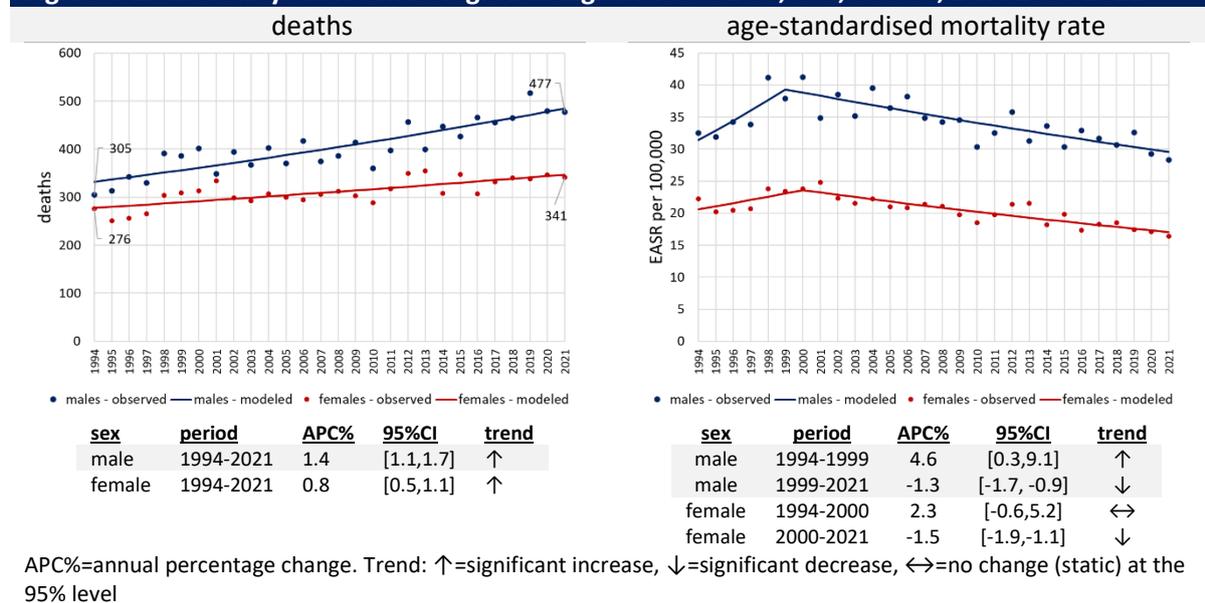
Annual averages are subject to rounding

The annual average number of deaths attributable to HMs was 833 deaths during 2019-2021 which accounted for 8.4% of all cancer related deaths, marginally lower than the annual average number of deaths attributable to colorectal cancer over the same period (1,012 deaths). During 2019-2021 there were 22 deaths per year due to Hodgkin lymphoma, or 2.7% of all HM related deaths. Non-Hodgkin lymphoma accounted for 34.5% of all HM deaths (287 deaths per year). Multiple myeloma and leukaemia comprised 22.8% (190 deaths per year) and 33.1% (276 deaths per year) respectively of all HM attributable deaths over the same period. Immunoproliferative and other/unspecified

neoplasms accounted for the smallest proportion of HM deaths (6.9%, 57 deaths per year), (Table 4-2).

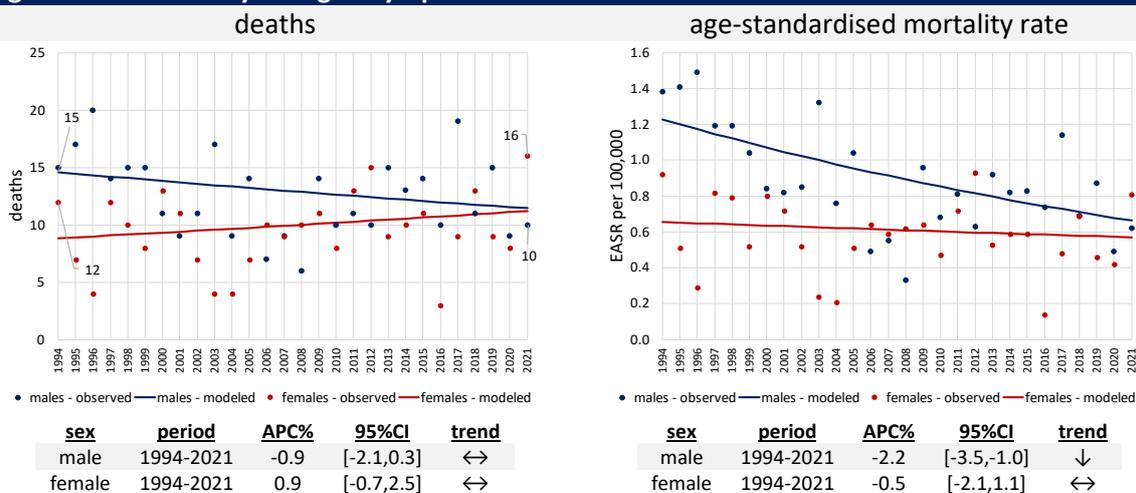
Mortality trends 1994-2021

Figure 4-1. Mortality: all haematological malignancies C81-85, C88, C90-96, D47: 1994-2021



