National Collaborating Centre for Cancer

Haematological cancers

Addendum to Haematological Cancers:

improving outcomes (update)

Service Guidance Addendum

Appendices A-F

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Contents

Appendix A: The cost effectiveness of co-located and networked centralised specialist laboratories offering integrated diagnostic reporting in comparison to local reporting in the diagnosis of haematological cancers

A.1 Background

There is evidence of a significant misdiagnosis rate in haematological malignancies (5-15%) sometimes with major clinical consequences (Lester et al. 2003, Proctor et al. 2011). This type of error can be difficult to detect after a patient has been treated and therefore a premium must be placed on being able to demonstrate that a diagnosis is correct and supported by strong evidence across several independent investigative modalities.

A Specialist Integrated Haematological Malignancy Diagnostic Service (SIHMDS) has been suggested as an approach to improve diagnosis rates and clinical outcomes over local reporting. These can either be co-located (centred at one physical site) or networked (located at multiple physical sites but under one management structure). For either approach to be effective this multi-modality approach to diagnostic quality assurance requires a systematic approach to the investigation of specimens and a clear process to interpret and integrate the results obtained (via integrated diagnostic reporting), most crucially to identify inconsistencies between the results obtained by different investigative techniques. This is potentially most effectively delivered within an integrated diagnostic service able to provide the full range of diagnostic techniques required and to provide a report to the end users that integrates these results into a single diagnostic assessment. It may also reduce costs through the avoidance of repeat testing of patients, more effective use of tissue samples and through the economies of scale of running a large SIHMDS.

SIHMDS are likely to only be cost effective if they are of sufficient size as the availability of suitably trained staff (pathologists, clinical and biomedical scientists) is limited and constrains the number of centres able to offer this service. SIHMDS, especially those that are co-located are likely to require reasonable building space to house all staff and testing facilities.

A.2 Existing Economic Evidence

A systematic literature review was performed to assess the current economic literature for this topic. The review identified 99 possibly relevant economic papers relating to the topic of the diagnosis of haematological malignancies. Of these, no papers were deemed relevant for this topic and therefore no papers were included in the review of existing economic evidence.

A.3 De Novo Economic Model

The current economic literature did not adequately address the decision problem; therefore a de novo economic evaluation was created to assess cost effectiveness. All analyses were conducted in Microsoft Excel 2007.

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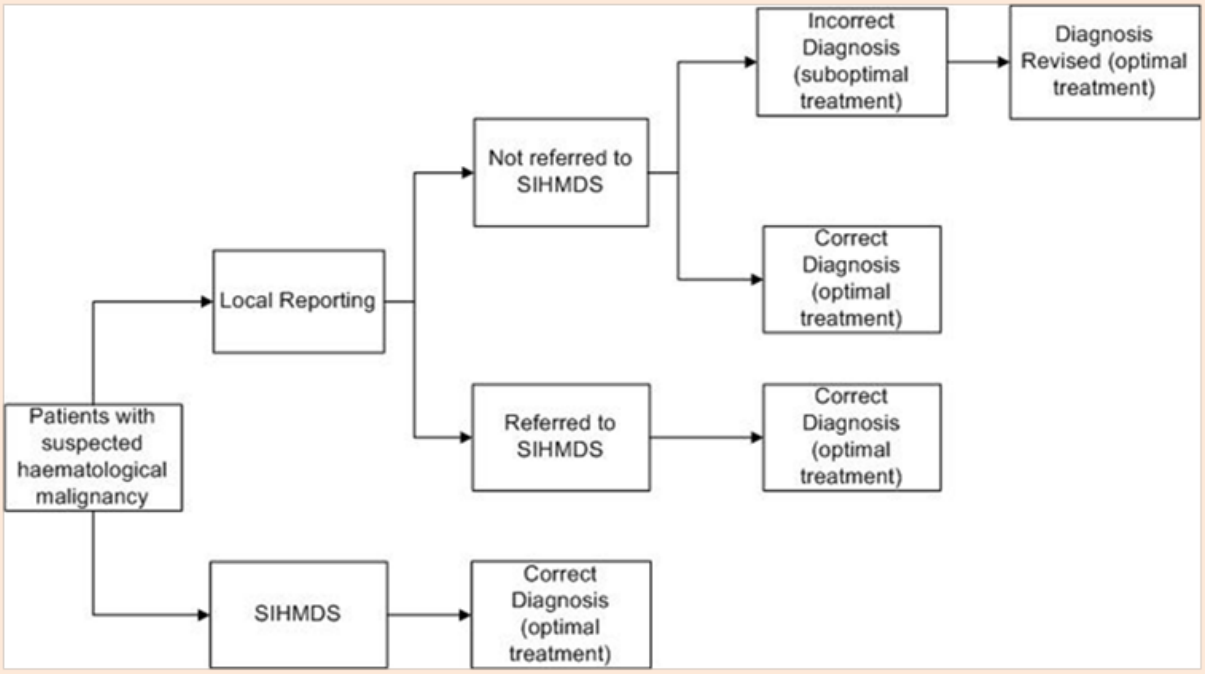
A.3.1 Aims of Analysis

The aim of the economic analysis was to assess the cost effectiveness of both a co-located and networked SIHMDS compared to local reporting. All analyses were conducted from a National Health Service (NHS) and Personal Social Services (PSS) perspective.

A.3.2 Model Structure

The economic model considered three potential ways of configuring diagnostic services for haematological cancers. The base case was assumed to be local reporting with a proportion of samples referred to SIHMDS for review. This was compared to an alternative of sending all samples in people with suspected haematological malignancies immediately for review by SIHMDS. Two configurations of SIHMDS were compared to local reporting- a co-located approach and a networked approach. Detailed definitions of each configuration are presented earlier in this IOG.

Figure 1: Model structure



The local reporting arm of the model assumes that all samples in people where a haematological malignancy is suspected would have all diagnostic testing in the diagnostic pathway (bone trephine, flow cytometry etc) performed locally and these various tests synthesised into an integrated report by a local haematologist. A proportion of these tests would be sent on to a SIHMDS after testing for verification of diagnosis (see later section on proportion of samples referred for further details). The results of these tests would either be concordant or discordant with the initial diagnosis made locally, based on discordance rates identified in the literature review (see section on 'discordance rates' below for further details). Concordant diagnoses result in the patients current treatment regimen being maintained (i.e. the treatment decision based on information obtained locally was found to be correct). Patients with a discordant diagnosis would have their diagnosis revised and may require a change in treatment (although some patients will not require a change in treatment). If the treatment strategy is changed, then there could be updated resulting in one of four possible changes to their current treatment regimen – 'no major change in treatment', 'treatment to no treatment', 'no treatment to treatment' or 'change in oncological treatment'. The proportions of patients requiring a change in management, including the type of change required were

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based on figures identified in the evidence review and are described in more detail in the 'change in treatment' section below.

In both SIHMDS arms of the model samples are sent off to the SIHMDS for review without any diagnostic workup at a local level. The MDT responsible for the patient's care would then receive an integrated report and treatment would be planned accordingly. The model assumes that diagnoses from the SIHMDS are always correct and optimal treatment would be received. Discussion of this assumption is presented later. Whilst this is an unlikely scenario, SIHMDS is considered the 'gold standard' for diagnosing haematological malignancies and consequently there is a paucity of evidence around its diagnostic accuracy. The number of incorrect diagnoses is likely to be very small in comparison to local reporting and any non-perfect diagnostic accuracy in the SIHMDS arms would be captured during sensitivity analysis when varying the discordance rate.

Total costs were estimated for each of the diagnostic service configurations. Total costs were estimated based upon the upfront costs associated with the diagnostic service (such as testing costs and staff costs) as well as the costs associated with a change in management after a discordant diagnosis (see later sections on costs for further details).

Quality adjusted life years (QALYs), which represent the number of life years that patients spend in a health state weighted by the quality of life (QoL) valuation associated with that health state, were also estimated for each of the diagnostic service configurations. The analysis focused on QALY losses that might be associated with a discordant diagnosis as this is the area where there was likely to be a difference in QALYs between the strategies (see later section on QALYs for further details).

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A.3.2.1 Prevalence

The prevalence of different haematological malignancies was taken from papers identified as part of both the economic and clinical evidence review. Prevalence for the base case was taken from one networked SIHMDS, managed from Sheffield serving a population of approximately two million. (Dalley et al. 2015) Dalley et al recorded the prevalence of disease referred between 1st October and 30th November 2011 as part of an activity based costing of the SIHMDS. (Table 1) This study was the most recent of the UK studies identified and the costings was also used to inform the network SIHMDS arm of the economic model.

As there will be variation across regions in terms of prevalence as a result of differing socio-economic factors across England. Prevalence was therefore varied, across a dirichlet distribution (Briggs, Ades, and Price 2003) during probabilistic sensitivity analysis (PSA), to capture this variance using numbers reported in the study.

Table 1: Prevalence of haematological malignancies for base case of economic model

Haematological Malignancy	Prevalence
Acute Lymphoblastic Leukaemia	0.9%
Acute myeloid leukaemia	3.0%
Acute Promyelocytic Leukaemia	0.7%
Aplastic Anaemia	0.5%
Lymphoma - bone marrow	6.7%
Lymphoma - other biopsy	7.6%
Lymphoma - lymph node	14.6%
Chronic Lymphocytic Leukaemia	6.5%
Hairy Cell Leukaemia	0.2%
Waldenstrom/Lymphoplasmacytic Lymphoma	0.2%

Haematological Malignancy	Prevalence
Myelodysplastic Syndrome	17.4%
Myeloproliferative Neoplasm: Chronic Myeloid Leukaemia	1.9%
Myeloproliferative Neoplasm: Chronic Myeloid Leukaemia ET	0.9%
Myeloproliferative Neoplasm: Chronic Myelomonocytic Leukaemia	1.2%
Myeloproliferative Neoplasm: Essential Thrombocythemia	9.5%
Myeloproliferative Neoplasm: Graft-Versus-Host Disease	0.2%
Myeloproliferative Neoplasm: Hyper Eosinophilic Syndrome	0.7%
Myeloproliferative Neoplasm: Myelofibrosis	1.4%
Myeloproliferative Neoplasm: Myelofibrosis Essential Thrombocythemia	0.2%
Myeloproliferative Neoplasm: -Unspecified	2.5%
Systemic mastocytosis	0.2%
Myeloproliferative Neoplasm: Polythemia Vera	9.3%
Myeloma	13.7%

A.3.2.2 Discordance Rate

The discordance rates between local reporting and SIHMDS were estimated in the accompanying clinical evidence review. The review identified 9 papers, 2 of which were UK based which compared initial haematological pathological diagnoses with expert review (Bowen et al. 2014, Chang et al. 2014, Herrera 2014, Lester et al. 2003, Proctor et al. 2011, Siebert et al. 2001, van de Schans et al. 2013) One US study reported a discordance rate of 60%, an outlier to other reported values. The guideline committee (GC) expressed that this discordance rate was likely to be much higher than the true value in England and was excluded from the estimate for the economic model. The base case model used the mean value from the included studies a discordance rate of 16%. As there was no evidence comparing diagnostic accuracy between the different configurations of SIHMDS they were assumed to be identical for both the networked and co-located approaches. Given a lack of consensus between the GC on any likely difference between the two on diagnostic accuracy this assumption remained for all baseline and sensitivity analyses in the economic analyses. This value was varied during sensitivity analysis, along a uniform distribution, over the reported range from the evidence review (6.0%-27.4%).

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A.3.2.3 Change in treatment

Only one study identified in the accompanying evidence review reported a change in treatment as a result of discordant diagnosis (Lester et al. 2003) with one further study reporting on a hypothetical change in treatment as part of a review by an expert panel. (Proctor et al. 2011) Both studies were retrospective reviews in UK laboratory settings with initial diagnoses being reviewed by central review or expert panel. To inform the economic model, inputs were taken from Lester et al as this was an actual revision of treatment it was considered to be most reflective of current NHS practice in England. Lester et al considered a sample of patients (n=99) who have received a change in initial diagnosis as a result of central haematopathological review. Lester et al reported that 54% of discordant diagnoses resulted in a change of management. The proportion of patients and description of change in management are reported in Table 2. The study only included lymphomas although the clinical evidence review suggested that the vast majority of discordant diagnoses were in these disease areas. Patients with lymphoma were therefore likely to get the majority of the benefit from any improvement in diagnostic accuracy. The economic model therefore assumed that only patients with lymphomas would get discordant diagnoses and consequently all changes in treatment would be in this subgroup.

Table 2: Change in Treatment in patients who received a discordant diagnosis

Change in Treatment	Proportion
No major change in Treatment	54%
Treatment to No Treatment	20%
No Treatment to Treatment	10%
Change in Oncological Treatment	16%
(Of which) Change Chemotherapy	81%

A.3.2.4 Proportion of Samples referred from Local Reporting to SIHMDS

No evidence was identified for the proportion of samples that would be forwarded to SIHMDS for expert review from following local reporting. It was however considered by the GC for there to be wide variation across England around the proportion referred on with some centres referring almost all samples onwards with others only referring a much smaller proportion of the more complex diagnoses. Given the lack of evidence and the wide variation the GC were unable to assign a definitive value, for use in the economic model around this parameter. Therefore, a range of proportions were investigated along an uninformative range between 0% and 100% of samples referred on to SIHMDS. Threshold analysis was also performed around this parameter to investigate at which values the conclusions of the economic model, in terms of preferred option, would change. For the purposes of the base case analysis it was assumed that 70% of samples would be referred for expert review.

It was noted by the GC that samples referred on for SIHMDS review are often inadequate for further analysis. This can be for a number of reasons e.g. insufficient size of sample for testing, incorrect preparation/storage etc. Whilst this could lead to increased costs, delayed treatment and decreased patient quality of life (through re-biopsying and delay in treatment) it was not explicitly covered by the economic model given that no evidence was identified, comparing the possible interventions, in this area. This issue would weigh against local reporting and the consequences of not explicitly including it in the economic model are discussed later.

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A.3.2.5 Quality of Life

The clinical evidence review identified no evidence around ‘quality of life’ (QoL) for the three different interventions. A wider search of the evidence was performed looking for evidence around QoL in misdiagnosis, non optimal treatment and changes in treatment in haematological cancers although no evidence was identified to inform the economic model. For practical and ethical reasons clinical evidence, in terms of RCTS and observational studies looking at misdiagnosis, inappropriate treatment or lack of appropriate treatment which could be used to estimate difference in QALYs or life years are not available in this area. It was therefore decided to estimate a range of likely lifetime QALY detriments, in terms of ‘quality adjusted life years’ (QALYs) associated with discordant diagnosis. (Table 3)

Table 3: Estimated Lifetime QALY detriment of a discordant diagnosis

	Estimate Lifetime QALY Detriment
Lower	0
Basecase	0.53
Upper	1.06

The lower end of the range estimated the detriment in QALYs, as a result of an incorrect diagnosis, to be zero. Whilst the GC felt this was very unlikely to be the true value it represented a conservative estimate where misdiagnoses would be identified and appropriate treatment started in a relatively short period of time and that any impact on QoL

would be relatively small. Whilst being conservative it also represents the absolute minimum value possible for any treatment for which total QALYS, as a result of treatment, are non negative (i.e. not harmful).

The middle estimate for QALY detriment was taken from the TA243 comparing the addition of rituximab(R) in addition to cyclophosphamide, doxorubicin/adriamycin, vincristine and prednisolone (CHOP) compared to CHOP alone in the treatment of follicular lymphoma. The base case analysis estimated by the TA243 assessment group estimated an incremental QALY of 0.53. Effectiveness data in the model was from RCT evidence with QoL data collected using EQ-5D: NICE's preferred measure of quality of life.

Lymphomas make up approximately 30% of all diagnoses in the estimated prevalence for the model and are associated with the largest proportion of discordant diagnoses. R-CHOP is standard treatment for follicular lymphoma in the UK and it was hypothesised that the incremental QALY would provide an estimate, in the absence of strong evidence, of the difference in QALY between optimal treatment (as a result of a correct diagnosis) and inappropriate treatment.

An upper QALY detriment was also estimated equal to double the base case estimate. Whilst treatment with CHOP alone may be considered suboptimal treatment it is still likely to be effective and lead to a lower QALY detriment compared to inappropriately not treating a patient or treating them with a potentially harmful intervention. For example the inappropriate treatment of Burkitt lymphoma with R-CHOP, due to a misdiagnosis of lymphoma subtype, increases the likelihood of remission and relapse. It is therefore quite likely that our baseline estimate underestimates the true detriment. Given the lack of evidence around inappropriately not treating or incorrectly treating patients discussed above this was considered to represent an upper estimate of total QALY detriment. QALY detriment was given a uniform distribution between the lower and upper estimate during probabilistic sensitivity analysis (PSA).

We were also unable to estimate baseline quality of life values for the patient cohort in this model however as economic evaluation is primarily an incremental analysis the differences in total QoL in the analysis as a result of differences in diagnostic accuracy would be captured and the conclusions of the model identical regardless of the baseline value.

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A.3.3 Costs

A.3.3.1 Networked SIHMDS

The cost for the networked SIHMDS were taken from the one identified published costing of an English SIHMDS (Dalley et al. 2015). The study, discussed earlier, used Activity Based Costing (ABC) to create a cost model, based on activity data between 1st October to 30th November 2011. The number of tests for each disease and diagnostic pathway were calculated by this study. These numbers were converted into the percentage of diagnoses receiving each diagnostic test, grouped by disease, to inform the economic model (Table 4).

From this workload Dalley et al calculated a resource use per diagnosis using Welcan units (Sims 1992). Dalley et al assigned each Welcan unit a cost of 94p and a cost per disease to calculate a cost per diagnosis (Table 5).

Table 4: Percentage of diagnoses receiving each diagnostic test

	Bone marrow aspirate	Flow	Bone marrow trephine	Trephine immunos	Lymph morph-ology	Lymph immuno	Cyto-genetics	FISH	Jak2	BCR-ABL1 break-point	BCR-ABL1/ ABL1 ratio	IgH/ TCR	Chimer-ism
Acute Lymphoblastic Leukaemia	100	100	50	0	0	0	0	0	0	0	0	0	0
Acute myeloid leukaemia	77	77	69	23	0	0	54	31	0	0	0	0	0
Acute Promyelocytic leukaemia	67	100	67	0	0	0	100	100	0	0	0	0	0
Aplastic Anaemia	100	50	100	0	0	0	0	0	0	0	0	0	0
Lymphoma	90	41	100	45	0	0	24	7	0	0	0	0	0
Lymphoma	0	0	0	0	100	97	0	3	0	0	0	0	0
Lymphoma	0	0	0	0	100	89	0	0	0	0	0	3	0
Chronic Lymphocytic Leukaemia	0	96	0	0	0	0	0	4	0	0	0	0	0
Hairy Cell Leukaemia	0	100	0	0	0	0	0	0	0	0	0	0	0
Waldenstrom	100	100	100	0	0	0	0	0	0	0	0	0	0
Myelodysplastic Syndrome	100	25	97	33	0	0	95	3	0	0	0	1	0
Chronic Myeloid Leukaemia	50	0	38	0	0	0	50	75	25	13	0	0	0
Chronic Myeloid Leukaemia Essential Thrombocythemia	50	25	50	0	0	0	50	50	100	0	0	0	0
Chronic Myelomonocytic Leukaemia	100	20	100	20	0	0	80	60	0	0	0	0	0
Essential Thrombocythemia	32	2	32	2	0	0	5	24	76	0	0	0	0

	Bone marrow aspirate	Flow	Bone marrow trephine	Trephine immunos	Lymph morph-ology	Lymph immuno	Cyto-genetics	FISH	Jak2	BCR-ABL1 break-point	BCR-ABL1/ ABL1 ratio	IgH/ TCR	Chimer-ism
Graft-Versus-Host Disease	0	0	0	0	0	0	0	0	100	0	0	0	0
Hyper Eosinophilic Syndrome	67	0	67	33	0	0	67	100	33	0	0	0	0
Myelofibrosis	33	0	50	0	0	0	50	17	83	0	0	0	0
Myelofibrosis Essential Thrombocythemia	0	0	0	0	0	0	0	0	100	0	0	0	0
Myeloproliferative Neoplasm - Unspecified	9	0	9	9	0	0	0	9	91	0	0	0	0
Systemic mastocytosis	100	0	100	0	0	0	0	0	0	0	0	0	0
Polythemia Vera	8	0	8	0	0	0	5	0	95	0	0	0	0
Myeloma	97	3	98	64	0	0	30	0	0	0	0	2	0

Table 5: Cost per diagnosis-Networked SIHMDS

Haematological Malignancy	Cost
Acute Lymphoblastic Leukaemia	£608
Acute myeloid leukaemia	£473
Acute Promyelocytic Leukaemia	£695
Aplastic Anaemia	£286
Lymphoma - bone marrow	£321
Lymphoma - other biopsy	£206
Lymphoma - lymph node	£191
Chronic Lymphocytic Leukaemia	£206
Hairy Cell Leukaemia	£204
Waldenstrom/Lymphoplasmacytic Lymphoma	£553
Myelodysplastic Syndrome	£481
Myeloproliferative Neoplasm: Chronic Myeloid Leukaemia	£423
Myeloproliferative Neoplasm: Chronic Myeloid Leukaemia ET	£444
Myeloproliferative Neoplasm: Chronic Myelomonocytic Leukaemia	£572
Myeloproliferative Neoplasm: Essential Thrombocythemia	£189
Myeloproliferative Neoplasm: Graft-Versus-Host Disease	£66
Myeloproliferative Neoplasm: Hyper Eosinophilic Syndrome	£586
Myeloproliferative Neoplasm: Myelofibrosis	£280
Myeloproliferative Neoplasm: Myelofibrosis Essential Thrombocythemia	£66
Myeloproliferative Neoplasm: -Unspecified	£112
Systemic mastocytosis	£185
Myeloproliferative Neoplasm: Polythemia Vera	£88
Myeloma	£242

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These costs included all costs associated with diagnosis including administrative costs (£23.50 per test) and consultant haematopathologists time (£47.73 and £33.31 for haematology and histopathology laboratory test work respectively). The costs of genetic tests were taken from block contracts and previously defined prices. The paper estimated an annual running cost of £1,056,726. This estimate included costs for laboratory testing around monitoring, staging and post-chemotherapy assessment. As these were outside the scope of the economic model costs assigned to them were removed from the reported estimate to give a total cost of £723,192. As the SIHMDS estimated they would diagnose 2592 haematological malignancies per year from the activity data this equates to a cost of £279 per diagnosis.