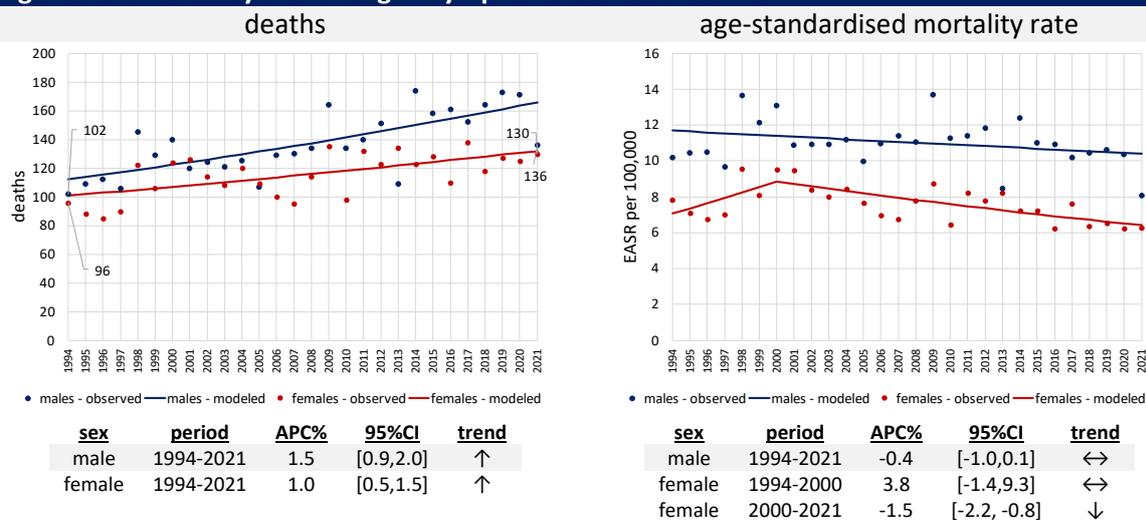
The number of deaths due to HMs increased steadily and significantly at +1.4% annually in males and +0.8% in females during 1994-2021. On adjusting for population increase and changes in the age structure of the population during 1994-2021 the age standardised rate for HM mortality declined significantly at -1.3% annually during 1999-2021 in males and -1.5% in females during 2000-2021, Figure 4-1.

Figure 4-2. Mortality: Hodgkin lymphoma C81: 1994-2021



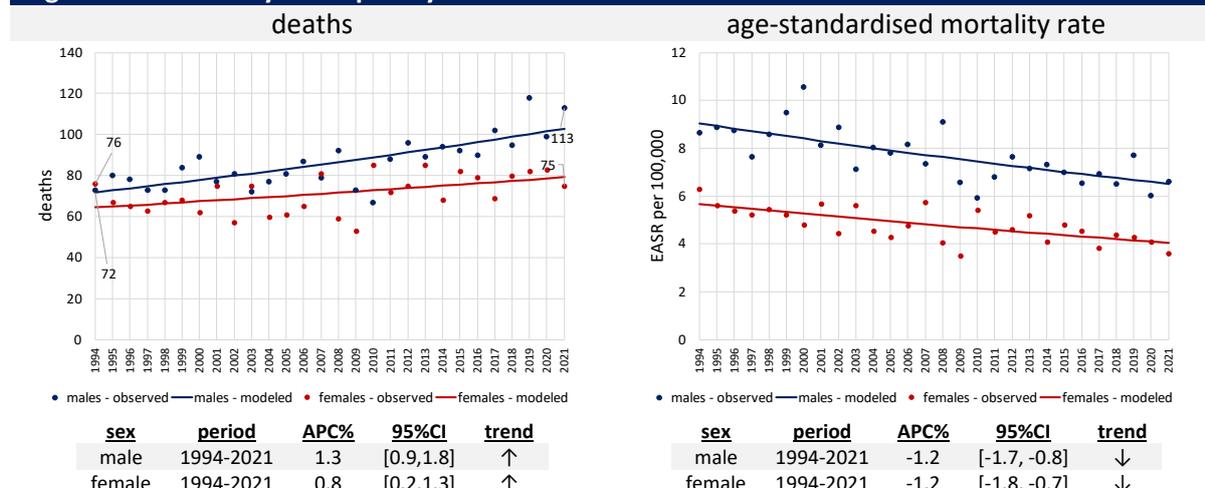
Deaths due to Hodgkin lymphoma are uncommon relative to other HMs and declined and increased marginally and non-significantly in males (-0.9%) and females respectively (+0.9%). The age-standardised rate declined significantly at -2.2% annually for males and was static (-0.5% annually) for females over the full period 1994-2021, Figure 4-2.

Figure 4-3. Mortality: non-Hodgkin lymphoma C82-85: 1994-2021



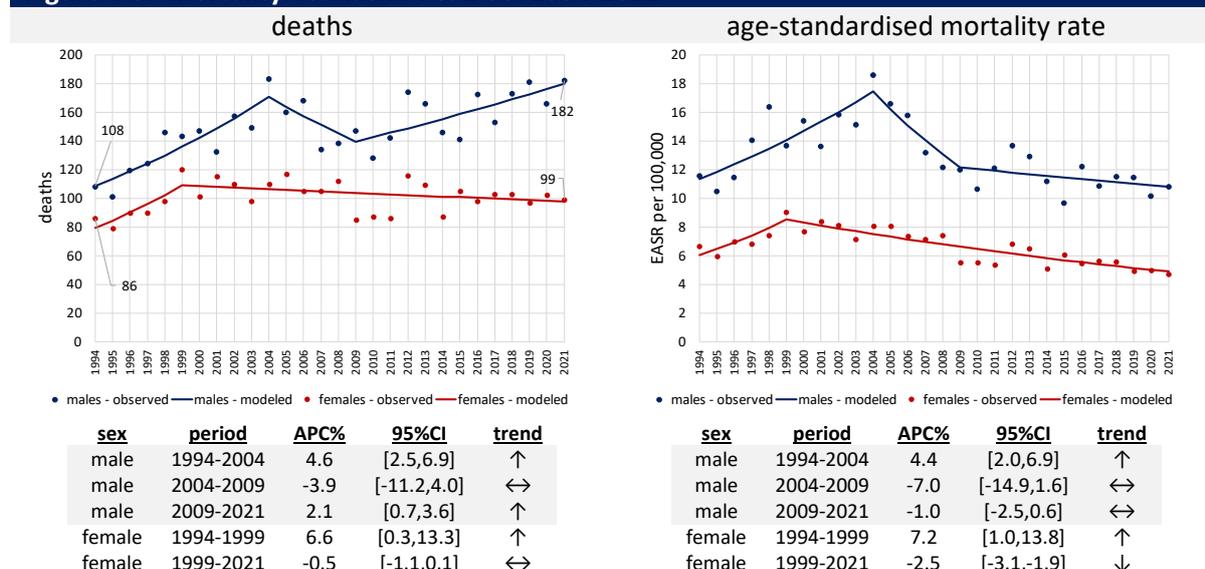
Death attributable to non-Hodgkin lymphoma increased at +1.5% annually in males and +1% annually in females over the full period (1994-2021). The age standardised mortality rate declined marginally and non-significantly at -0.4% annually in males during the full period and declined significantly at -1.5% annually in females during 2000-2021.

Figure 4-4. Mortality: multiple myeloma C90: 1994-2021



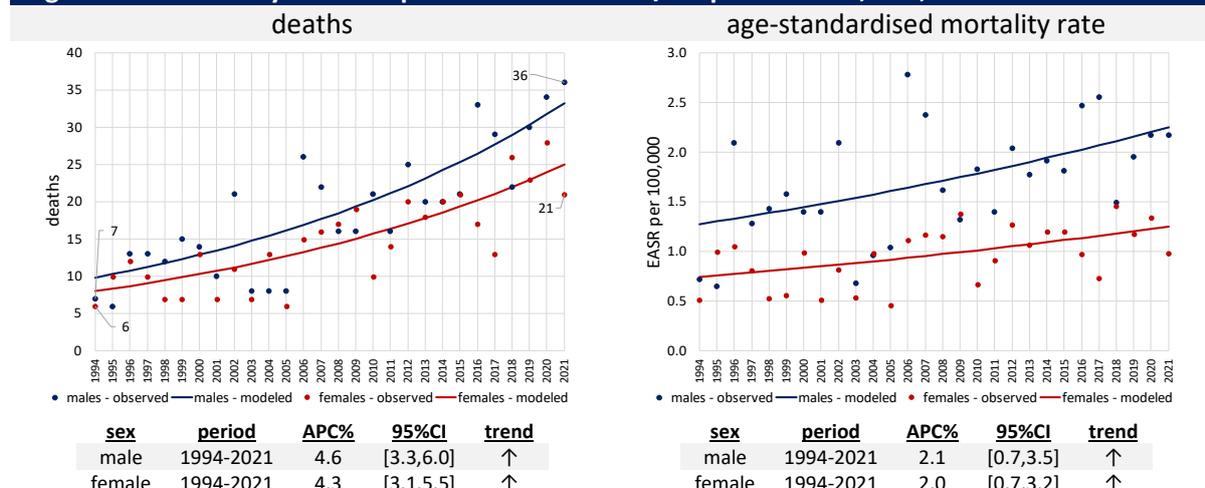
Deaths attributable to multiple myeloma increased significantly at +1.3% and +0.8% annually in males and females respectively during the full period (1994-2021). However, the age-standardised mortality rate declined significantly at -1.2% annually in both males and females during the full period (1994-2021), Figure 4-4.

Figure 4-5. Mortality: leukaemia C91-95: 1994-2021



The trend in leukaemia related deaths was complex. In males, after a significant annual +4.6% increase in deaths during 1994-2004, the number of deaths declined at -3.9% annually during 2004-2009 followed by a significant increase at +2.1% annually between 2009-2021. In females, deaths increased significantly at +6.6% annually during 1994-1999 and then declined marginally and non-significantly at -0.5% annually during 1999-2021. The age standardised mortality rate declined non-significantly at -1.0% annually in males during 2009-2021 and declined significantly at -2.5% annually in females during 1999-2021, (Figure 4-5).

Figure 4-6. Mortality: immunoproliferative & other/unspecified C88, C96, D47: 1994-2021



Deaths attributable to *immunoproliferative & other/unspecified neoplasms* increased significantly at +4.6% and +4.3% in males and females respectively. The mortality rate also increased at 2.1% and +2.0% in males and females respectively over the full range of years (Figure 4-6). Deaths attributable to *immunoproliferative & other/unspecified* were uncommon up to the mid-2000s but increased consistently from a low base in 1994 (13 deaths) up to 2021 (57 deaths). It is possible that the increase in deaths attributable to this category could be due to changes in coding practice on death certs over time.

Median age at death

Table 4-4.
Median age at death by ICD10 classification of HMs: 2019-2021

	males		females		M&F	
	median	IQR	median	IQR	median	IQR
	age		age		age	
all haematological malignancies (C81-85, C88, C91-96, D47)	77	[69,84]	78	[71,86]	78	[70,84]
Immunoproliferative & other/unspecified neoplasms (ICD10 C88, C96, D47)	81	[75,86]	84	[77,89]	82	[76,87]
Multiple myeloma (C90)	76	[69,83]	78	[71,86.5]	77	[70,84]
Non-Hodgkin lymphoma (C82-85)	77	[69,83]	79	[71,85]	78	[70,83]
Leukaemia (C91-95)	76	[68,84]	77	[70,86]	77	[68,84]
Hodgkin lymphoma (C81)	77	[68,83]	76	[72,84]	77	[71,84]

- The median age at death during 2019-2021 for all haematological malignancies combined was 78 years (M 77; F 78).
- Median age at death for *Immunoproliferative & other/unspecified neoplasms* for was 82 years (M 81; F 84) during the same period, followed by *multiple myeloma* 77 (M 76; F 78), *non-Hodgkin lymphoma* 78 years (M 77; F 79), *leukaemia* 77 years (M 76; F 77) and *Hodgkin lymphoma* 77 (M 77; F 76), (Table 4-4).