A.3.3.2 Co-Located SIHMDS

No published evidence was identified for the costs of a co-located SIHMDS. Costs were therefore calculated from annual accounting data for 2014-2015 from one co-located centre, serving a population of 3.8 million in the Yorkshire area of England. (Haematological Malignancy Diagnostic Service: Leeds, Personal Communication, July 2015) The accounting data reported an annual running cost of £1,881,021 again including all administrative (£13.59 per test) and consultant costs (£31.83 per test). As with Dalley et al the data included costs for monitoring, staging and post-chemotherapy assessment.

The accounting data reported costs in terms of cost per test performed and not an aggregated total cost per diagnosis. To try and make the results comparable we used the same prevalence and proportion of tests per case as those reported by Dalley et al but used

the test, administrative and consultant costs as reported from Jaks et al. The costs of diagnosis at a co-located SIHMDS per diagnosis are reported in Table 6.

Table 6: Cost per diagnosis-Co-Located SIHMDS

Haematological Malignancy	Cost
Acute Lymphoblastic Leukaemia	£258
Acute myeloid leukaemia	£384
Acute Promyelocytic Leukaemia	£516
Aplastic Anaemia	£294
Lymphoma - bone marrow	£375
Lymphoma - other biopsy	£229
Lymphoma - lymph node	£215
Chronic Lymphocytic Leukaemia	£82
Hairy Cell Leukaemia	£76
Waldenstrom/Lymphoplasmacytic Lymphoma	£400
Myelodysplastic Syndrome	£392
Myeloproliferative Neoplasm: Chronic Myeloid Leukaemia	£328
Myeloproliferative Neoplasm: Chronic Myeloid LeukaemiaET	£327
Myeloproliferative Neoplasm: Chronic Myelomonocytic Leukaemia	£490
Myeloproliferative Neoplasm: Essential Thrombocythemia	£170
Myeloproliferative Neoplasm: Graft-Versus-Host Disease	£34
Myeloproliferative Neoplasm: Hyper Eosinophilic Syndrome	£501
Myeloproliferative Neoplasm: Myelofibrosis	£210
Myeloproliferative Neoplasm: Myelofibrosis Essential Thrombocythemia	£34
Myeloproliferative Neoplasm: -Unspecified	£88
Systemic mastocytosis	£256
Myeloproliferative Neoplasm: Polythemia Vera	£55
Myeloma	£350

This approach estimated a total cost of the diagnostic portion of the co-located SIHMDS as £675,662 an average cost of £261 per diagnosis, less costly than a networked approach. These estimates however should be interpreted with caution. Both centres are likely to differ in their case mix, the diagnostic pathways and tests used to get to a diagnosis. Both centres serve different sized populations with different demographics. As we only had cost evidence for two centres, one of each configuration, we were unable to do any analysis around any potential 'economies of scale' of running a service for a larger population or optimal population size for each configuration of SIHMDS. Differences in demographics may also skew unit costs e.g. if one demographic has a higher prevalence of a disease that requires testing through high, one-off fixed cost equipment. As a result of this very large uncertainty around differences in cost extensive sensitivity analysis was carried out around this area.

The cost of samples sent on from local reporting to SIHMDS for review were assumed to cost the same as a sample sent directly to SIHMDS with no local testing.

A.3.3.3 Local Reporting

Given the large variations in local reporting across England discussed earlier it was difficult to assign a cost to local reporting. The conservative assumption was made that it would be less per diagnosis than SIHMDS. In the base case the cost of local reporting was assigned an arbitrary cost of £100. The GC considered this to be a significant underestimate of the true costs of local reporting and would favour local reporting during the economic analysis.

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The assumption was tested during threshold analysis varying the cost from £0 to the same cost as SIHMDS. The assumption that local reporting would be more costly than SIHMDS was also investigated during probabilistic sensitivity analysis.

A.3.3.4 Set Up Costs

All three alternative approaches considered are already operating in different centres throughout England and that a recommendation towards any approach will be associated with both set up costs (building of accommodation, recruitment, administrative costs etc) and decommissioning costs (redundancy, removal of out dated equipment etc). No estimates of these set up and decommissioning costs were identified although there would be wide variation across England dependant on the current configuration of services locally. Given these difficulties in estimating this cost it was not explicitly considered in the economic analysis although sensitivity analysis was performed to investigate any changes to the preferred option as a result of increased diagnostic costs.

A.3.3.5 Cost Discordant Diagnosis

No evidence on the costs of treatment in patients misdiagnosed in haematological malignancies was identified in the economic evidence review. The cost of a discordant diagnosis which resulted in a change from treatment to no treatment was therefore estimated to be £2,981, the cost of one cycle of R-CHOP as estimated in TA243. As discussed earlier lymphoma remains the disease area with the highest proportion of discordant diagnoses and R-CHOP remains standard treatment for this group. It was assumed that a correct diagnosis would be ascertained after one cycle of treatment. Given the uncertainty around this value it was varied along a uniform distribution during PSA between £0 and twice its value.

The GC conservatively estimated that there would be no additional cost for changes from ‘no treatment to treatment’ and for changes in treatment. No evidence was identified that patients who start therapy later in haematological malignancies incur additional costs compared with patients who start immediately and it was difficult to tell the direction of additional costs. Whilst patients may incur additional costs through worse outcomes and adverse events from untreated disease there may also be cost savings through decrease and delayed (discounted) use of expensive therapies. Similar is true in ‘change in treatment’ where 9 in 10 patients received a change from one potentially costly chemotherapy to another. Again increased costs from expensive incorrect chemotherapy may be offset by delayed and reduced use of the appropriate chemotherapy.

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A.3.3.6 Medico-legal costs

Medico-legal costs associated with misdiagnosis were not considered by the economic model. It was considered by the GC though that these would be much larger in the less diagnostically accurate intervention and that not including them would weigh in favour of local reporting in terms of the preferred intervention.

A.3.3.7 Cost Year

All costs incorporated in the economic model were at 2015 prices and in UK sterling. Therefore it was not necessary to inflate or convert any costs.

A.3.3.8 Discounting

All costs and QALYs were discounted at 3.5% per annum as recommended by the NICE Guidelines Manual 2014. (National Institute for Health and Care Excellence 2014)

A.3.3.9 Sensitivity analysis

For the base case analyses a range of deterministic and threshold sensitivity analyses were conducted to test the robustness of the results of the economic analysis to different input parameters. PSA was also conducted around the base case to assess the combined parameter uncertainty in the model. In this analysis, the mean values that are utilised in the base case are replaced with values drawn from distributions around the mean values. 1000 iterations were run, for the PSA, around total costs, total QALYs and the ICER. These iterations were used to produce the cost effectiveness planes (CEP) and to estimate the 95% confidence intervals around costs.

A.3.4 Results

A.3.4.1 Deterministic Base Case Results

Table 7 show the base case results for the different configurations of diagnostic services for haematological malignancies. In the base case analysis both SIHMDS approaches are dominant (cost saving and health improving) compared to local reporting. Both configurations of SIHMDS remained cost saving and health improving when the means of the 1000 probabilistic iterations were used (Table 8). A co-located approach led to the greatest cost saving per diagnosis in both the deterministic and stochastic results although the 95% confidence intervals always overlap. Whilst the probabalistic results show that a co-located approach is health improving compared to a networked approach, the assumptions around effectiveness are identical for both SIHMDS approaches and this difference was entirely due to chance and equivalent to an increased life expectancy of three hours in perfect health.

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Table 7: Deterministic Base Case Results

	Incremental Cost per diagnosis	Incremental QALY per Diagnosis	ICER
Local Reporting	Reference		
SIHMDS-Network	-£37	0.01129	Dominant
SIHMDS- Co-Located	-£56	0.01129	Dominant

Table 8: Probabalistic Results

	Incremental Cost per diagnosis (95 Confidence Interval)	Incremental QALY per Diagnosis	ICER
Local Reporting	Reference		
SIHMDS-Network	-£27(-£50,£167)	0.01144	Dominant
SIHMDS- Co-Located	-£29 (-£74,£146)	0.01175	Dominant

A.3.4.2 Deterministic and Threshold Sensitivity Analysis

The preferred option remains constant for all possible QALY detriments as a result of a discordant diagnosis with both SIHMDS approaches reaming dominant. Even under the unlikely assumption that a discordant diagnosis would lead to no QALY detriment and thus the effectiveness of all three interventions are identical, the SIHMDS approaches remains cost saving (Table 9).

Table 9: Impact on the preferred option of varying the lifetime QALY detriment

Lifetime QALY Detriment	0 QALYs		0.53 QALYs		1.06 QALYs	
	Incremental QALY	ICER	Incremental QALY	ICER	Incremental QALY	ICER
Local Reporting	Reference					
SIHMDS-Network	0	Dominant	0.01129	Dominant	0.02257	Dominant
SIHMDS- Co-Located	0	Dominant	0.01129	Dominant	0.02257	Dominant

For all values of laboratory costs for local reporting the ICER for SIHMDS compared to local reporting remains under £20,000 per QALY for both configurations of SIHMDS. Table 10 shows the results of the deterministic sensitivity analysis when zero testing costs are assumed at the local level: an unrealistic assumption but the most favourable possible towards local reporting. Whilst the SIHMDS approach is now estimated to be cost increasing, both ICERs are below the £20,000 per QALY threshold. The incremental costs in this example are identical to the maximum local reporting costs needed for each configuration to be cost saving and health improving. This equates to a maximum difference between the cost of either SIHMDS approach compared to local reporting of £217 per diagnosis for the SIHMDS approach to remain cost saving. For the ICER to remain under £20,000 per QALY the maximum difference would be £442.

Table 10: Sensitivity analysis with local reporting incurs zero cost

	Incremental Cost per diagnosis	Incremental QALY per Diagnosis	ICER
Local Reporting	Reference		
SIHMDS-Network	£63	0.01129	£5,556
SIHMDS- Co-Located	£44	0.01129	£3,931

A similar conclusion is identified with the proportion of samples being referred for review or testing to SIHMDS. Again when a hugely favourable assumption of 0% being referred to SIHMDS from local reporting the ICERs remained below £20,000 per QALY (Table 11). The GC felt again this assumption was unlikely and that whilst these sensitivity analyses assumed that QALY outcomes were not influenced by the proportion referred the evidence review suggested strongly that the two would have some covariance. It is likely therefore that even under this very favourable assumption it would be an underestimate of the true cost effectiveness of SIHMDS. The Co-Located and Networked configurations become cost saving when the proportions referred to SIHMDS are 50% and 57% respectively. Again the co-variance between the proportion referred and health outcomes mean these are again likely overestimates of the true proportion.

Table 11: Sensitivity analysis where proportion referred to SIHMDS is equal to zero

	Incremental Cost per diagnosis	Incremental QALY per Diagnosis	ICER
Local Reporting	Reference		
SIHMDS-Network	£152	0.01129	£13,441
SIHMDS- Co-Located	£133	0.01129	£11,816

When these two favourable assumptions are combined the ICERs for the two configurations of SIHMDS marginally exceed £20,000 per QALY (Table 12). With the covariance between referral and health outcomes these are again likely to underestimate the true cost-effectiveness of SIHMDS.

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Table 12: Threshold analysis where local reporting costs and proportion referred to SIHMDS is equal to zero

	Incremental Cost per diagnosis	Incremental QALY per Diagnosis	ICER
Local Reporting	Reference		
SIHMDS-Network	£252	0.01129	£22,300
SIHMDS- Co-Located	£233	0.01129	£20,676

A.3.4.3 Probabilistic Sensitivity Analysis

Figure 2 shows the CEP for a networked SIHMDS approach. The probabilistic result shows that 40.6% of the iterations were cost saving and health improving (in the South East quadrant of the CEP) with 84.6% being below the £20,000 per QALY threshold. Almost identical results are shown for co-located SIHMDS versus local reporting (Figure 3) with 46.5% of iterations being cost saving and health improving and 85.3% being below the £20,000 per QALY threshold. Again, for reasons discussed earlier this is likely to again be an underestimate of the cost effectiveness of the SIHMDS approach. These results are reiterated by the cost effectiveness acceptability curves (Figure 4, Figure 5). The networked and co-located approaches had a greater than 50 chance of being cost effective for willingness to pay values of £3,000 and £1,000 per QALY respectively, well below a threshold of £20,000 per QALY.

Co-located and networked SIHMDS were not directly compared in this way as the model assumed equal effectiveness for the two interventions throughout all sensitivity analyses. When the costs between the two interventions were compared probabilistically a co-located SIHMDS was cost saving compared to a networked approach in 56% of iterations.

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Figure 2: Cost effectiveness plane for Networked SIHMDS versus Local Reporting

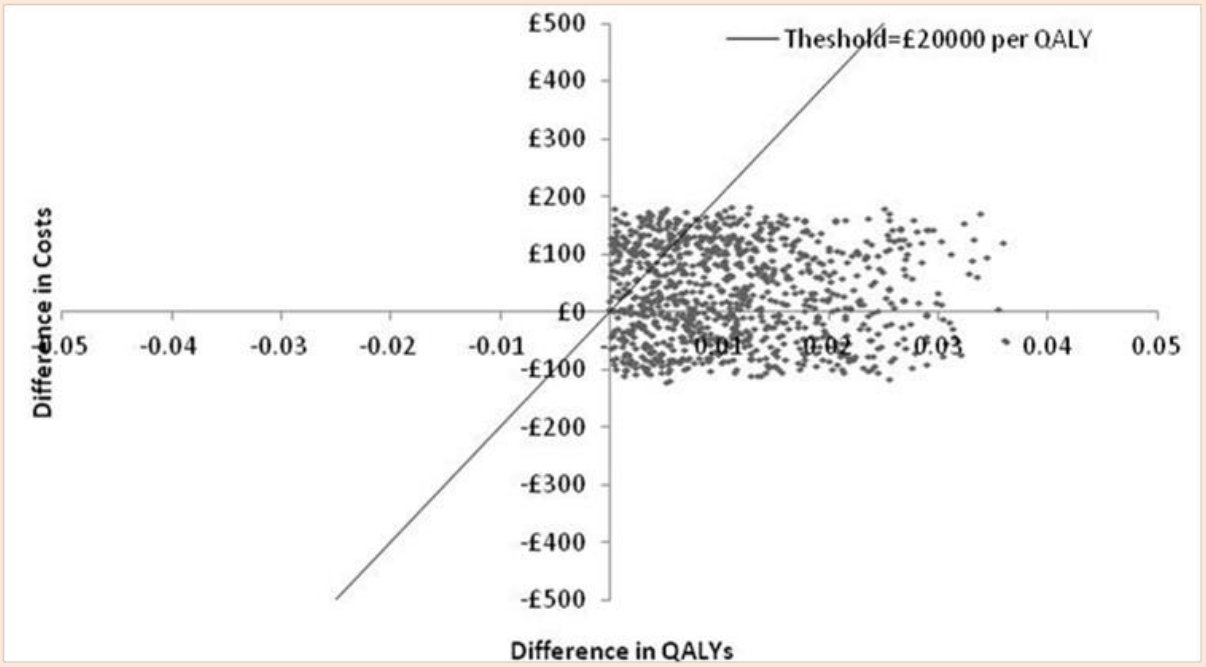

Figure 3: Cost effectiveness plane for Co-Located SIHMDS versus Local Reporting

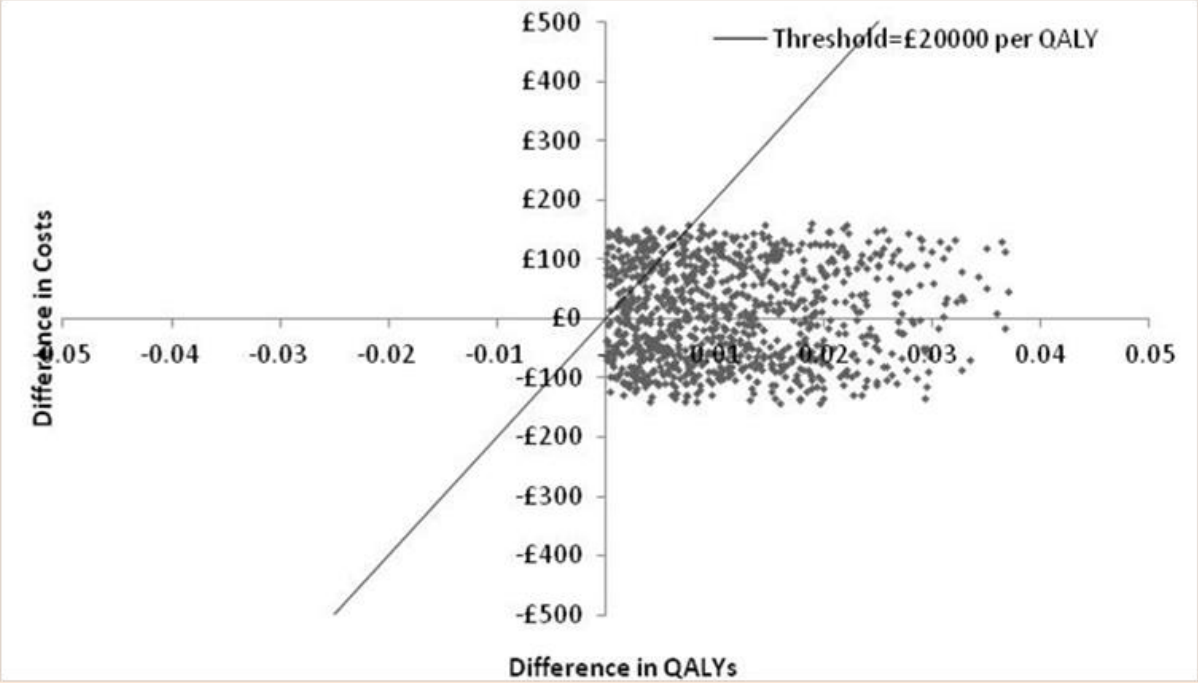

Figure 4: Cost effectiveness acceptability curve for Networked SIHMDS versus Local Reporting

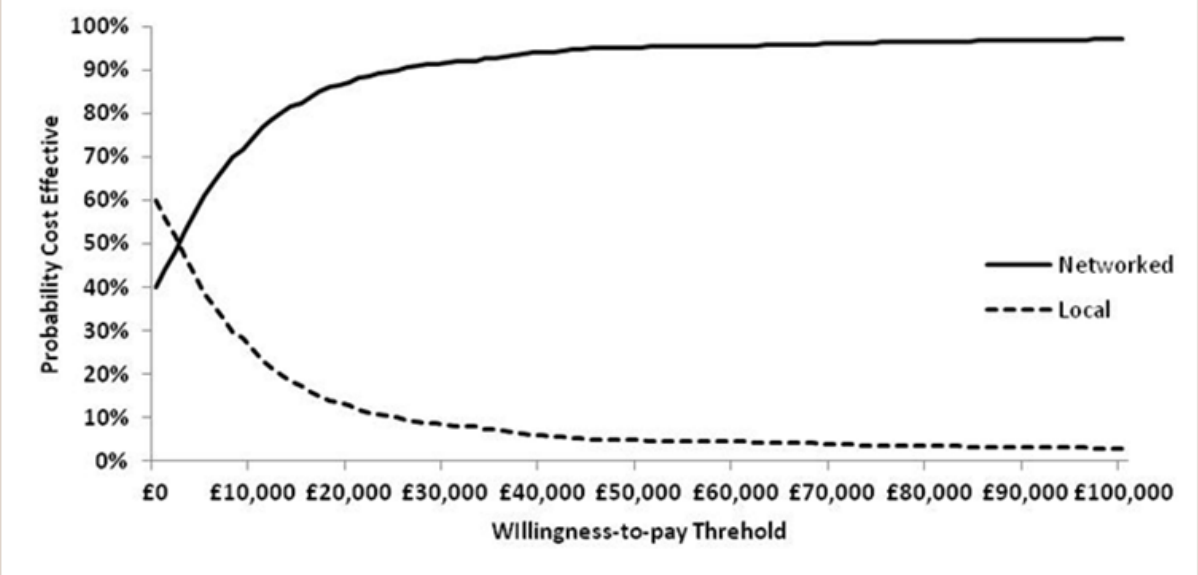

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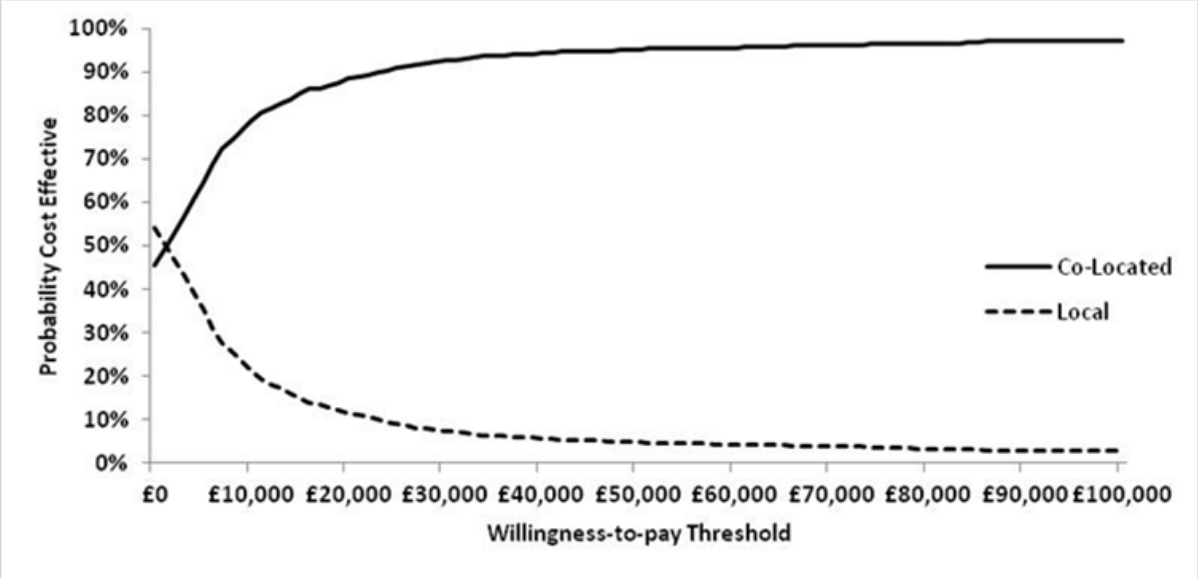
Figure 5: Cost effectiveness acceptability curve for Co-Located SIHMDS versus Local Reporting



A.3.5 Conclusions

The results of the base case analysis showed that both SIHMDS approaches were preferred over local reporting. This result was robust to sensitivity analysis even under unrealistically favourable assumptions around local reporting. The preferred option remained consistent even under large increases in cost again under otherwise favourable assumptions towards local reporting with the estimated costs of SIHMDS costs needing to increase by over 50% to a difference £442 per diagnosis between local reporting and SIHMDS. This equates to a cost of over £1,000,000 for a centre performing 2500 diagnoses a year, the number of diagnoses estimated for a population of two million (Dalley et al, 2014). The PSA again confirmed the robustness of the results to differing assumptions with over 85% of iterations estimating ICERs below £20,000 per QALY. Even though the results showed a preponderance towards a co-located SIHMDS over a networked configuration it was not possible, given the evidence available, to make any strong conclusions over the preferred configuration of SIHMDS from the results of the economic model.

Given the paucity of identified evidence around economies of scale, optimal population size, patient satisfaction and the need for repeat biopsies and viability of samples sent for reporting the model did not consider these aspects of the topic. With the exception of set-up costs, the GC felt strongly though that all of these factors would have strongly weighed in favour of SIHMDS increasing the robustness of the conclusions of the model. This again suggests that the conclusions of the economic model, already strongly supporting a SIHMDS approach as the preferred option, even under favourable assumptions towards local reporting, may even further underestimate its true cost effectiveness.

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Appendix B: Needs Assessment

B.1 Methods

Information in this report is drawn from a number of primary sources this section highlights key aspects of relevant methodologies, further details can be found through the reference section.

B.1.1 Definition of included cases and disease groups

Haematological cancers are a very diverse group of malignancies, and traditional disease classification systems (International Classification of Diseases version 10 ICD-10) do not always provide a good match to clinically relevant disease groups. However, the following ICD-10 codes (Table 13) have been used to categorise haematological cancers when national data on incidence, mortality and survival are presented.

Table 13: ICD10 codes for haematological malignancies

Disease Group	ICD10 code
Acute Lymphoblastic Leukaemia	C91.0
Acute Myeloid Leukaemia	C92.0, C92.4, C92.5, C93,0 C94.0 C94.2
Chronic Lymphoid Leukaemia	C91.1
Chronic Myeloid Leukaemia	C92.1
Hodgkin Lymphoma	C81
Non Hodgkin Lymphoma	C82, C83, C84, C85
Myeloma	C90
Other	C91.2, C91.3 C91.4, C91.5, C91.7, C91.9, C92.2, C92.3, C92.7, C92.9, C93.1, C93.2, C93.7, C93.9,C94.3, C94.4, C94.5, C94.7, C95.0, C95.1, C95.2, C95.7, C95.9, C96.0, C96.1, C96.2, C96.3, C96.7,C96.9

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B.1.2 Data sources

New cases of haematological cancers (incidence) in England are registered by the National Cancer Registration Service (NCRS), which is part of Public Health England (PHE).

All deaths in England are certified by a medical professional and then processed by the Office for National Statistics (ONS). The ONS derive a single underlying cause of death – this is what is counted for official statistics.

B.1.3 Age-standardised Rates

To adjust for variation in the age distributions between areas and across time age-standardised rates have been used for measures of incidence and mortality. Rates have been standardised to the European Standard Population (ESP). 1976 ESP weights and ONS mid-year population estimates have been used throughout.

B.1.4 Relative Survival

In a cohort of cancer patients, overall (observed) mortality can be divided into two components: the background mortality, also known as the expected mortality representing all-cause deaths in the general population, and the excess mortality due to cancer. Background mortality is calculated from life tables for England.

Relative survival reflects the excess mortality among cancer patients, over and above the background mortality in the country or region where they live. It is the ratio of the observed survival rate and the expected survival rate of the general population with a similar age/sex structure to the cancer patients in the study.

The survival analyses undertaken in this report use relative survival estimated using the maximum likelihood method for individual records, developed by Estève Et al (1) using the strel2 command in Stata version 13. This method assumes that the hazard is constant within each interval.

B.1.5 Routes to diagnosis

The Routes to Diagnosis study, established by the National Cancer Intelligence Network (NCIN), defines a methodology by which the route the patient follows to the point of diagnosis can be categorised, in order to examine demographic, organisational, service and personal reasons for delayed diagnosis. Administrative Hospital Episode Statistics (HES) data are combined with Cancer Waiting Times (CWT) data, data from the cancer screening programmes and cancer registration data from the National Cancer Data Repository (NCDR). Using these datasets every case of cancer registered in England which was diagnosed in 2006-2013 is categorised into one of eight 'Routes to Diagnosis' listed in the table below (Table 14) (Elliss-Brookes et al (2012).

The methodology is described in detail in the British Journal of Cancer article "Routes to Diagnosis for cancer - Determining the patient journey using multiple routine datasets".

Table 14: Categories of 'route to diagnosis'

Route	Description
Screen Detected	Detected via the breast, cervical or bowel screening
Two Week Wait	Urgent GP referral with a suspicion of cancer
GP Referral	Routine and urgent referrals where the patient was not referred under the TWO week wait referral route
Other outpatient	An elective route starting with an outpatient appointment, either self referral, consultant to consultant, other referral
Inpatient Elective	Where no earlier admission can be found prior to admission from a waiting list booked or planned
Emergency Presentation	An emergency route via A & E, emergency GP referral, emergency transfer, emergency consultant outpatient referral, emergency admission or attendance
Death Certificate Only	No date available from Inpatient or Outpatient HES, CWT, screening and with a death certificate only from diagnosis flagged by the registry in NCDR
Unknown	No data available from Inpatient or Outpatient HES, CWT, screening within set time parameters or unknown referral

Update 2016

B.1.6 Patient experience survey

The Cancer Patient Experience Survey 2014 is the fourth iteration of the survey following its successful implementation in 2010, 2012, and 2013. The survey covers all 153 acute and specialist NHS Trusts in England that provide adult acute cancer services.

The 2014 Cancer Patient Experience Survey covered over 118,000 NHS patients who were seen for treatment in hospital in the period 1st September 2013 and 30th November 2013

and who had a primary diagnosis of cancer. More than 70,000 cancer patients responded to the survey[a].

B.1.7 National Audit of Cancer Diagnosis in Primary Care

An audit of cancer diagnosis in primary care was undertaken in 2009/10 as part of the National Awareness and Early Diagnosis Initiative (NAEDI) with the intention to better understand and address the reasons for later diagnosis of cancer in England. Information was collected on patient demographics and the nature of the assessment process in primary care, including the time taken from first presentation to referral.

B.2 Key points

Population-based national incidence rates for England (as estimated by cancer registrations) rose over the period 2001-2010 for some haematological cancers: Hodgkin lymphoma, non-Hodgkin lymphoma (NHL) and myeloma. There are no haematological cancers for which incidence rates were in decline over that period.

Registration rates for haematological cancers were subject to change as a consequence of improvements in the ascertainment of new cases and developments in diagnosis and classification of disease; therefore not all observed changes may represent true differences in underlying incidence.

Population-based mortality rates fell over the period 2001-2010 for some haematological cancers: acute lymphoblastic leukaemia, chronic myeloid leukaemia, non-Hodgkin lymphoma and myeloma.

Relative survival improved for individuals in specific age groups who were diagnosed between 2000 and 2010 for a number of haematological cancers: acute lymphoblastic leukaemia (0-14 years males and females; 15-64 years males), acute myeloid leukaemia (15-64 years), chronic myeloid leukaemia, non-Hodgkin lymphoma, and myeloma.

For the most commonly encountered forms of leukaemia in older adult life (65+), acute myeloid leukaemia and chronic lymphocytic leukaemia, there was no evidence of significant change in the outcome for patients diagnosed and registered over this time period.

Although the incidence of haematological malignancy does not generally differ by deprivation, significant differences in the outcomes of patients depending on the level of deprivation in the area in which they live have been noted. For the data examined here, there were some differences observed in incidence by deprivation with higher incidence in the most deprived quintile for acute myeloid leukaemia (AML) and Hodgkin lymphoma. Both Hodgkin lymphoma and NHL showed significantly higher mortality rates in the most deprived quintiles compared to the least deprived; and there were significant differences in relative survival by quintile of deprivation for chronic lymphocytic leukaemia (CLL), chronic myeloid leukaemia (CML) and Hodgkin lymphoma at five years, and myeloma and NHL at one and five years.

For the majority of haematological malignancies GP referral was the most common route to diagnosis, with the exception of AML and ALL where emergency presentation was the most common route with over half of all presentations being via this route. CML and myeloma had similar proportions of GP referral and emergency presentations. All haematological malignancies with the exception of Hodgkin lymphoma had a significantly higher proportion of emergency presentation than all malignancies combined (23%). Relative survival was significantly poorer for emergency presentations for the majority of haematological malignancies. The exception to this was ALL where one-year relative survival for emergency

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a Quality Health – National Cancer Patient Experience Survey: https://www.quality-health.co.uk/surveys/national-cancer-patient-experience-survey

presentations was similar to all other routes. For some acute haematological malignancies emergency presentation may be the most appropriate route to diagnosis.

The majority of patients included in an audit which asked how many times a patients had consulted their GP prior to diagnosis had consulted their GP once or twice (66%), however a third of myeloma patients (33%) had consulted their GP three or more times, and 14% had consulted their GP five or more times. For lymphoma patients 22% of patients had consulted their GP three times or more, and 8% more than five times.

B.3 Introduction

Haematological malignancies are diseases originating in the bone marrow and lymph nodes and include leukaemias, lymphomas and myeloma. They are a very diverse group of diseases affecting people across the whole life course, but with their greatest incidence among the elderly. The prognosis and responsiveness to treatment of these conditions also varies very widely.

Haematological malignancies accounted for 8.4% of all malignant disease (excluding non-melanoma skin cancer) diagnosed in England in the years 2001 to 2010v.

B.3.1 Data quality and availability

Accurate capture of information on haematological malignancies nationally is an ongoing challenge, although data capture has improved over the period reported. Haematological malignancies are extremely diverse, ranging from highly aggressive forms; to some types so benign that are often only picked up incidentally. Some blood changes which could be classified as chronic leukaemias often producing no symptoms, and incidence of these conditions is therefore dependent on looking at blood samples from these individuals and clinicians' criteria for deciding whether a malignancy exists. Even when it is clear that malignancy exists, identifying the specific type requires sophisticated diagnostic techniques, and the integration of information from clinical and laboratory sources, the results of which are not always available to the registration service (NCIN 2013) leading to some registrations not including sufficient detailed information (NICE 2003) to accurately capture the precise diagnosis. This is particularly true of non-Hodgkin lymphoma (NHL), a large and varied group of conditions, which are often considered as a single group as coding has not been of sufficient quality to distinguish individual types of lymphoma.

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Although the National Cancer Registration Service (NCRS) now operates as one national system for England, historically there were eight separate cancer registries, with different practices and levels of ascertainment of haematological malignancies, this led to regional variations in capture of information, and changes in trends in incidence may be due to improved ascertainment in former registries.

As well as the national data, collected by the National Cancer Registration Service (NCRS) within Public Health England, we have also reported on regional data from the Haematological Malignancies Research Network (HMRN), and predictions for the UK based on these data. The HMRN is a collaboration across the former cancer networks of Yorkshire and Humber and Yorkshire Coast, between researchers from the University of York, a clinical network operating across 14 hospitals, and an integrated Haematological Malignancy Diagnostic Service (HMDS) at St James's Hospital in Leeds.

Covering a population of 3.6 million, with a similar socio-demographic profile to the country as a whole, HMRN collects detailed information about all patients diagnosed with a haematological malignancy within the HMRN region[b]. Within HMRN, all haematological

b Haematological Malignancies Research Network (HMRN) website - https://www.hmrn.org/ [accessed August 2015]

malignancy diagnoses, are centrally coded using the latest World Health Organization (WHO) classifications by clinical staff at HMDS's laboratory. Following diagnosis, patients are individually tracked, and full details of all treatments, responses and outcomes are collected to clinical trial standardise[e].

There is a reasonable expectation that due to the incidence of haematological malignancies not being strongly influenced by social position or deprivation that the incidence observed in the HMRN data for the Yorkshire region is likely to be representative of the national picture. In 2013 the NCIN compared national registration data on haematological malignancies with assumptions about England incidence made using the HMRN data. This analysis found that for 2004-10 the two data sources were largely in agreement for acutely presenting conditions such as ALL, with very little notable variation in recording across the country. However, for conditions for which require integration of information from clinical and laboratory sources there was variation; both between the two data sources and geographically – suggesting that this variation is due to different case ascertainment and coding procedures in different registries.

Clinical networks within the HMRN area apply standard treatment protocols in the management of haematological malignancies and therefore regional outcomes are also of value in estimating likely survival patterns for England as a whole.

B.3.2 What is covered in this report and what is not

This report focuses on presenting English national data on seven main groupings of haematological malignancies, which have been used in previous reports by the National Cancer Intelligence Network (NCIN). These are: Acute Lymphocytic Leukaemia (ALL), Acute Myeloid Leukaemia (AML), Chronic Lymphocytic Leukaemia (CLL), Chronic Myeloid Leukaemia (CML), Myeloma, Hodgkin lymphoma and non-Hodgkin Lymphoma grouped together. These groupings are felt to be the most accurate with the data currently available from NCRS. Due to the data quality issues outlined above these have been defined using ICD10 codes. Any specific known data quality issues with each condition are discussed in the relevant chapter.

Update 2016

Many haematological conditions are not included in this report in detail, but remain important in the picture of haematological malignancies as a whole. These particularly include the myeloproliferative disorders, information on which is not currently collected comprehensively by the NCRS. Where possible information the information presented here is supplemented with available regional data from the HMRN.

B.4 All haematological malignancies

B.4.1 Incidence

When considered overall, age-standardised rates of incidence for haematological malignancies have risen significantly from 2001-2010 in both men and women (Figure 6). Part of this trend is a consequence of improved ascertainment of these cancers particularly from 2008 onwards (NCIN 2010).

The incidence of all haematological malignancies in males is consistently significantly higher than females over this time period.

Figure 6: Incidence of all haematological malignancies by sex, all ages, England 2001 – 2010

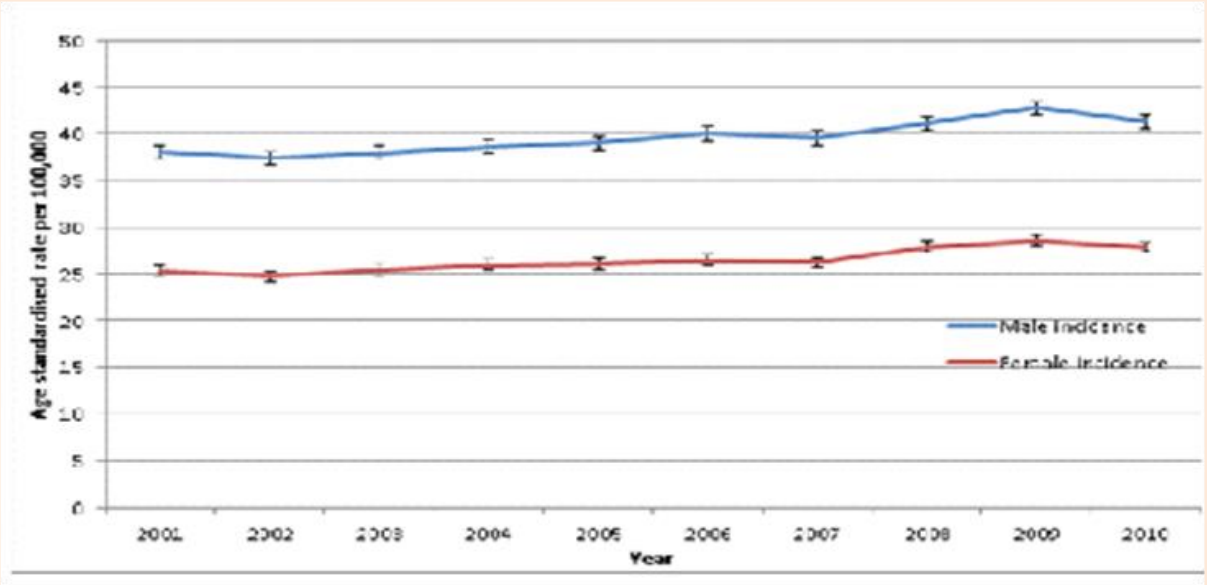


Table 15: Age-standardised incidence rates for haematological malignancies diagnosed in the period 2008-2010 by diagnostic group for males and females

	Males				Females			
Site	Cases	ASR	95% CI		Cases	ASR	95% CI	
All haematological malignancies	12779	41.7	41.3	42.1	10138	28.1	27.7	28.4
Acute Lymphoblastic Leukaemia	329	1.4	1.3	1.5	250	1.1	1.1	1.2
Acute Myeloid Leukaemia	1267	4.0	3.9	4.2	1038	2.8	2.7	2.9
Chronic Lymphoid Leukaemia	1666	5.2	5.0	5.3	1060	2.6	2.5	2.7
Chronic Myeloid Leukaemia	328	1.1	1.0	1.2	243	0.7	0.7	0.8
Hodgkin Lymphoma	860	3.2	3.1	3.3	669	2.4	2.3	2.5
Non-Hodgkin Lymphoma	5499	17.9	17.7	18.2	4680	12.9	12.7	13.2
Myeloma	2242	7.0	6.8	7.1	1792	4.5	4.4	4.6
Other	588	1.9	1.8	2.0	407	1.0	1.0	1.1

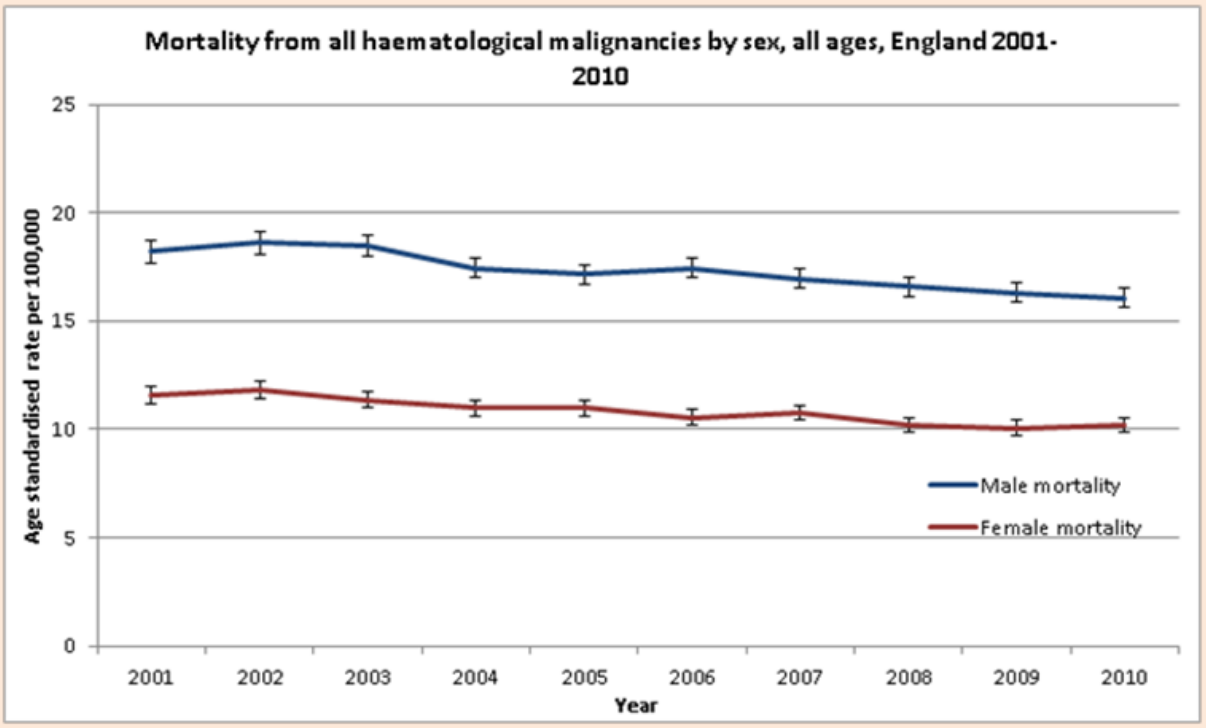
Update 2016

B.4.2 Mortality

Figure 7 shows trends in age-standardised mortality from all haematological malignancies by sex for England between 2001 and 2010. Mortality rates have decreased significantly over this time.