5. PROJECTIONS

Table 5-1.
Projected case counts for subsets of haematological malignancies in 2030 based on demographic projection of average age-specific rates for HMs during 2015-2019

	average annual case count 2015-2019	projected cases in 2030	projected in 2030, 95%PI	% increase in 2030 on 2015-2019
ALL HAEMATOLOGICAL MALIGNANCIES (C81-85, C88, C90-96, D47)	2,387	3,162	(2,949,3,375)	32%
HODGKIN LYMPHOMA (C81)	147	183	(156,209)	24%
NON-HODGKIN LYMPHOMA (C82-85)	826	1,096	(1,019,1,174)	33%
MULTIPLE MYELOMA (C90)	351	506	(474,538)	44%
LEUKAEMIA (C92-95)	579	735	(648,821)	27%
IMMUNOPROLIFERATIVE & OTHER/UNSPECIFIED (C88, C96, D47)	475	633	(554,713)	33%

Average annual case counts, and projected cases are subject to rounding

Table 5-1 shows how many HM cases might be diagnosed in 2030. The projected cases in 2030 assume that average annual age-specific rates observed during 2015-2019 will still apply in 2030 and that population projections for 2030 will materialise, and that diagnostic criteria and the effect of risk factors for various HMs remain the same between 2015-2019 and 2030.

- The number of all HMs projected for 2030 was 3,162, a 32% increase on average case numbers observed during 2015-2019 (2,387).
- The largest projected increase in HMs in 2030 is seen in multiple myeloma cases (506), a 44% increase on average case numbers observed during 2015-2019 (351). Multiple myeloma tends to occur in older persons which is in keeping with the CSO M2F1 assumption of population growth where most of the population growth is expected in older age groups, whereas the smallest increase in projected cases in 2030 (24%) was seen for Hodgkin lymphoma which tends to occur in younger persons.
- The number of non-Hodgkin lymphoma and immunoproliferative/ other/ unspecified cases were projected to increase by 33% in 2030 over cases counts observed during 2015-2019.

5. DISCUSSION

Summary

HMs are a heterogeneous group of cancers differing in incidence, pathophysiology, prognosis, treatment options and survival. They account for 10% of the total cancer incidence in Ireland. The incidence and mortality of HMs overall are in the same range as colorectal cancer, but apart from *plasma cell neoplasms* and *diffuse large B-cell lymphoma*, most of the 26 individual HAEMACARE subsets we examined are considered rare cancers (<6 per 100,000) according to RARECARENet [9].

For HMs overall, the age-standardised mortality rate declined significantly during 1999-2021 in males and 2000-2021 in females reflecting advances in prevention, earlier detection, and treatment. Mortality rates declined significantly for the broad HM subtypes except for non-Hodgkin lymphoma and leukaemia in males and Hodgkin lymphoma in females where the mortality rates were stable.

For cases diagnosed during 2008-2021, 5-year net survival for all HMs combined was 67%, compared with 53% for cases diagnosed during the earlier period 1994-2007, a 14-percentage point (pp) improvement from the earlier period to the later period. This possibly reflects innovations in treatment over the latter diagnosis period.

There were improvements in survival between 1994-2007 and 2008-2021 for all HM subtypes. For *acute myeloid leukaemia*, which has the poorest survival prospect, survival improved from 19% to 29%. Also, for *ALL/LL, Precursor lymphoid neoplasm/ acute lymphoblastic leukaemia/lymphoma* which occurs mostly in children and young adults, survival improved from 42% to 60%. For *plasma cell neoplasms (multiple myeloma)* survival improved from 34% to 58%.

Sex differences

The incidence rate of HMs overall was higher in males (57% higher than females), and the mortality rate was 40% higher. In males, for HMs overall, after a period of significant increase from 1994, the incidence rate stabilised during 2005-2019. This stabilisation was influenced by a decline in the rate of leukaemia during 2004- 2019 balanced against stabilisation of rates for NHL and immunoproliferative & other/unspecified neoplasms and increasing rates for HL and multiple myeloma.

In females, for blood cancers overall, the incidence rate increased steadily during the full period 1994-2019. As in males the rate of leukaemia declined significantly during 2009-2019 but was counterbalanced by increasing rates of HL (1994-2021) and *immunoproliferative & other/unspecified neoplasms* (2014-2019), and stabilisation of rates for NHL (2013-2019) and multiple myeloma (1994-2019).

International Comparisons

Incidence and Prevalence

Comparing average estimated European age standardised rates (EASRs) for HMs in the EU27 (2022) versus EASRs for Ireland (during 2012-2021 from this report), the EASR in Ireland was higher than the EU average for NHL (EU27 average 19.3; Ireland 22.1), HL (EU27 average 2.8; Ireland 3.3), and

multiple myeloma (EU27 average 7.3; Ireland 9.6), and lower than the EU average for leukaemia (EU27 average 15.3; Ireland 14.9).

Leukaemia rates are generally higher in countries with high socio-demographic indices particularly in western Europe and north America [10] possibly due to higher exposure to risk factors and greater resources to diagnose the condition, but incidence in many developed countries has been declining [11][10]. Incidence rates for leukaemia in Ireland declined significantly in both males (2004-2019) and females (2009-2019) after a period of increase from 1994 to the mid-2000s.