Mortality information is taken from the cause of death recorded on the death certificate for an individual and recorded by ONS. Therefore, accuracy of mortality recording for some of the more complex haematological malignancies must be interpreted with care.

Figure 7: Mortality from all haematological malignancies by sex, all ages, England 2001 - 2010

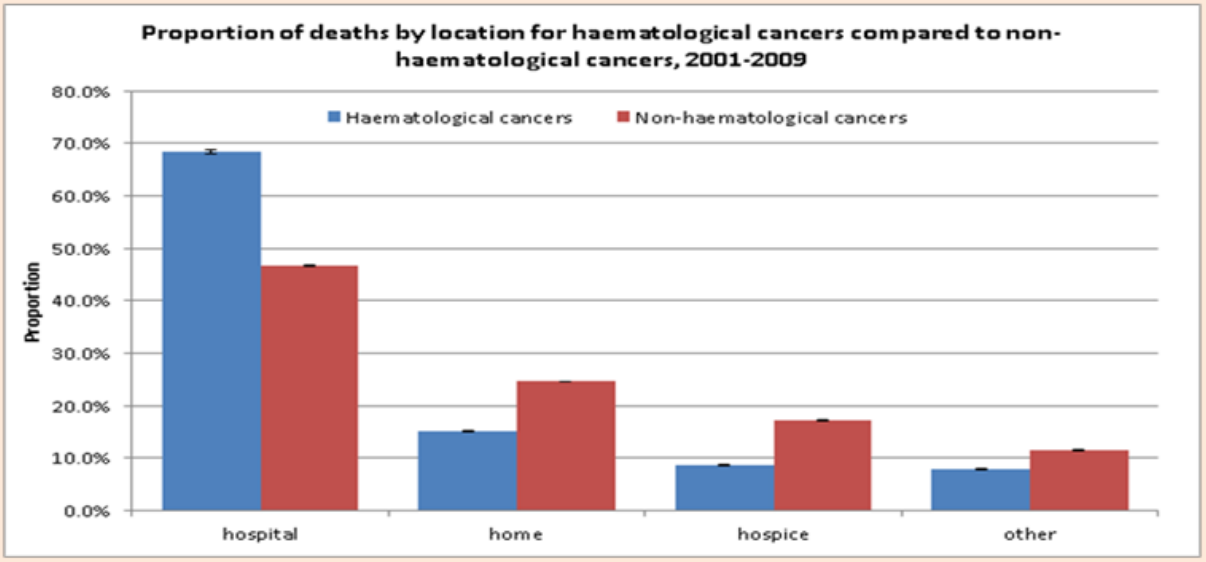


B.4.3 Survival

B.4.3.1 Place of death

Figure 3 shows the proportion of deaths by location of death for all haematological cancers compared to non-haematological cancers from a report done by NCIN in 2011. It shows that patients with haematological cancers are significantly more likely to die in hospital than patients with other cancers, with less than half (46.7%) of patients with other cancers dying in hospital compared to 68.4% of patients with haematological cancers.

Figure 8: Proportion of deaths by location for haematological cancers compared to non-haematological cancers, 2001 - 2009



Update 2016

B.4.4 Patient Experience

Results in this section come from the 2014 cancer patient experience survey[c]

64% of patients diagnosed with a haematological malignancy saw their GP no more than twice before being referred to hospital.

75% of patients diagnosed with a haematological malignancy said they had a completely understandable explanation of their test results.

83% of patients said they were told they had a haematological malignancy sensitively.

58% of patients said they completely understood what was wrong with them which is lower than the response from breast cancer where 81% of patients understood what was wrong with them. Haematology scored the lowest of all other cancer sites for this question.

70% of patients said their views were taken into consideration when discussing treatment and 72% said that side effects of the treatment were explained and only 51% said they were told of possible future side effects from the treatment they received.

87% of patients were given a named clinical nurse specialist which is lower when compared to breast, lower GI, lung, brain, gynaecological and upper GI cancer patients where between 90% and 93% of patients were given a named clinical nurse specialist.

55% of patients said they were given information on financial help/benefits by staff, this was low for all cancer sites included in the survey.

82% of patients were told they could get free prescriptions.

37% of patients said they taking part in research had been discussed with them, this was low for all cancer sites included in the survey.

59% of patients said they were given enough care/help from health or social services.

64% of patients said their general practice did everything to support them.

Update 2016

B.4.5 HMRN incidence data

As we have previously discussed national NCRS data do not allow a breakdown of all haematological malignancies into separate conditions, and does not include reliable data on conditions including myelodysplastic syndromes. Therefore Table 16 shows HMRN regional data on incidence of haematological cancers, including myelodysplasia, and expected UK cases per year, which have been estimated by applying HMRN age and sex specific rates to 2001 UK population census strata.

Table 16: HMRN regional age-standardised rates for haematological neoplasms, 2004-13, and expected UK cases per yr

	ASR per 100,000			Expected UK cases per year[d]
	Total	**Male**	**Female**	
All haematological neoplasms	51.2	64.5	41.1	38100
Leukaemias				
Chronic myeloid leukaemia	0.9	1.1	0.7	580
Acute myeloid leukaemia	3.2	4	2.6	2400

c Quality Health – National Cancer Patient Experience Survey: https://www.quality-health.co.uk/surveys/national-cancer-patient-experience-survey

d Estimated by applying HMRN age and sex specific rates to 2001 UK population census strata

	ASR per 100,000			Expected UK cases per year[d]
Acute promyelocytic leukaemia	0.3	0.3	0.3	170
B-lymphoblastic leukaemia	1	1.1	0.9	550
T-lymphoblastic leukaemia	0.3	0.4	0.2	160
Chronic lymphocytic leukaemia	5.4	7.8	3.5	4100
Hairy cell leukaemia	0.3	0.5	0.1	210
T-cell leukaemias	0.3	0.3	0.3	250
Chronic myelomonocytic leukaemia	0.5	0.8	0.3	440
Non-Hodgkin lymphoma	**14.2**	**16.8**	**12.1**	**10280**
Marginal zone lymphoma	2.7	3.4	2.1	2050
Follicular lymphoma	2.8	2.7	2.8	1860
Mantle cell lymphoma	0.7	1.0	0.4	510
Diffuse large B-cell lymphoma	6.8	8	5.8	4990
Burkitt lymphoma	0.4	0.6	0.2	210
T-cell lymphoma	0.9	1.2	0.7	650
Hodgkin lymphoma	**2.8**	**3.3**	**2.4**	**1730**
Classical Hodgkin lymphoma	2.8	2.8	2.2	1540
Lymphocyte predominant nodular Hodgkin lymphoma	0.3	0.5	0.2	190
Plasma cell neoplasms	5.5	7.4	4	4260
Plasmacytoma	0.3	0.5	0.2	250
Myeloma	5.1	6.9	3.8	4010
Other disorders	**16.5**	**20.5**	**13.7**	**12930**
Chronic myeloproliferative neoplasms	4.4	4.6	4.3	3320
Myelodysplastic syndromes	2.6	4.1	1.5	2180
Lymphoproliferative disorder NOS	1.4	1.8	1.1	1160
Monoclonal gammopathy of undetermined significance	5.6	6.8	4.7	4290
Primary myelofibrosis	0.4	0.5	0.3	300
Myelodysplastic/Myeloproliferative neoplasms unclassifiable	0.1	0.1	0	50

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The most common specific types of haematological malignancies are diffuse large B-cell lymphoma (a type of NHL) which accounts for 13.1% of the estimated incidence; monoclonal gammopathy of undetermined significance (MGUS) which accounts for 11.3% and chronic lymphocytic leukaemia and myeloma, which each account for 10.8% and 10.6% respectively. If the non-Hodgkin lymphomas are grouped together, they account for around 27.1% of all haematological malignancies using these data.

These data are not directly comparable to those captured nationally by the NCRS, due to data collection and coding methodological issues discussed earlier. For instance MGUS is not registered as it is an asymptomatic potential precursor to myeloma, which is not easily ascertainable through normal reporting systems.

Table 17 shows five-year relative survival for all individual haematological malignancies derived from the regional HMRN data. It shows that there is significant variation both between types of haematological malignancy and within the different types. Five-year relative survival for all haematological malignancies combined is 68.3%, however this varies from 45.4% for plasma cell neoplasms (including myeloma) to 85.7% for Hodgkin lymphoma.

Within types of malignancy there is also significant variation, for instance five-year survival from hairy cell leukaemia is 90.5%, whereas for acute myeloid leukaemia it is 15.2%.

Trends in one- and five-year relative survival for the specific conditions defined in the introduction are discussed in the relevant chapters later on in this report.

Table 17: HMRN regional 5-year relative survival estimates (%)

	5-Year Relative Survival (%)
All haematological neoplasms	68.3
Leukaemia	60.5
Chronic myeloid leukaemia	88.4
Acute myeloid leukaemia	15.2
Acute promyelocytic leukaemia	66.6
B-lymphoblastic leukaemia	64.9
T-lymphoblastic leukaemia	63.7
Chronic lymphocytic leukaemia	83.2
Hairy cell leukaemia	90.5
T-cell leukaemias	75.9
Chronic myelomonocytic leukaemia	18.8
Non-Hodgkin lymphoma	**66.9**
Marginal zone lymphoma	77.8
Follicular lymphoma	86.9
Mantle cell lymphoma	36.2
Diffuse large B-cell lymphoma	59.6
Burkitt lymphoma	57.1
T-cell lymphoma	48.6
Hodgkin lymphoma	**85.7**
Classical Hodgkin lymphoma	83.3
Lymphocyte predominant nodular Hodgkin lymphoma	99.7
Plasma cell neoplasms	**45.4**
Plasmacytoma	61.7
Myeloma	44.1
Other disorders	**79.4**
Monoclonal B-cell lymphocytosis	96.1
Chronic myeloproliferative neoplasms	92.7
Myelodysplastic syndromes	28.4
Lymphoproliferative disorder NOS	75.3
Monoclonal gammopathy of undetermined significance	88.4
Primary myelofibrosis	40.5

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B.5 Acute lymphoblastic leukaemia (ALL)

B.5.1 Incidence

Acute lymphoblastic leukaemia (ALL) is most common in children, with a higher incidence in males than females (Figure 9). Over the period of this report the age-standardised incidence has not changed significantly for either sex (Table 18).

Figure 9: age-specific incidence rates by age group for ALL in males and females between 2006-08 in England

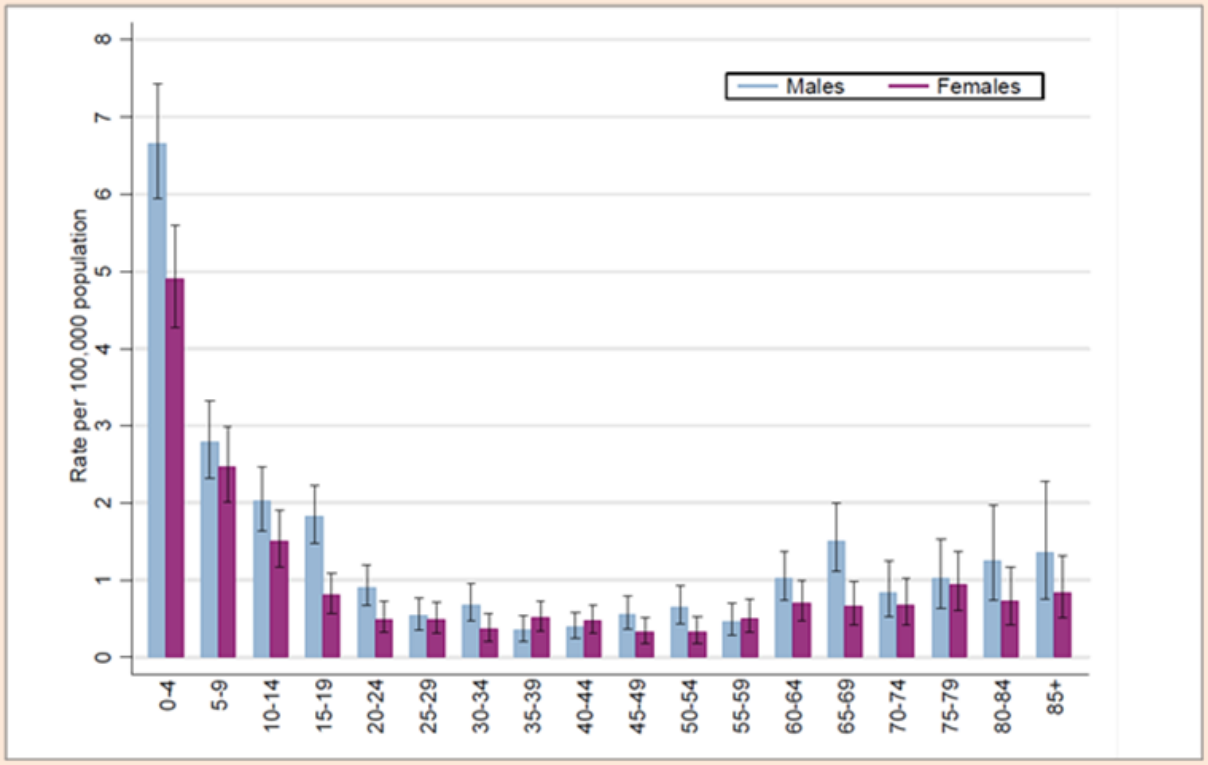

Table 18: Incidence; Acute Lymphoblastic Leukaemia by sex, all ages, England 2001-2003 to 2008-2010. Three year averages

	Male incidence				Female incidence			
Year	Cases	ASR	95% CI		Cases	ASR	95% CI	
2001-2003	337	1.5	1.4	1.6	261	1.2	1.1	1.2
2002-2004	344	1.5	1.4	1.6	263	1.2	1.1	1.3
2003-2005	341	1.5	1.4	1.65	265	1.2	1.1	1.3
2004-2006	3.45	1.5	1.4	1.6	266	1.2	1.1	1.3
2005-2007	342	1.5	1.4	1.6	244	1.1	1.0	1.2
2006-2008	335	1.5	1.4	1.6	243	1.1	1.0	1.1
2007-2009	328	1.4	1.3	1.5	246	1.1	1.0	1.1
2008-2010	329	1.4	1.3	1.5	250	1.1	1.0	1.2

Figure 10 shows the incidence of ALL by deprivation quintile and sex, it shows there is no significant relationship between deprivation and the incidence of ALL.

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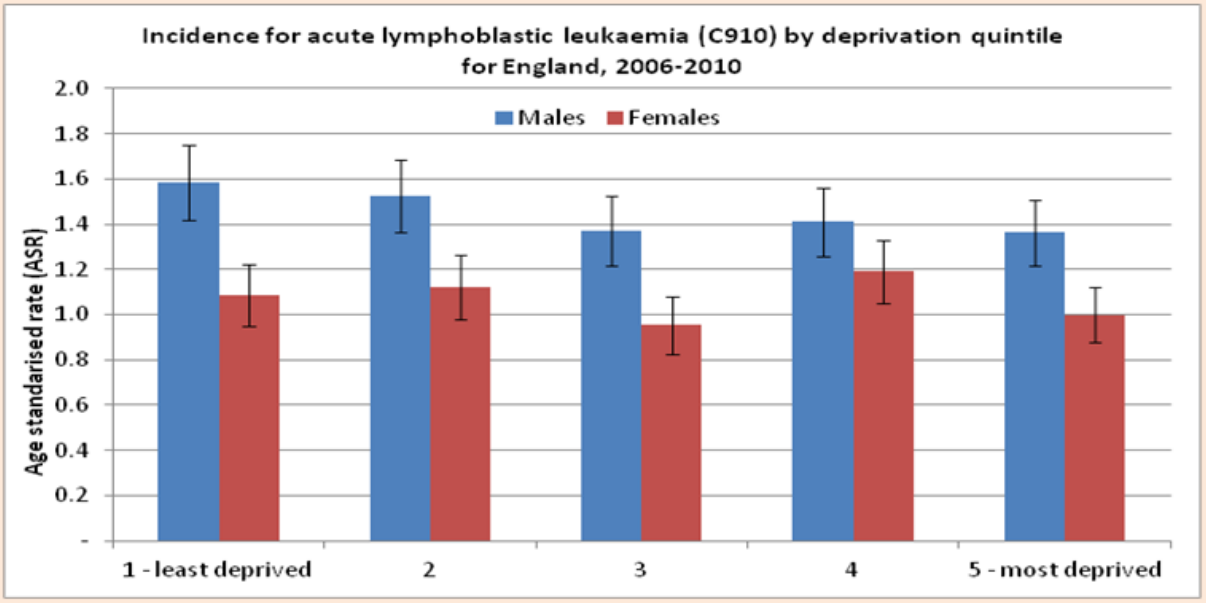
Figure 10: Incidence of ALL by deprivation quintile and sex



B.5.2 Mortality

Table 19 shows trends in mortality rates from ALL between 2001-03 and 2008-10; there is a small decline in the mortality rates in both sexes.

Table 19: Mortality; Acute Lymphoblastic Leukaemia by sex, all ages, England 2001-2003 to 2008-2010. Three year averages

	Male mortality				Female mortality			
Year	Deaths	ASR	95% CI		Deaths	ASR	95% CI	
2001-2003	148	0.6	0.5	0.6	110	0.4	0.4	0.4
2002-2004	139	0.5	0.5	0.6	108	0.4	0.3	0.4
2003-2005	129	0.5	0.4	0.5	103	0.4	0.3	0.4
2004-2006	126	0.5	0.4	0.5	100	0.3	0.3	0.4
2005-2007	122	0.5	0.4	0.5	97	0.3	0.3	0.4
2006-2008	125	0.5	0.4	0.5	93	0.3	0.3	0.4
2007-2009	116	0.5	0.4	0.5	94	0.3	0.3	0.4
2008-2010	111	0.4	0.4	0.5	88	0.3	0.3	0.3

Figure 11 shows mortality rates for ALL by quintile of deprivation. It shows no significant difference in mortality rates for males by deprivation quintile. For females in the least deprived quintiles the mortality rate is significantly higher than in males, however, in the two most deprived quintiles the mortality rates are more similar to the male mortality rates. The numbers of registered cases are small so patterns should be interpreted with caution.

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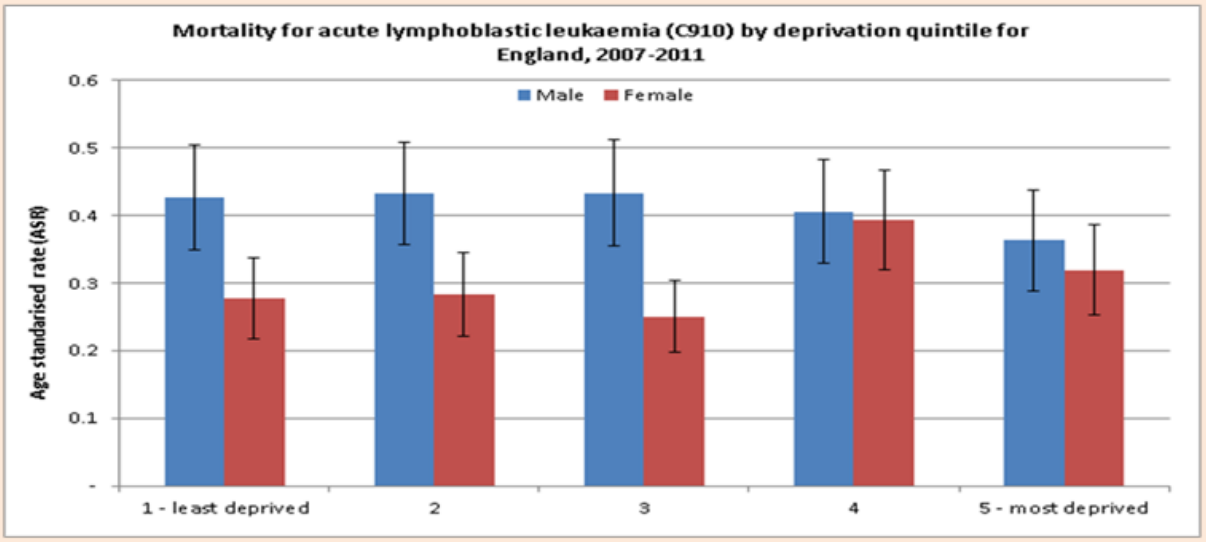
Figure 11: Mortality for acute lymphoblastic leukaemia (C910) by deprivation quintile for England 2007 - 2011



B.5.3 Survival

For all ages one-year relative survival for ALL increased between 2000-2003 and 2008-2010, significantly for males from 76.9% (95% CI: 74.5-79.2%) to 83.1% (95% CI:80.4-85.4%) although not significantly for females 77.5% (95% CI: 74.7-80.0%) to 81.0% (95% CI: 77.8-83.7%). Five-year relative survival for ALL increased significantly for both sexes (Figure 12).