The incidence rate of multiple myeloma increased in males and marginally in females over the whole period as seen in other countries in western Europe [11]. Incidence rates of Hodgkin lymphoma increased in both males and females over the whole period as seen in western Europe, whereas rates of non-Hodgkin lymphoma stabilised in males (2014-2019) and females (2013-2019) after periods of significant increase from 1994 which was also the case in western Europe [11].

Mortality & Survival

Comparing average estimated European age standardised rates (EASRs) for HM mortality in the EU27 (2022) versus EASRs for Ireland (during 2012-2021). The EASR for mortality in Ireland was higher than the EU average for NHL (EU27 average 7.3; Ireland 8.5), HL (EU27 average 0.5; Ireland 0.7), and multiple myeloma (EU27 average 4.6; Ireland 5.5), and lower than the EU average for leukaemia (EU27 average 9.2; Ireland 8.1).

The HM subtypes that showed the highest 5-year net survival (>80%) during the diagnosis period 2008-2021 were: *hairy cell leukaemia* (highest), *essential thrombocythemia*, *polycythaemia vera*, *B-cell CLL/SLL small lymphocytic lymphoma*, *histiocytosis* and *marginal zone lymphoma*, *follicular lymphoma*, *primary cutaneous T-cell lymphoma* and *immunoproliferative disease* which was also the case for a similar epidemiological study conducted by the Belgian cancer registry [5].

The HM subtypes with the lowest 5-year net survival (<60%): *acute myeloid leukaemia* (lowest), *peripheral NK/T-cell lymphoma*, *myelodysplastic/myeloproliferative*, *myelodysplastic syndrome* and *plasma cell neoplasm (multiple myeloma)* were also the same subtypes with lowest net-survival in the Belgian study, e.g., 5-year net survival for *plasma cell neoplasms (multiple myeloma)* was 58% in Ireland and 57% in Belgium. Notably, overall, the survival estimates and the order of survival probabilities for each HM subtype (best to worst) was very similar in both studies using the same HM classification.

Limitations of international comparisons

In the interpretation of these results, it is important to note that international comparison of data between population-based registries is challenging due to variations in selection criteria, different reference populations and methods used for standardisation of incidence, mortality and survival rates, changes in classification over time, and different interpretations in the applications of coding recommendations.

Cancer incidence data on cancers are available on the European Cancer Information System (ECIS) (<https://ecis.jrc.ec.europa.eu>). The ECIS provides estimated European age-standardised incidence rates (EASR) for EU27 member states for 2022 for the four broad categories of HMs: Hodgkin lymphoma, non-Hodgkin lymphoma, leukaemia and multiple myeloma. For Ireland, the ECIS estimates for 2022 were based on an extrapolation of trends extant during the period from 1994 to 2017 [12] which may not be realised when HM incidence data is complete for 2022 (in November

2024), and do not consider the impact of COVID-19 on cancer registration during 2020-2022. Also, unlike Ireland which has a national registry with virtually complete coverage, incidence figures from some of the bigger countries in the EU27 (e.g. Italy, France, Germany and Spain) come from an amalgamation of data from regional cancer registries which may not fully capture cancer incidence in those countries.

Possible factors affecting observed trends

Risk factors

More research needs to be done to fully understand risk factors for haematologic malignancies in the Irish population. Nevertheless, the existing body of knowledge suggests familial history, lifestyle and environmental factors are possible reasons for observed trends. Increasing age and male sex are associated with increased risk of developing HMs [10]. Genetics and family history have been cited as risk factors for NHL [13], as well as adult leukaemia [14] and childhood ALL, CLL and AML [15].

Lifestyle factors such as smoking and physical activity have been shown to increase risk of leukaemia [10], NHL [13], follicular lymphoma [16] and MM [17]. Alcohol consumption has been cited to increase risk of multiple myeloma [17] while obesity has been cited as risk factor for incidence of *diffuse large B-cell lymphoma* [18], multiple myeloma and lymphoma [11].

Work related exposures to ionising radiation and organic solvents such as benzene have been cited as risk factors for leukaemia [19]. Cancer patients with solid tumours treated with adjuvant radiation, platinum and topoisomerase II inhibitors have an increased risk of subsequent therapy-related myeloid neoplasms such as AML and MDS [20].

Certain infections can also pre-dispose towards developing lymphomas. *Helicobacter pylori* causes most gastric mucosa-associated lymphoid tissue lymphomas [21]. Epstein-Barr virus is associated with Burkitt lymphoma [22] while the hepatitis C virus has been associated with splenic marginal zone lymphoma and DLBCL [23].

There is an increased risk of NHL in persons with autoimmune diseases, possibly attributable to immunosuppressive therapies [24]. Persons immunosuppressed for other reasons, such as transplantation or HIV infection, are also known to be at an increased risk of developing NHL [13].

While not all these risk factors are avoidable, lifestyle modifications such as quitting smoking, increasing physical activity, weight control, and management of hypercholesterolaemia might reduce the risk of developing HMs [13][16].

Changes in diagnostic & therapeutic innovation over time

Improvements in diagnostic methods and treatment modalities could have partly explained observed trends in incidence, mortality and survival. In part, because tumour material is comparatively readily accessible i.e. via the blood and/or bone marrow, HMs have been at the forefront of development and implementation of precision medicine in the use of genetic analyses for diagnosis, classification, prognosis, and therapeutic decision-making [25][26].

Genetic testing has been increasingly applied over the last decades in the diagnosis and management of HMs and is now routine in the clinical evaluation of nearly all HMs. Additionally, access to innovative drugs over the last two decades [27] especially the monoclonal antibody anti-CD20 (Rituximab) in most B-cell mature lymphomas and tyrosine kinase inhibitors in CML, were

progressively introduced in the early 2000s. For example, the identification of the BCR::ABL1 gene fusion in CML and the use of tyrosine-kinase inhibitors [25] has markedly changed CML treatment and led to marked improvements in prognosis for patients [28] and improvements in survival which are reflected in the Irish data presented here.

Changes in classification

Precision diagnostics have greatly increased the complexity of classification and registration procedures, which have changed markedly over the period covered by this report. Such continuous refinement in classification poses significant challenges for population-based cancer registries which seek to capture complete and accurate data for the full spectrum of HMs. To accurately measure the burden of the different types of HM and facilitate comparison over time data must be consistently classified over the entire study period, in this instance from 1994-2021. The NCRI coded cancer types according to ICDO-2 during 1994-2004, ICDO-3 during 2005-2011, ICDO-3.1 during 2012-2019 and ICDO-3.2 from January 2020. The effect of updates to the coding system was evident over time with the steady decline in HMs with non-specific morphology which was also observed in other countries [5][29].

Data from population-based cancer registries are an important adjunct to data from clinical trials. The oldest, those with complex comorbidity and/or with a prior history of malignancy are typically underrepresented in clinical trials thus population-level cancer registry data is important in providing a real-world picture of overall HM incidence and outcome.

Conclusions

This report, which includes data on adults and children, serves to better inform about HM burden in Ireland and identify HM subsets that need improvement (such as AML). These data will help policy makers and healthcare managers plan future health-care services in terms of number of cases projected at the end of the decade and monitor the effect of service and therapeutic changes at the population level.

The increase in both incidence and survival of HMs over time is likely explained by diagnostic and therapeutic innovations since 1994. Still, the heterogeneous and complex genetic and molecular landscape of HMs presents ongoing challenges [26] - the full promise of precision medicine in oncology is yet to be realised [30]. These data describing the heterogeneity in incidence and outcomes for HMs should help clinicians, policy makers and researchers better address the burden of HMs in the Irish population.

6. METHODS

The data presented in this report were abstracted from the National Cancer Registry, Ireland (NCRI) database. Data were anonymised and not considered personal level data. Population data derived from census data were downloaded from the Central Statistics Office website. The study included all HMs, both paediatric and adult cases registered by the NCRI during the period 1994-2021 with follow-up to 31/12/2021 (Table 6-1).

Table 6-1. Period of study, number of cases, and quality indicators of data

Cancer registry	Period	HM cases	Microscopically verified cases (%)	Unspecified cases (NOS) ¹ (%)	Death certificate only or autopsy only cases (%)
Ireland	1994-2007	20,353	95.6%	16.9%	2.21%
Ireland	2008-2019	26,200	95.2%	7.5%	0.78%
Ireland	2020-2021	4,701	84.6%	7.5%	0.30%

¹ NOS cases refer to ICDO-3 morphology codes: 9800, 9898, 9911, 9967, 9590, 9591, 9820, 9832

Incident HMs cases were classified using the International Classification of Diseases for Oncology (ICD-O), third edition – based on the 2008 WHO classification [31] – and grouped according to the HAEMACARE project scheme [4], a European project aimed to improve standardisation of epidemiological information on HMs (Appendix I).

Descriptive statistics are presented for age, expressed as median and interquartile range (IQR), and absolute frequencies and percentages are presented for HM subsets by sex. Age specific mid-year population and cause specific mortality were obtained from the Central Statistics Office (www.cso.ie).

Case counts, Crude (CR) and European age-standardized incidence and mortality rates (EASRs), using the 2013 European standard population [32], were calculated per 100,000 person years. Sex ratios were based on the EASR male/EASR female rate ratios for each HM subset.

5-year net-survival was calculated for each HM subset diagnosed during 1994-2007 and 2008-2021 using the Pohar-Perme estimator option [33] in Stata 15 'strs' command [8]. A case was included in the analyses if the HM of interest was the first or only primary tumour diagnosed in that person. The date of last follow-up (i.e. 'censor date') was 31/12/2021. Each HM subset was ranked from high to low survival probability.

The Joinpoint Regression programme [7] was used to assess significant annual percentage change (APC) and average annual percentage change (AAPC) in incidence and mortality rate trends for each HM subset over 1994-2021 inclusive. The default settings allowed a maximum of four change points and selection of the best fit Joinpoint model for each HM subset.

The number of expected cases in each HM subset was projected for 2030 by applying the average age-specific rates observed for years 2015-2019 to the projected population for 2030 under the M2F1 population assumption (a demographic projection) [34] and assuming that the effect of risk factors remained the same up 2030. Statistical analyses were performed using Stata 15 and the Joinpoint Regression Program [35] was used to examine trends in cases counts and rates (Version 4.9.1.0- April 2022).

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APPENDIX I. HM incident cases and rates 2012-2021