The outcome from ALL is strongly influenced by the age at diagnosis, with poorer relative survival in older teenagers and adults.

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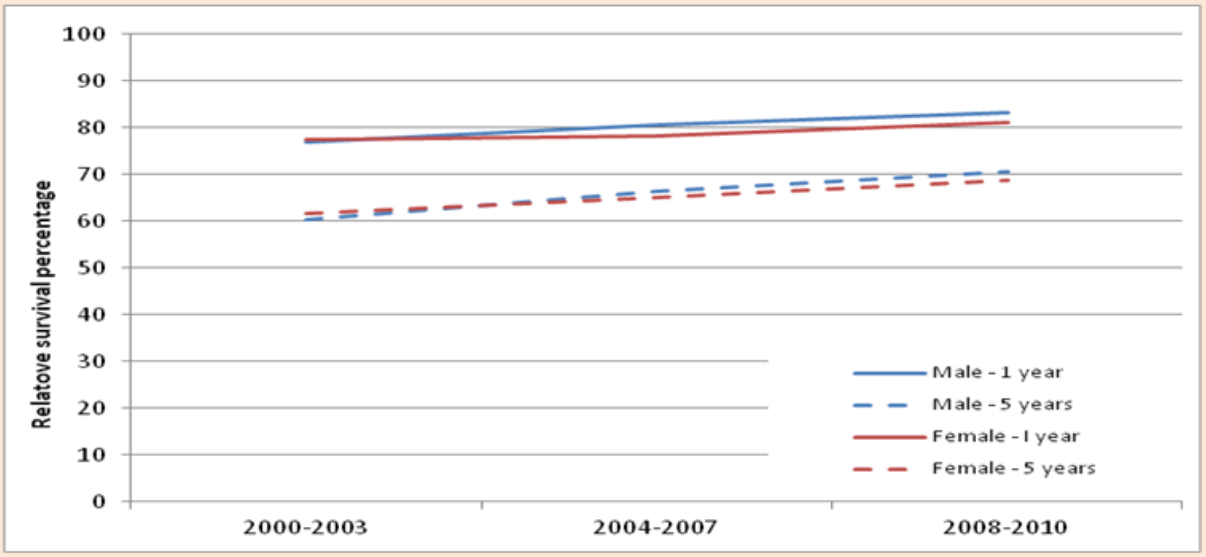
Figure 12: Relative 1 and 5 year survival - Acute Lymphoblastic Leukaemia, by sex , diagnosed in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010 in England



Over the time period reported here improvements in relative survival are apparent in patients aged 0-14 years, with an increase in relative survival at five years among males and females combined from 83% (95% CI: 81-85%) for individuals diagnosed in 2000-03 to 92% (95% CI: 90- 94%) for those diagnosed in 2008-10 (Figure 13).

Figure 13: Trends in relative survival rates for acute lymphoblastic leukaemia diagnosed in persons in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010, by age group in England

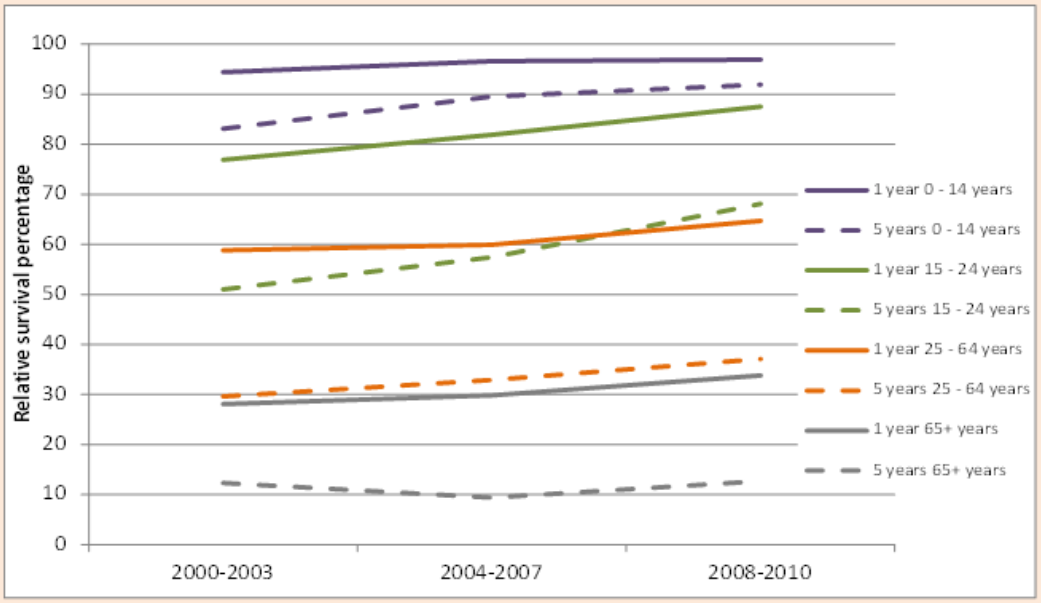
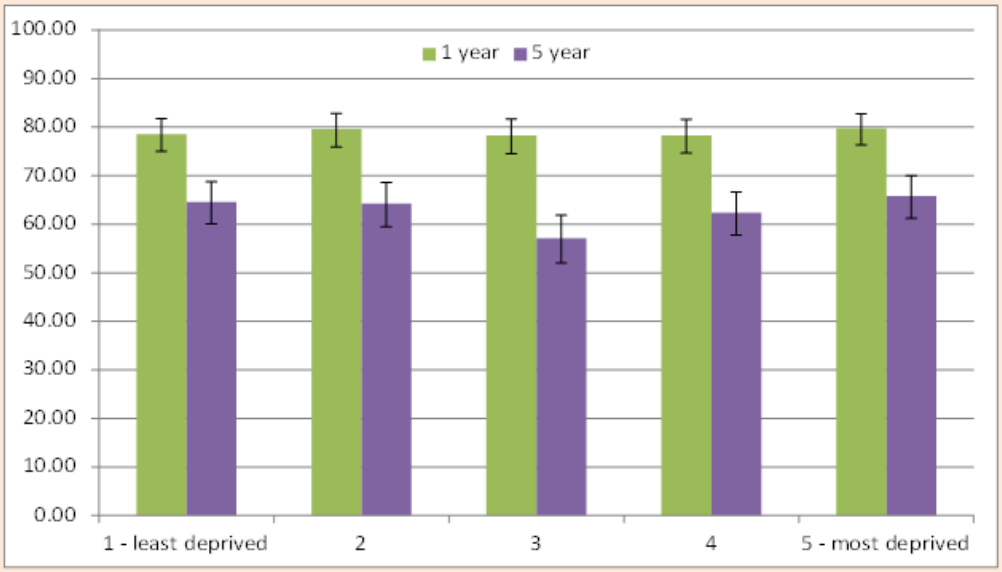


Figure 14 shows one- and five-year relative survival for patients with ALL by quintile of deprivation; there is no significant difference in relative survival by quintile of deprivation at either one or five years.

Figure 14: 1 and 5-year survival of patients (persons) diagnosed with Acute Lymphoblastic Leukaemia in England, 2000-2007 by deprivation (IMD2004)



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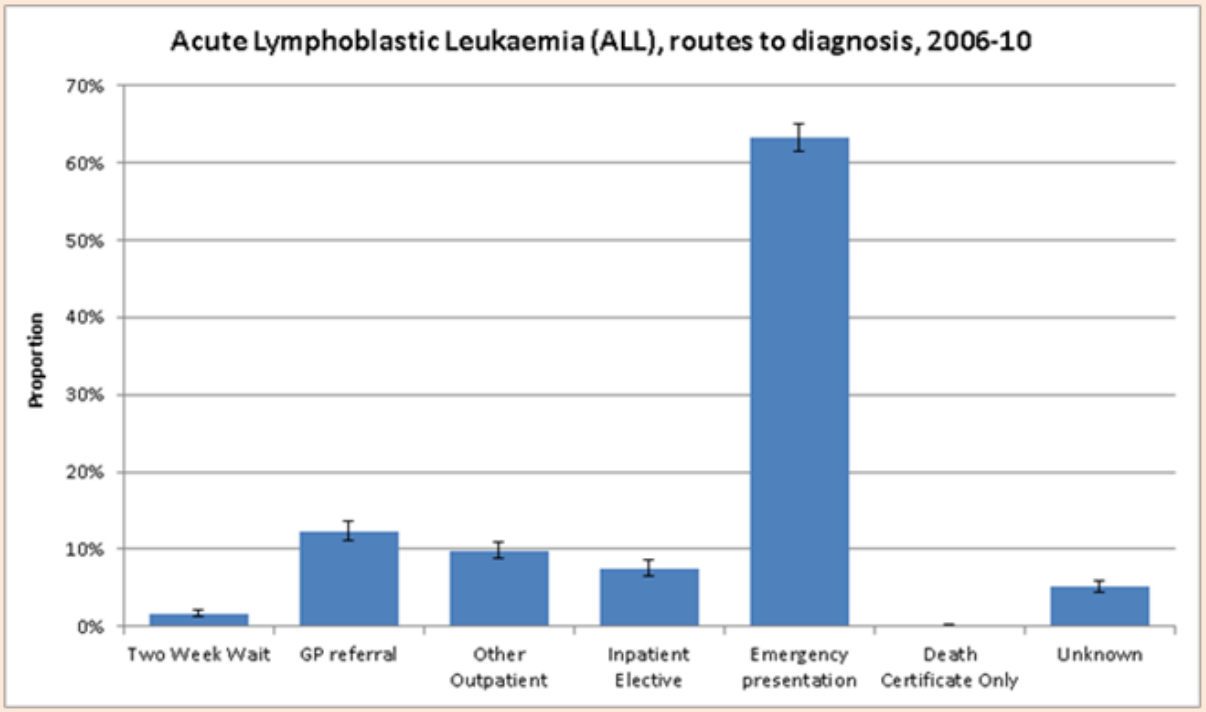
B.5.4 Routes to diagnosis – ALL

Figure 15 shows the routes to diagnosis for ALL from 2006-10; the vast majority of admissions for ALL (63.3%) came through the emergency route; this is almost three times the proportion observed for all malignancies combined (23%).

Figure 15: Routes to diagnosis for ALL from 2006-10



B.5.5 Survival by route

Unlike some other cancer types, where emergency presentations tend to have poorer relative survival, there are no significant differences in survival time by route to diagnosis for ALL (Figure 16). This reflects the fact that diagnosis as an emergency is not an indication of late presentation as is the case for many tumour types.

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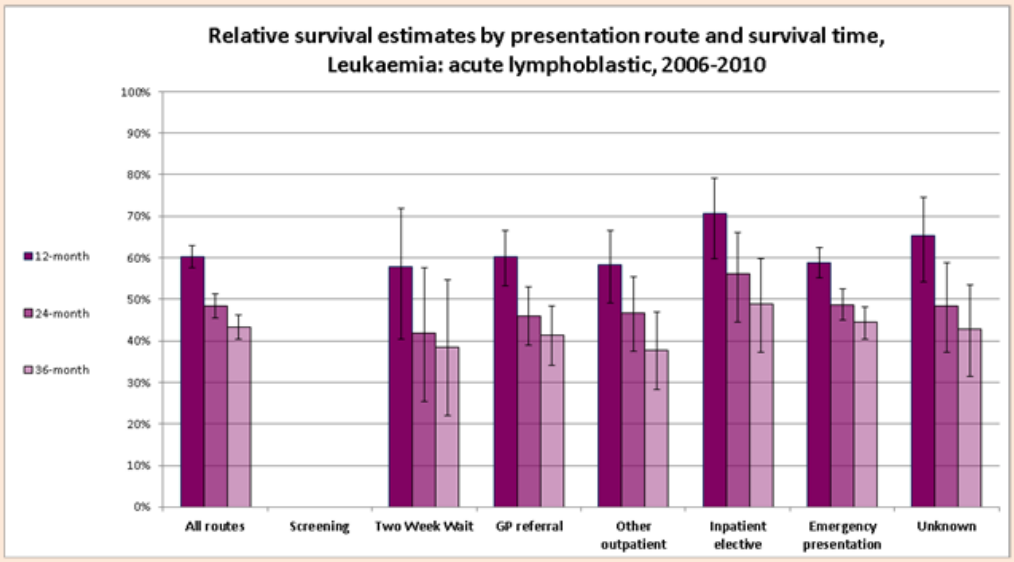
Figure 16: Relative survival estimates by presentation route and survival time, Leukaemia: acute lymphoblastic, 2006-2010



B.6 Acute Myeloid Leukaemia (AML)

B.6.1 Incidence

Acute myeloid leukaemia is most common in people over the age of 60 and age-standardised incidence is significantly higher in men (Figure 17). Over the period 2001-2010 there was little or no change in the age-standardised incidence of AML (Table 20).

Figure 17: Age-specific incidence rates by age group for acute myeloid leukaemia in males and females in the period 2006-2008 in England

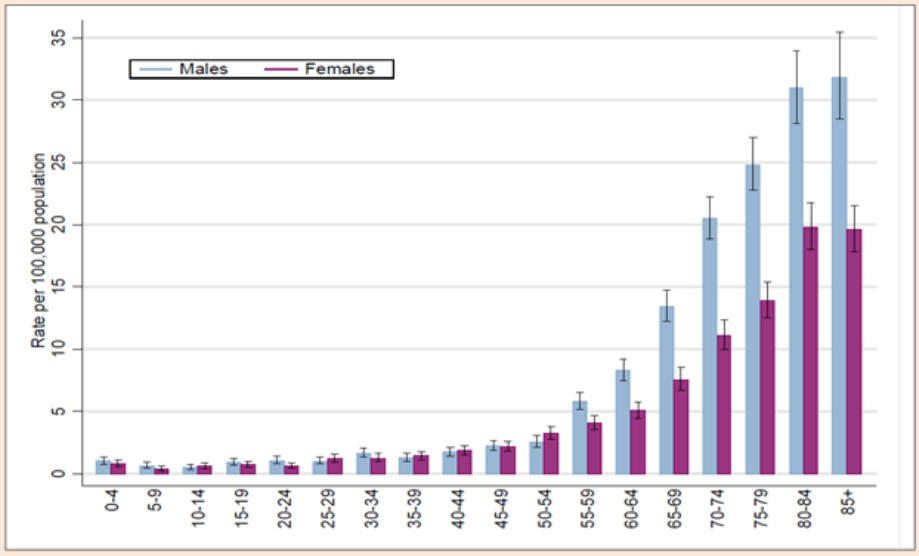


Table 20: Incidence - Acute Myeloid Leukaemia, by sex, all ages, England 2001-2003 to 2008-2010. Three year averages

	Male Incidence				Female incidence			
Year	Cases	ASR	95% CI		Cases	ASR	95% CI	
2001-2003	1086	3.9	3.7	4.0	945	2.8	2.7	2.9
2002-2004	1130	4.0	3.8	4.1	972	2.8	2.7	2.9
2003-2005	1176	4.1	3.9	4.2	990	2.9	2.8	3.0
2004-2006	1179	4.0	3.9	4.2	998	2.8	2.7	2.9
2005-2007	1197	4.0	3.9	4.2	1010	2.9	2.7	3.0
2006-2008	1222	4.0	3.9	4.2	1003	2.8	2.7	2.9
2007-2009	1264	4.1	4.0	4.2	1029	2.8	2.7	2.9
2008-2010	1267	4.0	3.9	4.2	1038	2.8	2.7	2.9

Figure 18 shows incidence of AML by quintile of deprivation and sex. There is some evidence of a relationship between deprivation and incidence of AML, with incidence in the most deprived group of males being significantly higher than incidence in the least deprived group (3.8 per 100,000 compared to 4.3). There was no such observable relationship for females.

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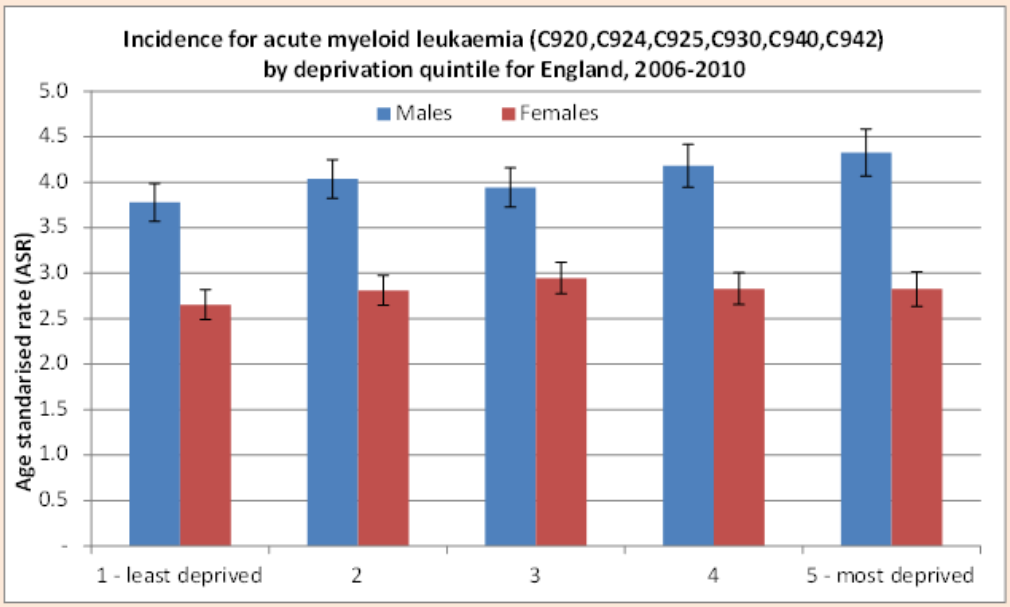
Figure 18: Incidence for acute myeloid leukaemia by deprivation for England. 2006 – 2010)



B.6.2 Mortality

Table 21 presents trends in mortality rates for AML by sex, there has been almost no change in the AML mortality rate for either sex over this time period.

Table 21: Mortality - Acute Myeloid Leukaemia, by sex, England 2001-2003 to 2008-2010. Three year averages.

	Male mortality				Female mortality			
Year	Deaths	ASR	95% CI		Deaths	ASR	95% CI	
2001-2003	914	3.2	3.1	3.3	778	2.1	2.0	2.2
2002-2004	941	3.2	3.1	3.3	792	2.1	2.0	2.2
2003-2005	962	3.2	3.1	3.3	799	2.1	2.0	2.2
2004-2006	980	3.2	3.1	3.4	800	2.1	2.0	2.2
2005-2007	999	3.2	3.1	3.4	808	2.1	2.0	2.2
2006-2008	1013	3.2	3.1	3.3	805	2.0	1.9	2.1
2007-2009	1040	3.2	3.1	3.3	836	2.1	2.0	2.2
2008-2010	1065	3.2	3.1	3.3	863	2.1	2.0	2.2

Figure 19 shows mortality from AML by deprivation quintile and sex, there is no significant differences in mortality rate by quintile of deprivation for AML.