Incident cases and rates of HMs in males diagnosed during 2012-2021, by HM

	cases No.	%	CR	95%CI	EASR	95%CI
ALL HAEMATOLOGICAL MALIGNANCIES	13,266	100%	55.97	[52.9-58.9]	77.71	[73.3-82.1]
NON-HODGKIN LYMPHOMA (ICD10, C82-85)	4,527	34.1%	19.10	[17.3-20.8]	26.19	[23.6-28.6]
MULTIPLE MYELOMA (ICD10, C90)	2,006	15.1%	8.44	[7.2-9.6]	12.22	[10.4-13.9]
LEUKAEMIA (ICD10, C91-95)	3,411	25.7%	14.41	[12.8-15.9]	19.95	[17.7-22.1]
IMMUNOPROLIFERATIVE & OTHER/UNSPECIFIED (ICD10, C88, C96, D47)	2,494	18.8%	10.52	[9.2-11.8]	15.55	[13.5-17.5]
01) HL, Hodgkin lymphoma (ICD10, C81)	828	6.2%	3.49	[2.74-4.24]	3.81	[2.96-4.66]
02) CLL/SLL, B-cell CLL/small lymphocytic lymphoma	1,595	12.0%	6.76	[5.71-7.80]	9.97	[8.36-11.57]
03) HCL, Hairy cell leukaemia	136	1.0%	0.57	[0.27-0.87]	0.72	[0.31-1.11]
04) Other MBCL, Other Mature B-cell leukaemia and related lymphoma	18	0.1%	0.07	[0.01-0.16]	0.10	[0.01-0.22]
05) IPD, Immunoproliferative disease	191	1.4%	0.80	[0.44-1.16]	1.19	[0.64-1.73]
06) PCN, Plasma cell neoplasm	2,006	15.1%	8.44	[7.27-9.60]	12.22	[10.46-13.97]
07) MZL, Marginal zone lymphoma	208	1.6%	0.87	[0.49-1.24]	1.17	[0.64-1.69]
08) FL, Follicular lymphoma and related lymphoma	822	6.2%	3.47	[2.72-4.21]	4.44	[3.45-5.42]
09) MCL, Mantle cell lymphoma	298	2.2%	1.25	[0.80-1.70]	1.81	[1.13-2.49]
10) DLBCL, Diffuse large B-cell lymphoma and related large B-cell lymphoma	1,703	12.8%	7.18	[6.10-8.25]	10.00	[8.43-11.56]
11) BL, Burkitt lymphoma / leukaemia	123	0.9%	0.52	[0.23-0.80]	0.55	[0.23-0.86]
12) pCTCL, Primary cutaneous T-cell lymphoma	165	1.2%	0.69	[0.36-1.02]	0.93	[0.46-1.39]
13) PNK/TCL, Peripheral NK/T-cell lymphoma	312	2.4%	1.32	[0.85-1.77]	1.70	[1.08-2.30]
14) ALL/LL, Precursor lymphoid neoplasm or acute lymphoblastic leukaemia/lymphoma	373	2.8%	1.58	[1.07-2.0]	1.42	[0.94-1.89]
15) AML, and related precursor neoplasm (incl. AL of ambiguous lineage)	850	6.4%	3.58	[2.82-4.34]	5.01	[3.87-6.13]
16) CML, Chronic myeloid leukaemia	250	1.9%	1.05	[0.64-1.46]	1.35	[0.79-1.8]
17) PV, Polycythaemia vera	278	2.1%	1.17	[0.736-1.60]	1.50	[0.92-2.07]
18) ET, Essential thrombocythemia	406	3.1%	1.70	[1.18-2.22]	2.28	[1.55-3.00]
19) PMF, Primary myelofibrosis	83	0.6%	0.35	[0.11-0.57]	0.51	[0.15-0.85]
20) Other MPN, Other MPN and related neoplasm	330	2.5%	1.39	[0.91-1.86]	1.95	[1.24-2.65]
21) MCN, Mast cell neoplasm	13	0.1%	0.05	[0.01-0.14]	0.06	[0.01-0.15]
22) MDS, Myelodysplastic syndrome	1,135	8.6%	4.80	[3.91-5.68]	7.82	[6.33-9.31]
23) MDS/MPN, Myelodysplastic / myeloproliferative neoplasm	196	1.5%	0.83	[0.46-1.19]	1.28	[0.69-1.85]
24) HDCN, Histiocytic and dendritic cell neoplasm	50	0.4%	0.21	[0.03-0.39]	0.20	[0.02-0.38]
25) Other leukaemia	122	0.9%	0.52	[0.22-0.80]	0.94	[0.38-1.50]
26) Other lymphoid neoplasm	234	1.8%	0.98	[0.58-1.37]	1.45	[0.84-2.05]

95%CI: 95% confidence interval; CR: crude rate; EASR: age-standardized incidence rate per 100,000 weighted using the European standard population 2013