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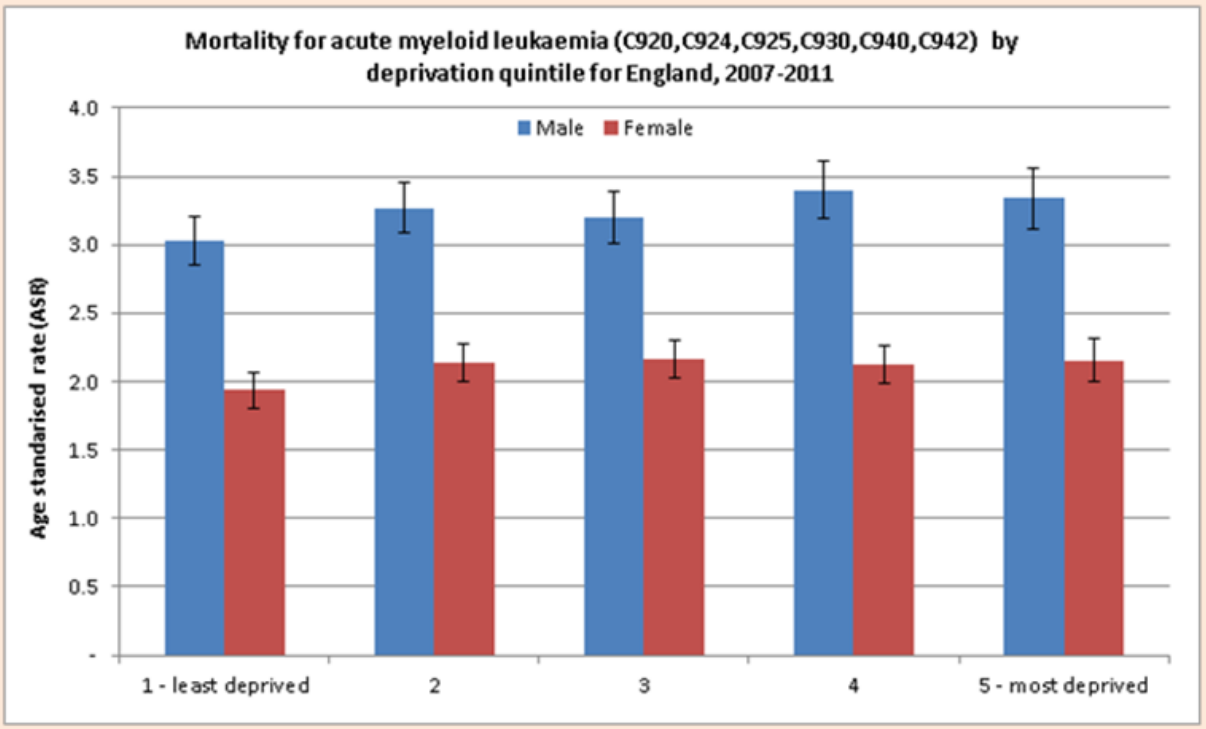
Figure 19: Mortality for acute myeloid leukaemia by deprivation for England, 2007-2011



B.6.3 Survival

Overall, there was a small, but not significant, increase in one-year relative survival for males and females for AML over the period 2000-2010. There was a significant increase in five-year relative survival for males, but not for females. Female five-year relative survival remained slightly higher than male five-year relative survival (Figure 20).

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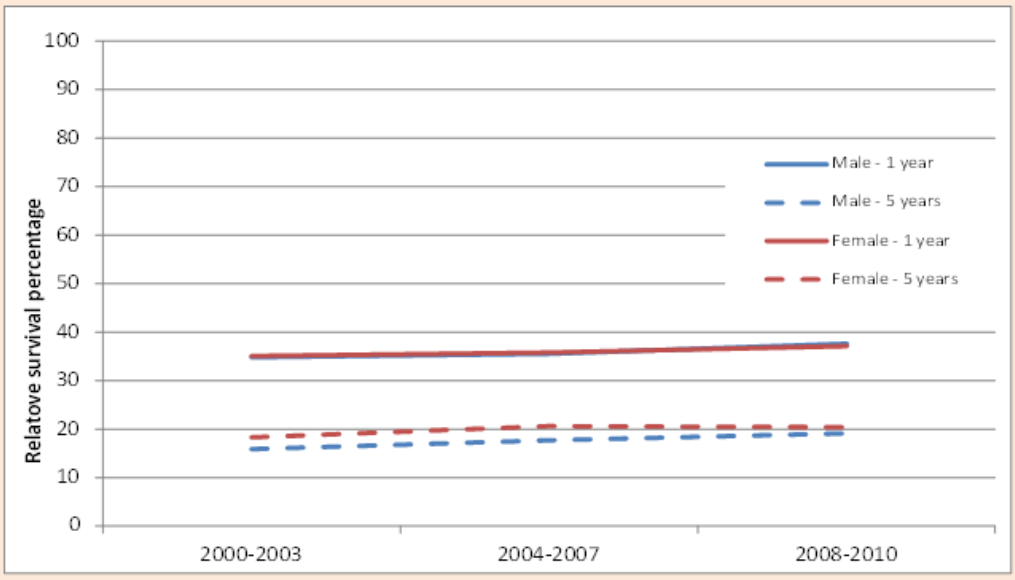
Figure 20: Relative 1 and 5 year survival - Acute Myeloid Leukaemia, by sex, diagnosed in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010 in England



While relative survival among older adults (65+ years) diagnosed with AML was unchanged over this period, a small improvement in outcome was seen in the 25-64 year age range, with

an increase in relative survival at five years among males and females combined from 30% (95% CI 28 to 31%) for individuals diagnosed in 2000-03 to 38% (95% CI:36-40%) for those diagnosed in 2008-10 (Figure 21).

Figure 21: Trends in Relative survival rates for acute myeloid leukaemia diagnosed in persons in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010, by age group in England

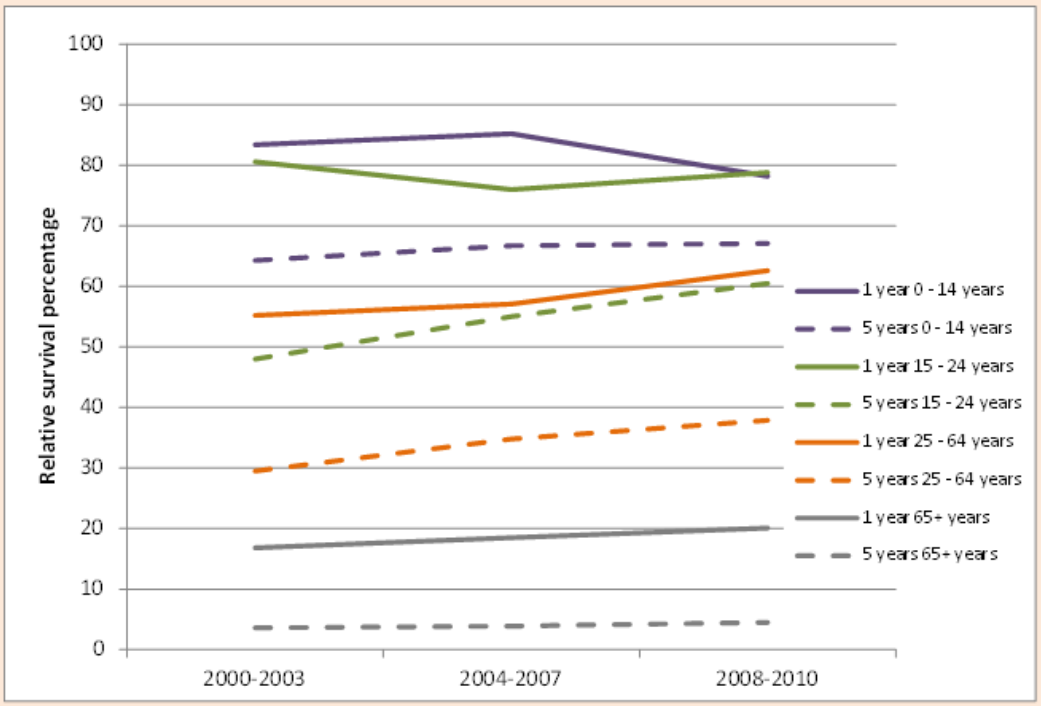
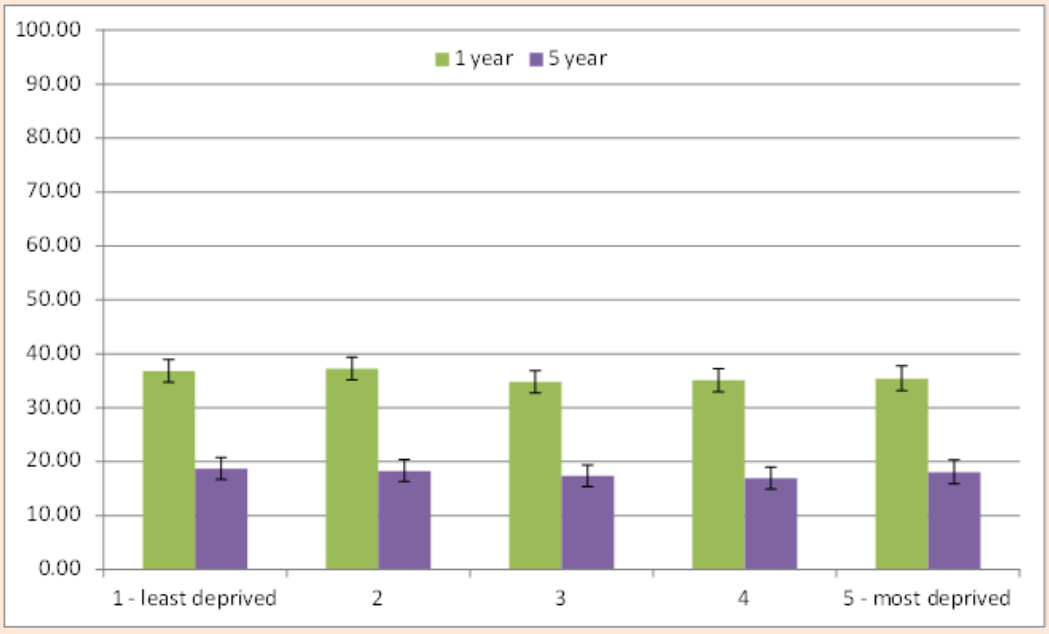


Figure 22 shows one- and five-year relative survival for patients diagnosed with AML by quintile of deprivation, there was no significant relationship between deprivation and relative survival for AML.

Figure 22: 1 and 5-year survival of patients (persons) diagnosed with Acute Myeloid Leukaemia in England, 2000-2007 by deprivation (IMD2004)



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B.6.4 Routes to diagnosis

Figure 23 shows a breakdown of routes to diagnosis for AML. The majority of admissions for AML are via the emergency route (52.9%), followed by GP referral (22.6%).The proportion of emergency admissions is almost three times the proportion for all malignancies combined (23%), however, given the acute nature of AML it may be that the emergency route to treatment is entirely appropriate.

Figure 23: Acute myeloid leukaemia (AML) routes to diagnosis, 2006-10

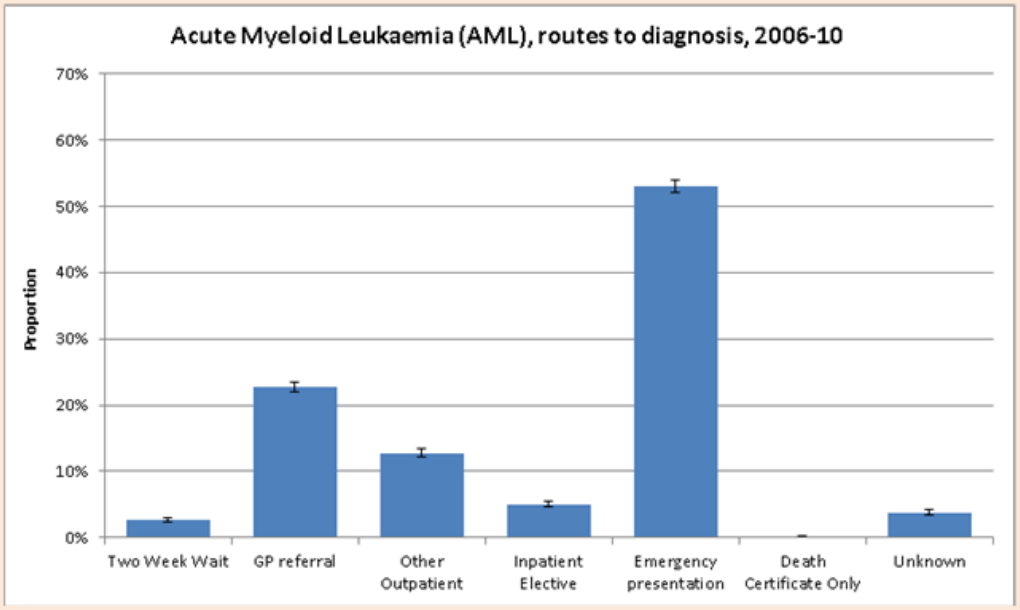

Figure 24 shows relative survival by route to diagnosis for AML. One-year relative survival is significantly lower for emergency presentations than all other routes. Diagnosis following inpatient elective admissions had significantly better relative survival than all routes combined at one, two and three years.

Figure 24: Relative survival by route to diagnosis for AML

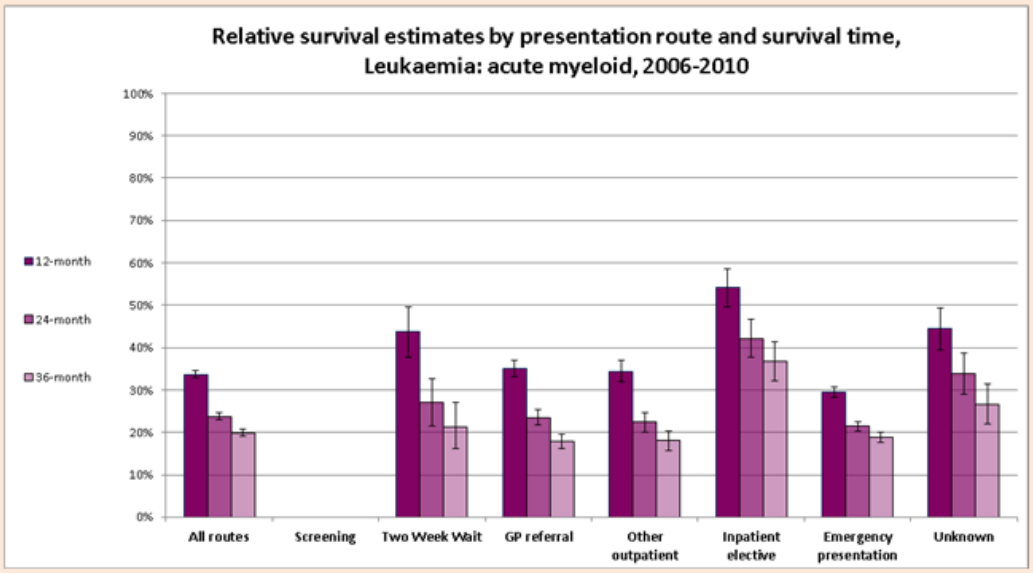

Figure 25 shows one-year relative survival estimates by age and route to diagnosis. It shows that for the younger age group (0-64) one-year relative survival for emergency admissions (60%) was similar to the overall relative survival (61%), however, one-year relative survival

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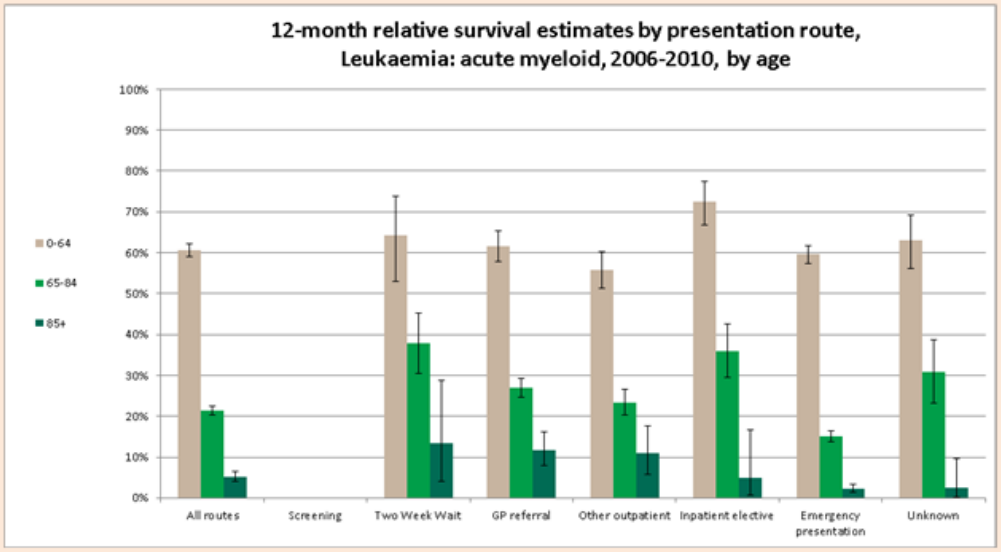
for the 65-84 and 85+ year age groups was significantly worse for emergency admissions than for all other routes combined.

Figure 25: One-year relative survival estimates by age and route to diagnosis



B.7 Chronic Lymphocytic Leukaemia (CLL)

CLL is a relatively indolent cancer for which histopathology laboratories will not necessarily be involved in diagnosis and where treatment can be delivered in an outpatient setting, factors which combine to reduce the likelihood of notification to cancer registries. There is evidence of wide variation in registration rates at a sub-national level for CLL1 and improvements in ascertainment over time. Therefore, both absolute levels of incidence and trends in incidence should be treated with caution. In addition, as variable levels of ascertainment of CLL may be related to the stage of disease at presentation (with the most indolent cancers probably those least likely to be registered), changes in survival may also be subject to artefact.

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B.7.1 Incidence

Chronic lymphocytic leukaemia (CLL) is predominantly a disease of the elderly, with higher age-standardised incidence in males (Figure 26). Table 22 shows the trends in incidence of CLL; there were no marked changes in age-standardised of incidence of CLL over this time period.

Figure 26: Age-specific incidence rates by age group for Chronic Lymphocytic Leukaemia in males and females in the period 2006-2008 in England

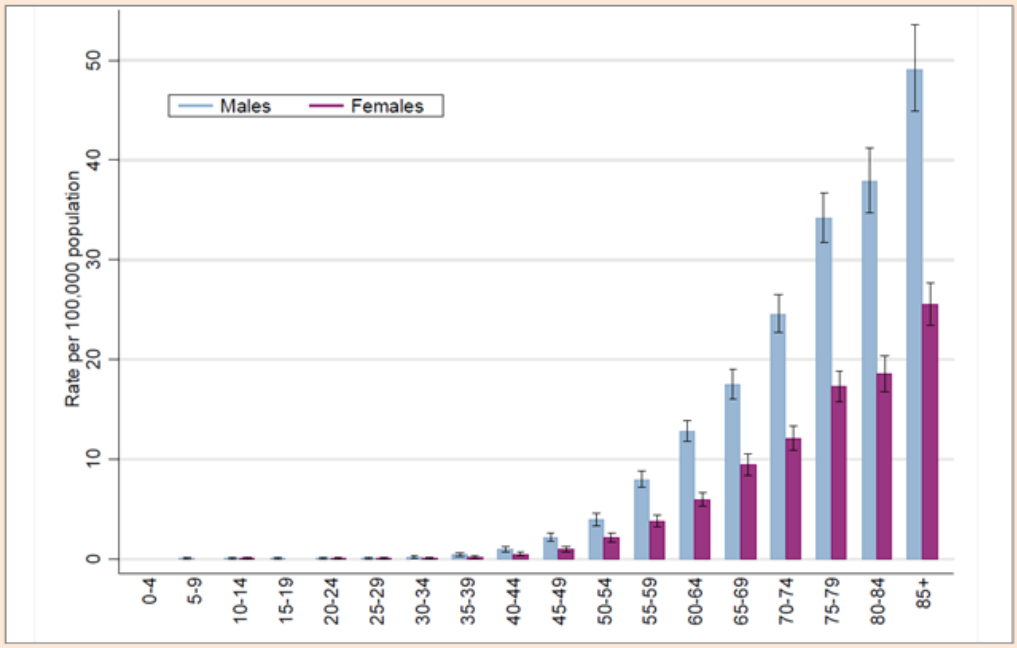

Table 22: Incidence - Chronic Lymphocytic Leukaemia, by sex, England 2001-2003 to 2008-2010. Three year averages

	Male Incidence				Female incidence			
Year	Cases	ASR	95% CI		Cases	ASR	95% CI	
2001-2003	1413	4.9	4.8	5.1	946	2.4	2.3	2.5
2002-2004	1413	4.9	4.7	5.0	913	2.3	2.2	2.4
2003-2005	1423	4.8	4.7	5.0	918	2.3	2.2	2.4
2004-2006	1458	4.9	4.7	5.0	940	2.3	2.2	2.4
2005-2007	1423	4.7	4.5	4.8	923	2.3	2.2	2.4
2006-2008	1483	4.8	4.6	4.9	958	2.4	2.3	2.5
2007-2009	1555	4.9	4.8	5.0	1007	2.5	2.4	2.6
2008-2010	1666	5.2	5.0	5.3	1060	2.6	2.5	2.7

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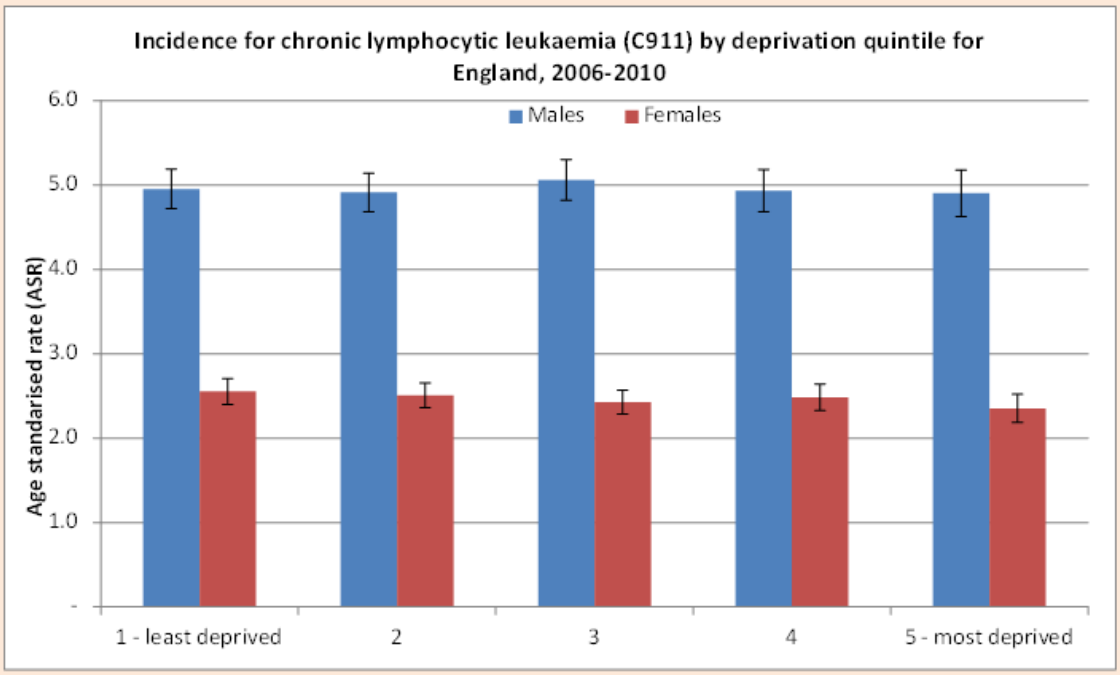
Figure 27 shows the incidence of CLL by quintile of deprivation and sex over the period 2006-2010; there was no relationship between deprivation and the incidence of CLL.