Incident cases and rates of HMs in females diagnosed during 2012-2021, by HM

	cases No.	%	CR	95%CI	EASR	95%CI
ALL HAEMATOLOGICAL MALIGNANCIES	9,686	100%	40.08	[37.5-42.6]	49.95	[46.7-53.1]
NON-HODGKIN LYMPHOMA (ICD10, C82-85)	3,542	36.6%	14.68	[13.1-16.2]	18.64	[16.6-20.6]
MULTIPLE MYELOMA (ICD10, C90)	1,376	14.2%	5.68	[4.7-6.6]	7.38	[6.1-8.6]
LEUKAEMIA (ICD10, C91-95)	2,139	22.1%	8.86	[7.6-10.0]	10.71	[9.2-12.1]
IMMUNOPROLIFERATIVE & OTHER/UNSPECIFIED (ICD10, C88, C96, D47)	1,965	20.3%	8.12	[6.9-9.2]	10.32	[8.8-11.7]
01) HL, Hodgkin lymphoma (ICD10, C81)	662	6.8%	2.74	[2.07-3.39]	2.89	[2.18-3.59]
02) CLL/SLL, B-cell CLL/small lymphocytic lymphoma	838	8.7%	3.48	[2.73-4.21]	4.56	[3.58-5.53]
03) HCL, Hairy cell leukaemia	27	0.3%	0.11	[0.01-0.24]	0.13	[0.01-0.29]
04) Other MBCL, Other Mature B-cell leukaemia and related lymphoma	11	0.1%	0.04	[0.01-0.11]	0.06	[0.01-0.15]
05) IPD, Immunoproliferative disease	108	1.1%	0.45	[0.18-0.70]	0.58	[0.23-0.92]
06) PCN, Plasma cell neoplasm	1,376	14.2%	5.68	[4.73-6.62]	7.38	[6.13-8.62]
07) MZL, Marginal zone lymphoma	254	2.6%	1.05	[0.64-1.46]	1.34	[0.81-1.86]
08) FL, Follicular lymphoma and related lymphoma	839	8.7%	3.48	[2.73-4.22]	4.33	[3.39-5.25]
09) MCL, Mantle cell lymphoma	99	1.0%	0.41	[0.15-0.66]	0.54	[0.20-0.88]
10) DLBCL, Diffuse large B-cell lymphoma and related large B-cell lymphoma	1,317	13.6%	5.45	[4.52-6.38]	6.96	[5.75-8.16]
11) BL, Burkitt lymphoma / leukaemia	44	0.5%	0.18	[0.02-0.33]	0.21	[0.02-0.38]
12) pCTCL, Primary cutaneous T-cell lymphoma	103	1.1%	0.43	[0.16-0.68]	0.51	[0.19-0.82]
13) PNK/TCL, Peripheral NK/T-cell lymphoma	223	2.3%	0.92	[0.54-1.30]	1.14	[0.65-1.61]
14) ALL/LL, Precursor lymphoid neoplasm or acute lymphoblastic leukaemia/lymphoma	292	3.0%	1.21	[0.77-1.65]	1.08	[0.67-1.48]
15) AML, and related precursor neoplasm (incl. AL of ambiguous lineage)	656	6.8%	2.71	[2.05-3.36]	3.29	[2.47-4.09]
16) CML, Chronic myeloid leukaemia	166	1.7%	0.68	[0.35-1.01]	0.78	[0.40-1.16]
17) PV, Polycythaemia vera	210	2.2%	0.86	[0.49-1.23]	1.09	[0.61-1.55]
18) ET, Essential thrombocythemia	504	5.2%	2.07	[1.50-2.63]	2.52	[1.81-3.21]
19) PMF, Primary myelofibrosis	46	0.5%	0.19	[0.02-0.35]	0.25	[0.03-0.47]
20) Other MPN, Other MPN and related neoplasm	303	3.1%	1.25	[0.80-1.69]	1.56	[0.99-2.12]
21) MCN, Mast cell neoplasm	17	0.2%	0.07	[0.01-0.15]	0.08	[0.01-0.17]
22) MDS, Myelodysplastic syndrome	740	7.6%	3.07	[2.37-3.76]	4.12	[3.17-5.06]
23) MDS/MPN, Myelodysplastic / myeloproliferative neoplasm	90	0.9%	0.37	[0.13-0.61]	0.48	[0.16-0.79]
24) HDCN, Histiocytic and dendritic cell neoplasm	47	0.5%	0.20	[0.02-0.36]	0.18	[0.01-0.33]
25) Other leukaemia	106	1.1%	0.44	[0.17-0.70]	0.59	[0.23-0.94]
26) Other lymphoid neoplasm	194	2.0%	0.79	[0.45-1.13]	1.02	[0.56-1.46]

95%CI: 95% confidence interval; CR: crude rate; EASR: age-standardized incidence rate per 100,000 weighted using the European standard population 2013

APPENDIX II. HM deaths and mortality rates 2012-2021

Number of deaths and mortality rates of HMs during 2012-2021, by HM and sex						
Sex	HM	Deaths	CR	95%CI	EASR	95%CI
Males	All haematological malignancies	4,587	19.36	[17.58, 21.12]	31.62	[28.55, 34.67]
	Hodgkin lymphoma (C81)	126	0.54	[0.24, 0.82]	0.78	[0.33, 1.21]
	non-Hodgkin lymphoma (C82-85)	1,549	6.54	[5.51, 7.56]	10.44	[8.71, 12.16]
	immunoproliferative & other/unspecified (C88,C96,D47)	270	1.14	[0.70, 1.56]	2.03	[1.22, 2.84]
	multiple myeloma (C90)	988	4.17	[3.34, 4.98]	6.94	[5.50, 8.38]
	leukaemia (C91-95)	1,654	6.98	[5.91, 8.04]	11.43	[9.58, 13.27]
Females	All haematological malignancies	3,363	13.94	[12.44, 15.42]	18.59	[16.58, 20.59]
	Hodgkin lymphoma (C81)	103	0.43	[0.17, 0.68]	0.56	[0.22, 0.90]
	non-Hodgkin lymphoma (C82-85)	1,256	5.20	[4.29, 6.11]	6.97	[5.74, 8.19]
	immunoproliferative & other/unspecified (C88,C96,D47)	207	0.86	[0.48, 1.22]	1.14	[0.64, 1.63]
	multiple myeloma (C90)	778	3.22	[2.50, 3.93]	4.34	[3.36, 5.31]
	leukaemia (C91-95)	1,019	4.23	[3.40, 5.04]	5.58	[4.48, 6.67]
M&F	All haematological malignancies	7,950	16.62	[15.46, 17.77]	24.22	[22.50, 25.92]
	Hodgkin lymphoma (C81)	229	0.48	[0.28, 0.67]	0.66	[0.38, 0.93]
	non-Hodgkin lymphoma (C82-85)	2,805	5.87	[5.17, 6.55]	8.49	[7.48, 9.50]
	immunoproliferative & other/unspecified (C88,C96,D47)	477	1.00	[0.71, 1.27]	1.53	[1.08, 1.96]
	multiple myeloma (C90)	1,766	3.69	[3.14, 4.23]	5.45	[4.60, 6.26]
	leukaemia (C91-95)	2,673	5.59	[4.91, 6.26]	8.08	[7.09, 9.07]

95%CI: 95% confidence interval; CR: crude rate; EASR: age-standardized rate per 100,000 weighted using the European standard population 2013