Figure 27: Incidence for chronic lymphocytic leukaemia by deprivation for England, 2006-2010



B.7.2 Mortality

Table 23 shows trends in mortality from CLL; there were no marked changes across the period reported in the age-standardised mortality of CLL.

Table 23: Mortality- Chronic Lymphocytic Leukaemia, by sex, England 2001-2003 to 2008-2010. Three year averages

	Male mortality				Female mortality			
Year	Deaths	ASR	95% CI		Deaths	ASR	95% CI	
2001-2003	509	1.7	1.6	1.8	371	0.7	0.7	0.8
2002-2004	508	1.7	1.6	1.8	374	0.7	0.7	0.8
2003-2005	534	1.7	1.6	1.8	366	0.7	0.7	0.8
2004-2006	535	1.7	1.6	1.8	366	0.7	0.7	0.8
2005-2007	552	1.7	1.6	1.8	378	0.7	0.7	0.8
2006-2008	560	1.7	1.6	1.8	378	0.7	0.7	0.8
2007-2009	565	1.6	1.6	1.7	369	0.7	0.6	0.7
2008-2010	566	1.6	1.5	1.7	369	0.7	0.6	0.7

Figure 28 shows mortality rates for CLL by quintile of deprivation and sex; there was no significant relationship between deprivation and mortality from CLL.

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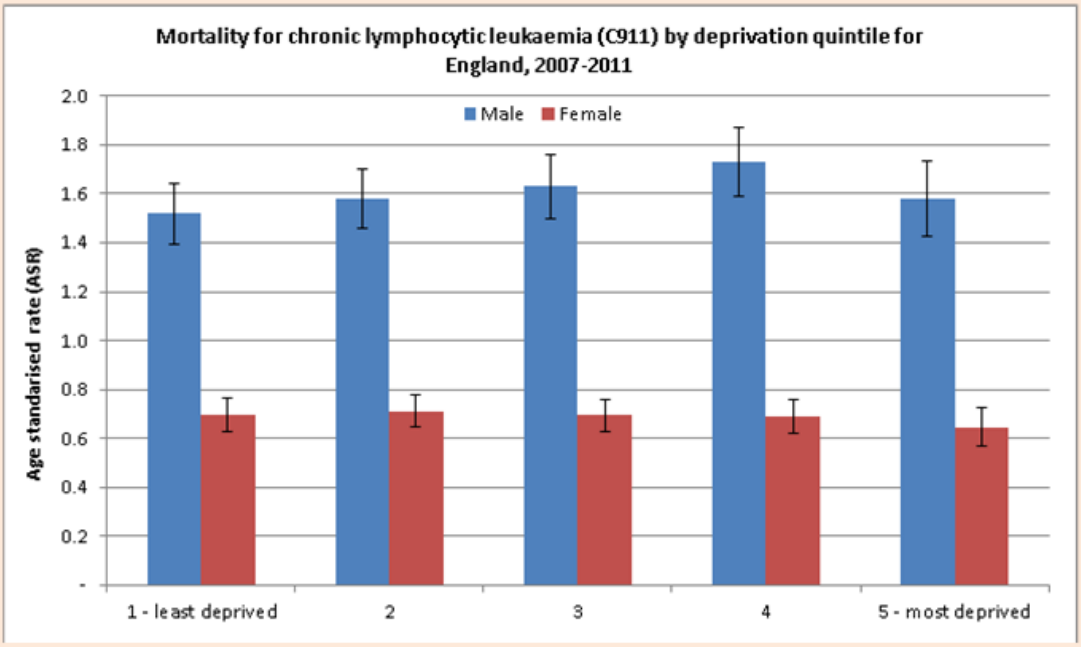
Figure 28: Mortality rates for CLL by quintile of deprivation and sex



B.7.3 Survival

Figure 29 and 30 show one - and five-year relative survival for males and females with CLL; no statistically significant change in relative survival was observed across this period.

Figure 29: Relative 1 and 5 year survival - Chronic Lymphocytic Leukaemia, by sex, diagnosed in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010 in England

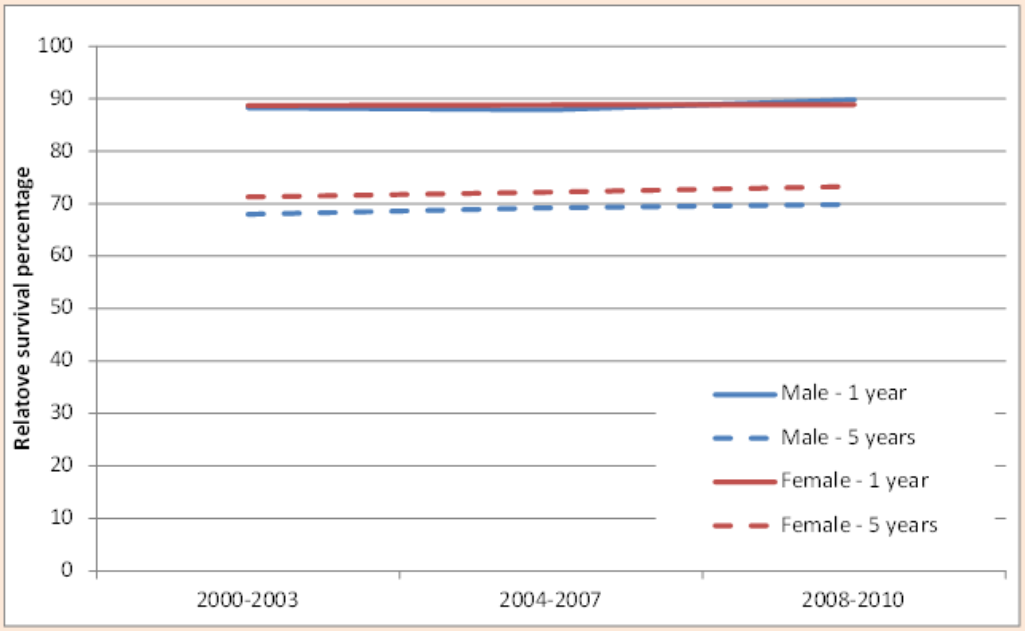


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Figure 30: Trends in relative survival rates for chronic lymphocytic leukaemia diagnosed in persons in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010, by age group in England

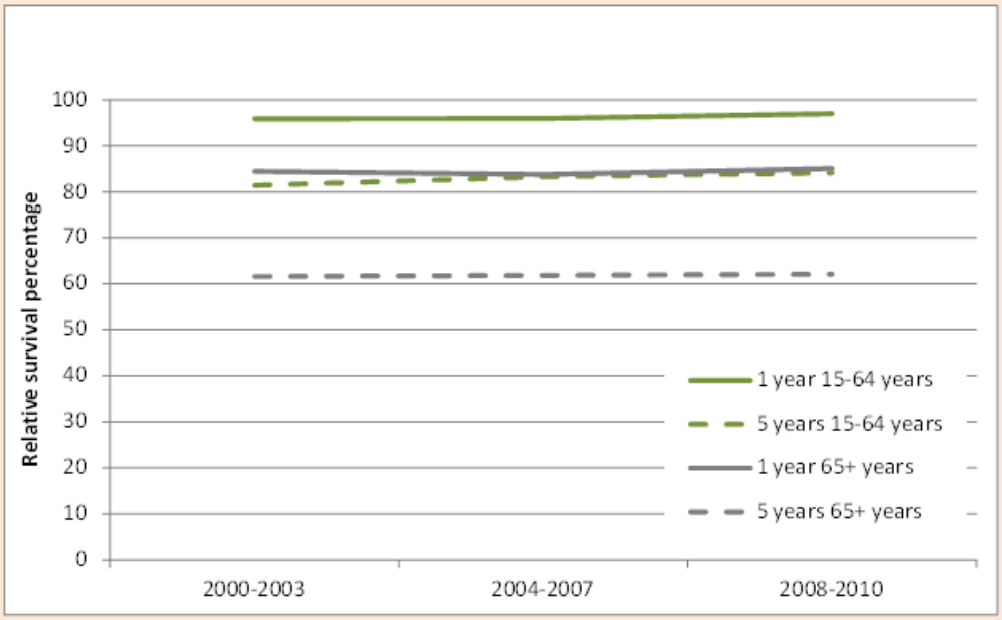

Figure 31 shows one- and five-year relative survival of patients with CLL by quintile of deprivation. Despite the lack of any association with incidence of CLL and deprivation, relative survival differs by quintile of deprivation, with poorer relative survival in the more deprived quintiles. This becomes significant at five years with five-year relative survival in the least deprived quintile being significantly better than that in the most deprived (76.3% compared to 66.5%).

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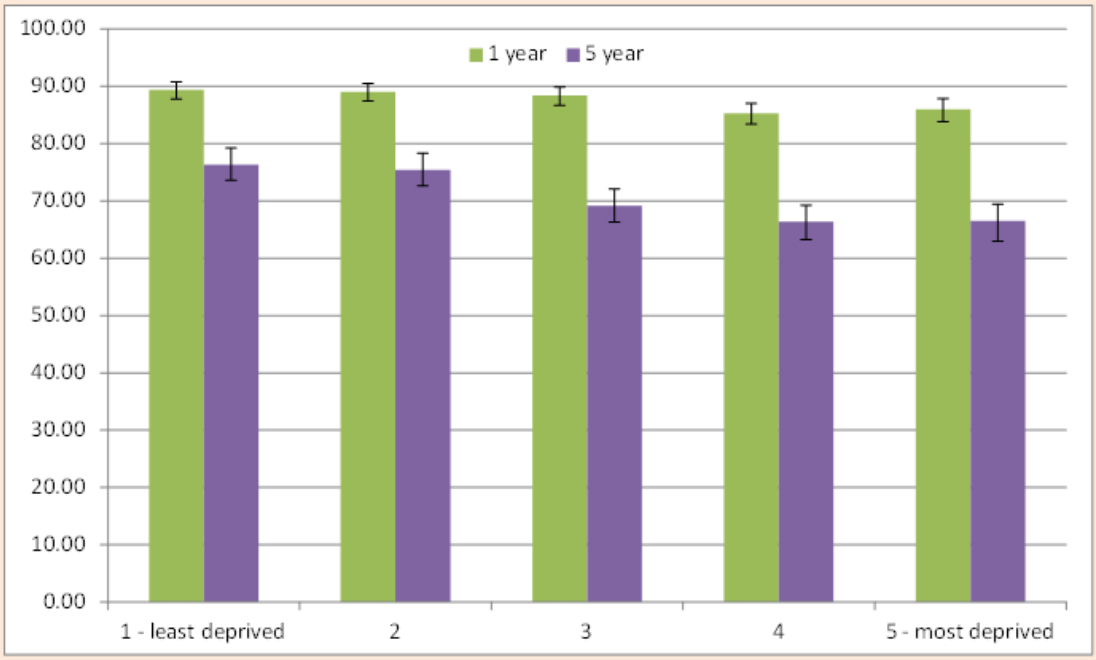
Figure 31: 1 and 5 year survival of patients (persons) diagnosed with Chronic Lymphocytic Leukaemia in England, 2000-2007 by deprivation (IMD2004)



B.7.4 Routes to diagnosis

Figure 32 shows a breakdown of the routes to diagnosis for CLL. It shows that the majority of patients were diagnosed via GP referral (43.4%), followed by emergency presentation (24.3%). Fewer patients came in via the two week wait route than for all malignancies combined (11.5% compared to 27.1%).

Figure 32: Routes to diagnosis for CLL

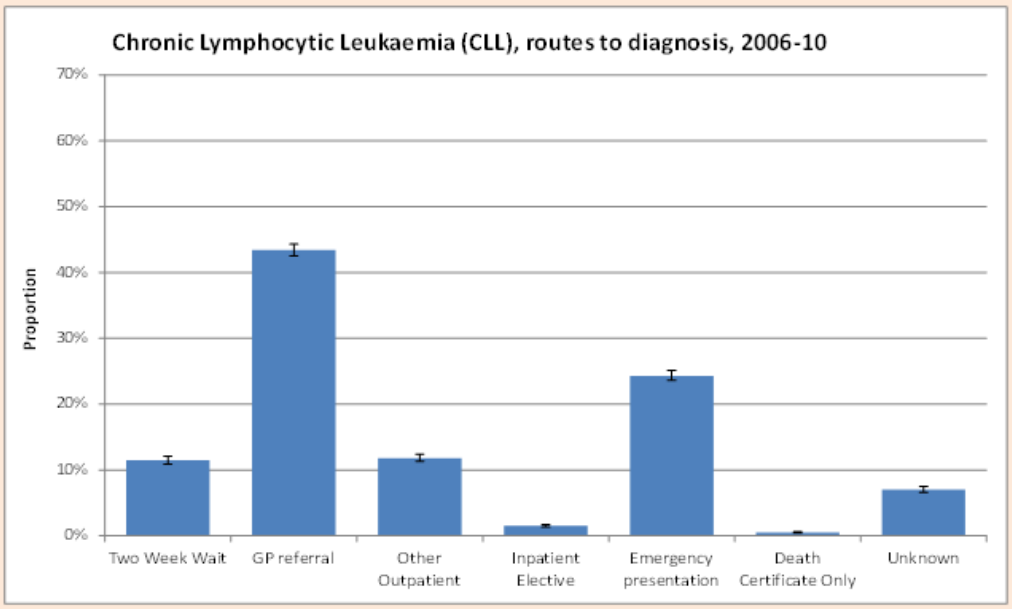


Figure 33 shows relative survival estimates by route to diagnosis; it shows that emergency presentations had significantly poorer one, two and three year relative survival than all other routes. Patients who came in via the two week wait and GP referral route had significantly better one, two and three year relative survival than all routes combined.

Figure 33: Relative survival estimates by route to diagnosis

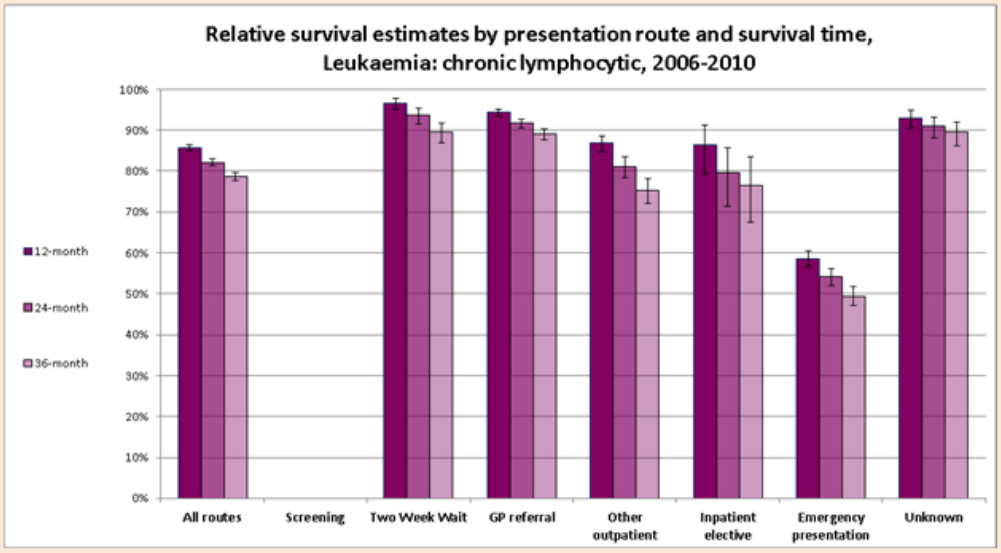


Figure 34 shows relative survival by presentation route and age for CLL. It shows that although one-year relative survival for emergency presentations in the younger age group (0-64) is significantly lower than one-year relative survival for all routes (88% compared to 96%), it is much more comparable than for the older age groups. For the 65-84 year age group one-year relative survival for emergency admissions is 60% compared to 85% for all

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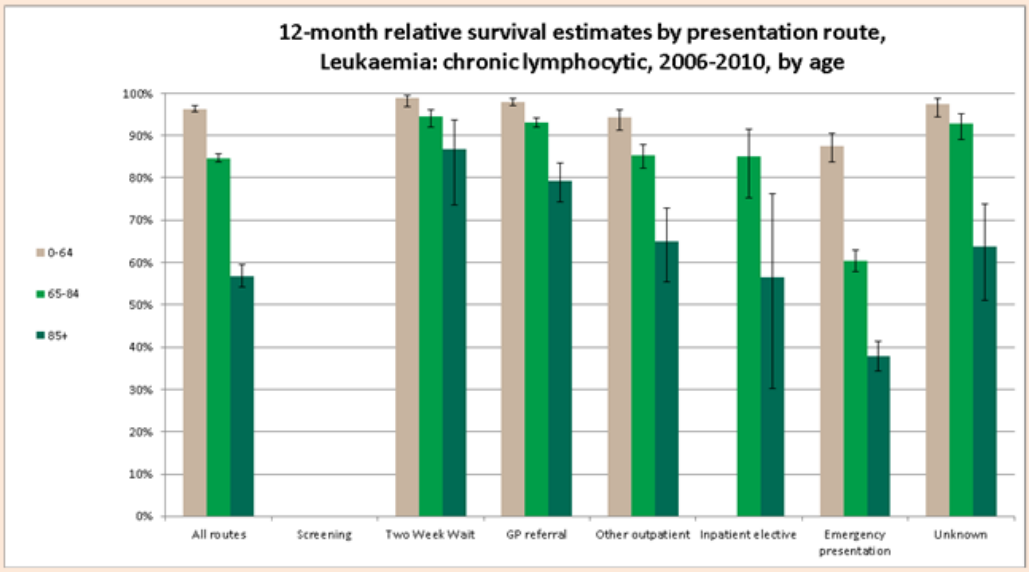
routes, and for the 85+ group it is 38% compared to 57% for all routes, and 87% in the 2 week wait group.

Figure 34: Relative survival by presentation route and age for CLL



B.8 Chronic Myeloid Leukaemia (CML)

Update 2016

Cases of CML have been difficult to capture and code accurately as coding systems prior to ICD-10 did not support the required levels of specificity (Caroline's poster). Since the introduction of ICD-10, these cases have been identified using the code C92.1. A recent publication by the National Cancer Intelligence Network (NCIN)v reported significantly poorer CML relative survival rates in the 65+ than the <65 age group which was not consistent with previously reported outcomes by the Haematological Malignancy Research Network (HMRN)2 or with clinical observation. This presented the hypothesis that some cases of CML in the elderly were potentially miscoded.

A recent review of a subset of CML cases by the NCRS team in Northern and Yorkshire confirmed inaccuracies in the final coding, finding that the majority of miscoded CML cases were in the 60+ age groups, confirming the suspicion that some cases of CML, particularly in the elderly, were miscoded. Therefore, interpretation of incidence and relative survival figures for CML presented here should be done with caution.

B.8.1 Incidence

Chronic myeloid leukaemia (CML) is a relatively rare cancer, predominantly affecting people over the age of 60, with higher age-standardised incidence in males (Figure 35). Table 24 shows trends in incidence of CML by sex; there were no changes in the incidence of CML between 2001 and 2010.

Figure 35: Age-specific incidence rates by age group for chronic myeloid leukaemia in males and females between 2006-2008 in England

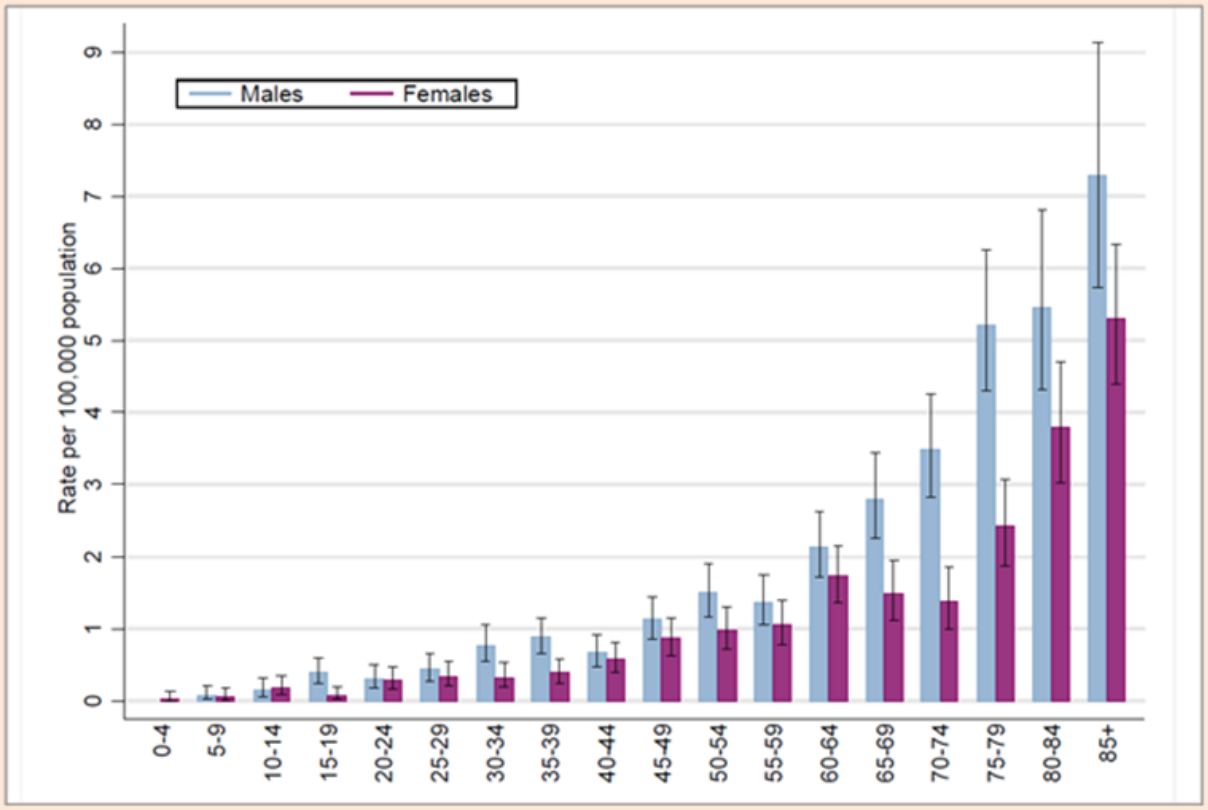


Table 24: Incidence - Chronic Myeloid Leukaemia, by sex, England 2001-2003 to 2008-2010. Three year averages

	Male Incidence				Female incidence			
Year	Cases	ASR	95% CI		Cases	ASR	95% CI	
2001-2003	307	1.1	1.1	1.2	239	0.7	0.7	0.8
2002-2004	299	1.1	1.0	1.2	236	0.7	0.7	0.8
2003-2005	307	1.1	1.0	1.2	238	0.7	0.7	0.8
2004-2006	313	1.1	1.0	1.2	234	0.7	0.6	0.7
2005-2007	310	1.1	1.0	1.2	230	0.7	0.6	0.7
2006-2008	306	1.1	1.0	1.1	232	0.7	0.6	0.7
2007-2009	308	1.1	1.0	1.1	234	0.7	0.6	0.7
2008-2010	328	1.1	1.0	1.2	243	0.7	0.7	0.8

Figure 36 shows incidence of CML by quintile of deprivation and sex; it shows there is no significant relationship between incidence of CML and deprivation.

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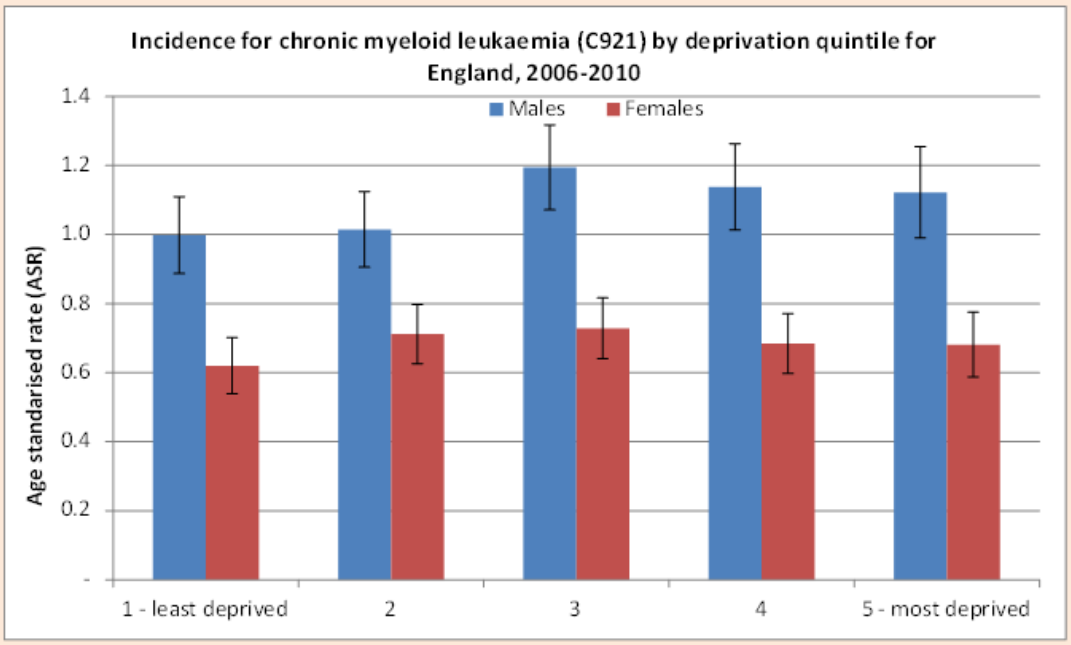
Figure 36: Incidence of CML by quintile of deprivation and sex



B.8.2 Mortality

Table 25 shows the mortality rates over time for CML by sex; it shows marked changes in the mortality rates over this time, with a significant decrease in mortality for both males (from 0.6 to 0.3 per 100,000) and females (0.4 to 0.2 per 100,000).

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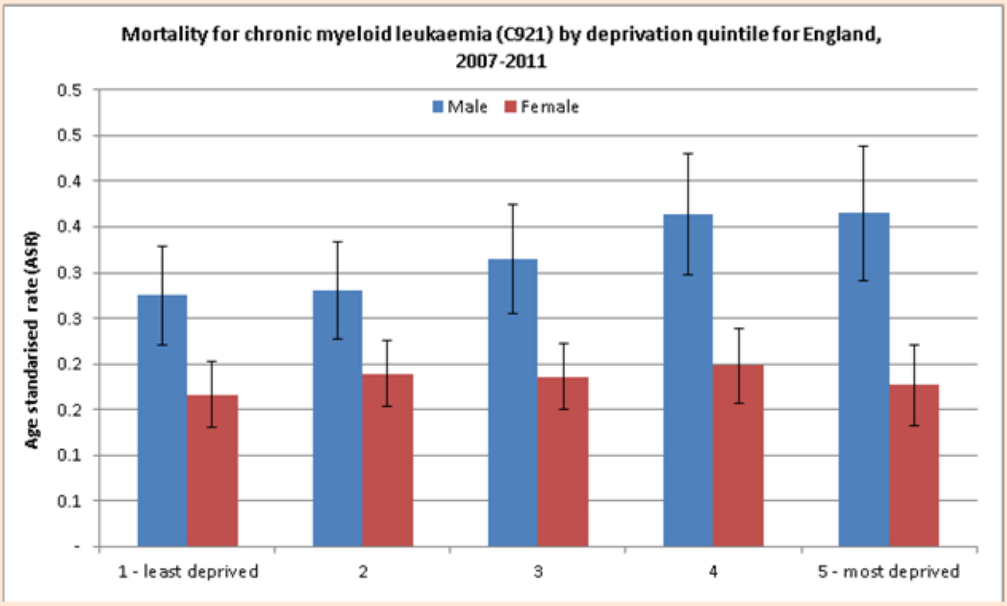
Table 25: Mortality - Chronic Myeloid Leukaemia, by sex, England 2001-2003 to 2008-2010. Three year averages

	Male mortality				Female mortality			
Year	Deaths	ASR	95% CI		Deaths	ASR	95% CI	
2001-2003	163	0.6	0.5	0.6	140	0.4	0.3	0.4
2002-2004	149	0.5	0.5	0.6	126	0.3	0.3	0.4
2003-2005	136	0.5	0.4	0.5	110	0.3	0.2	0.3
2004-2006	114	0.4	0.3	0.4	101	0.2	0.2	0.3
2005-2007	102	0.3	0.3	0.4	92	0.2	0.2	0.2
2006-2008	105	0.3	0.3	0.4	96	0.2	0.2	0.2
2007-2009	102	0.3	0.3	0.4	90	0.2	0.2	0.2
2008-2010	107	0.3	0.3	0.4	91	0.2	0.2	0.2

Figure 37 shows mortality from CML by quintile of deprivation; it shows that although there is a slighter increasing mortality rate with increasing deprivation for males, this relationship is not statistically significant.

Figure 37: Mortality from CML by quintile of deprivation



B.8.3 Survival

Figure 38 shows trends in one- and five-year relative survival by sex. It shows a significant improvement for both sexes in both one and five-year relative survival. One-year relative survival has increased from 75.7% to 83.2% for males, and 76.9% to 85.9% in females. Five-year relative survival has increased from 45.8% to 72.2% in males, and 42.8% to 74.3% in females.

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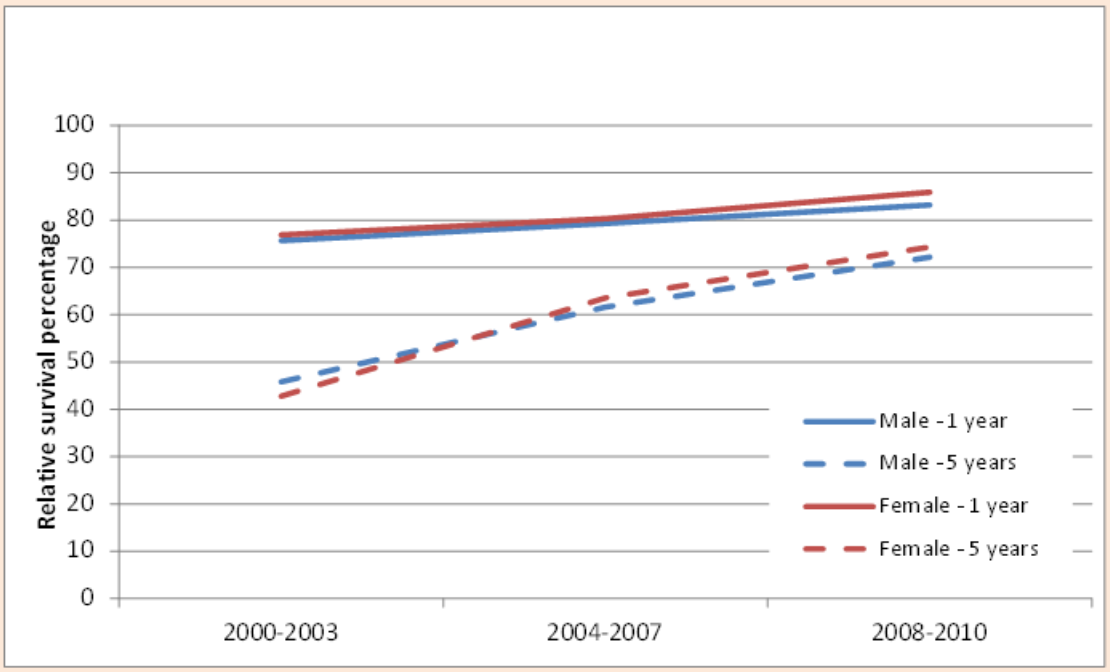
Figure 38: Relative 1 and 5 year survival - Chronic Myeloid Leukaemia, by sex , diagnosed in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010 in England



For patients aged 15-64 years relative survival at five years among males and females combined rose from 59% (95% CI: 56-63%) for individuals diagnosed in 2000-03 to 87% (95% CI: 84-90%) for those diagnosed in 2008-10. Improvement in outcomes has also been

observed in older individuals, for patients aged 65 and over relative survival at five years among males and females combined rose from 22% (95% CI 19-26%) for individuals diagnosed in 2000-03 to 44% (95% CI 39-48%) for those diagnosed in 2008-10. However, as discussed above, the observation that reported CML relative survival in older people remains low, may be reflective of miscoding of CML in older patients.

Figure 39: Trends in relative survival rates for chronic myeloid leukaemia diagnosed in persons in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010, by age group in England

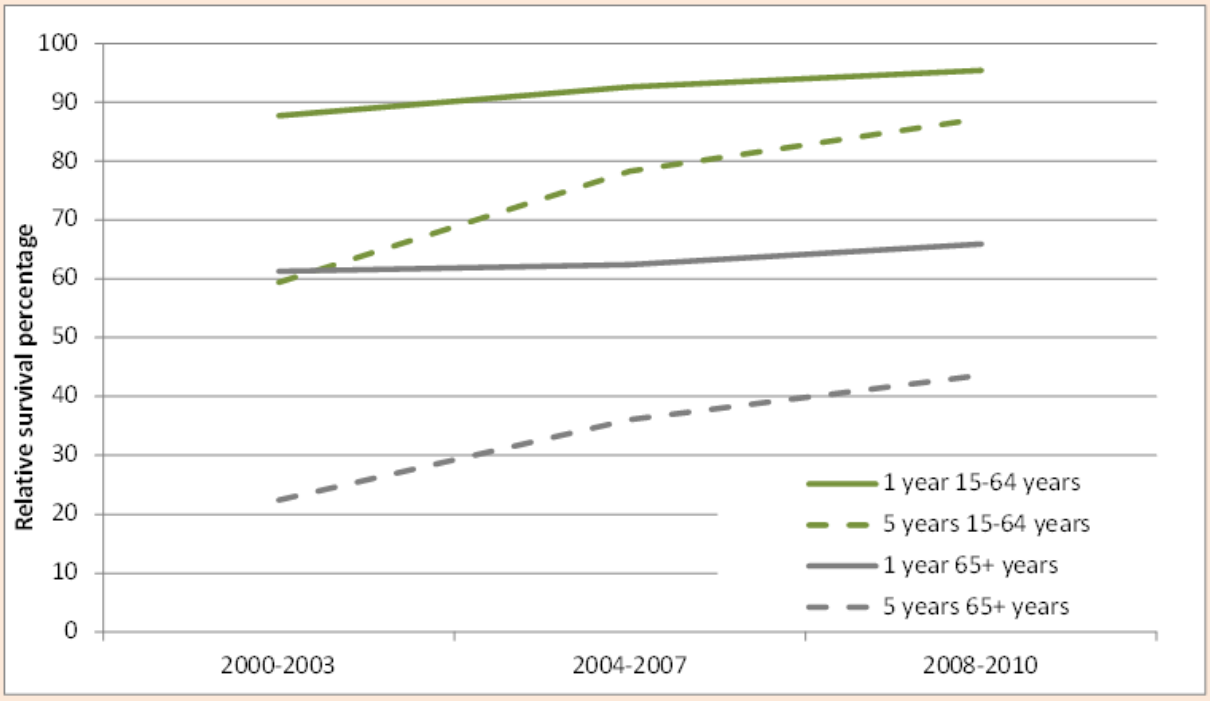


Figure 40 shows one- and five-year relative survival of patients with CML by quintile of deprivation. It shows that although there is no significant association with deprivation seen with one-year relative survival, at five years relative survival is significantly better in the least deprived quintile than in any other quintile (68.5% in quintile 1 compared to 52.8% in quintile 5).

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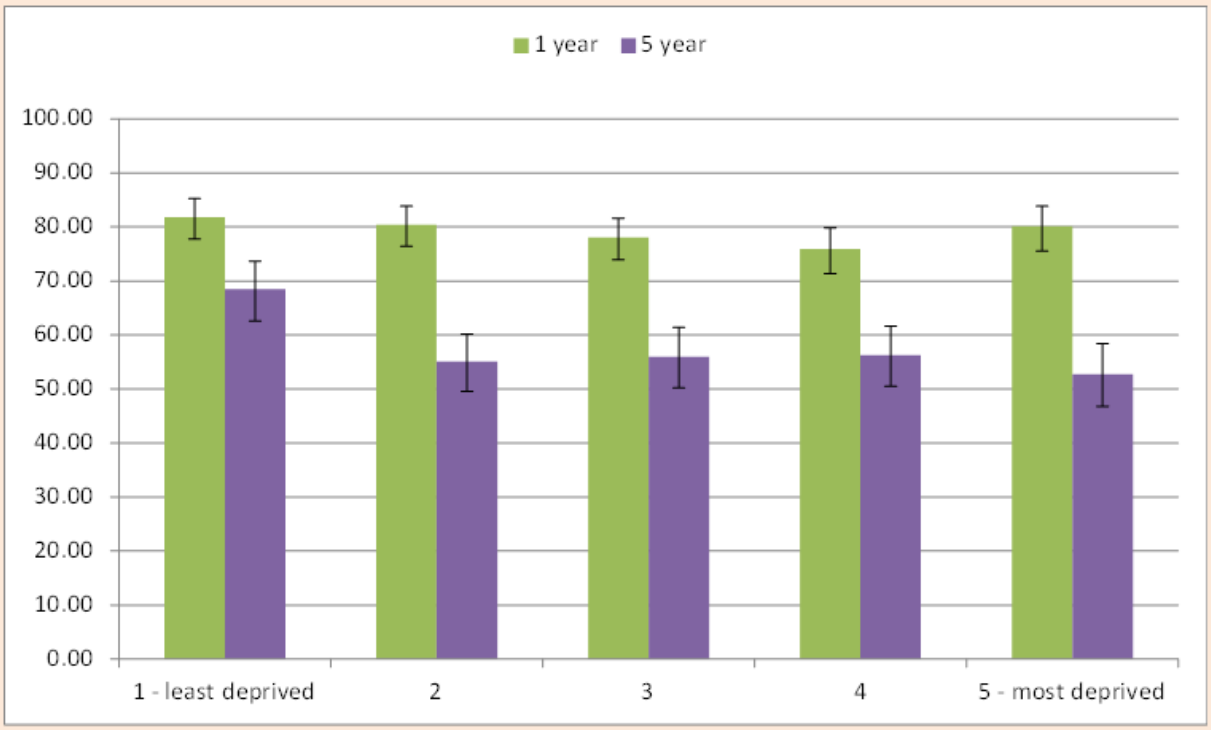
Figure 40: 1 and 5-year survival of patients (persons) diagnosed with Chronic Myeloid Leukaemia in England, 2000-2007 by deprivation (IMD2004)



B.8.4 Routes to diagnosis

Figure 41 shows a breakdown of the routes to diagnosis for CML. The majority of patients with CML are diagnosed either via GP referral (32.5%) or emergency presentation (34.2%) routes. The proportion of emergency presentations were higher than for all malignancies combined (22.9%).

Figure 41: Breakdown of the routes to diagnosis for CML

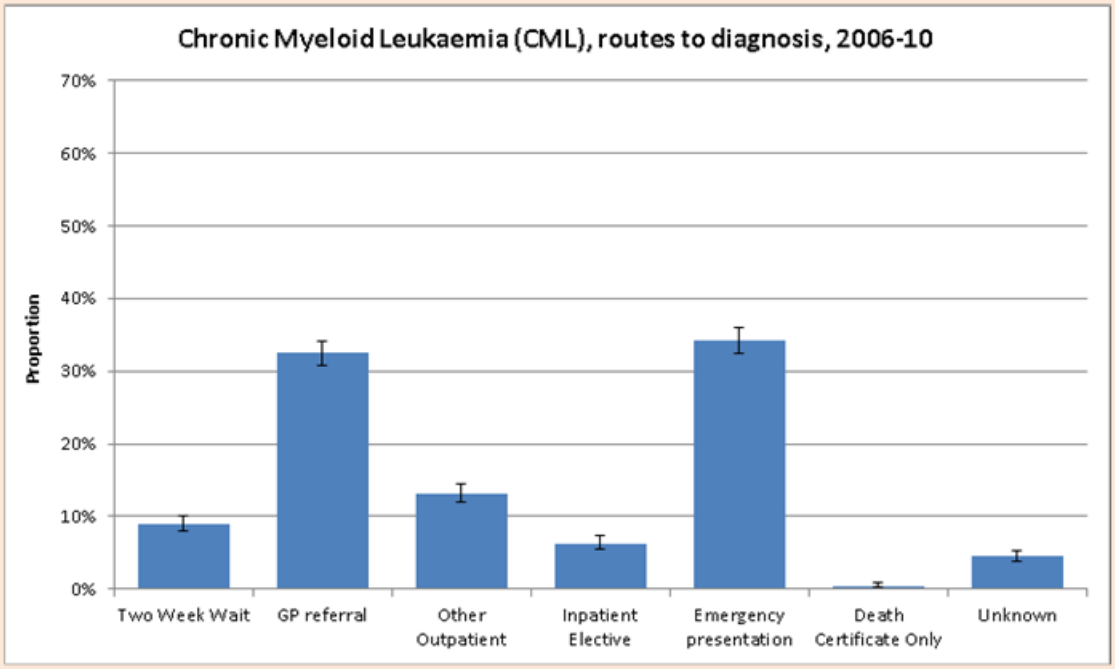


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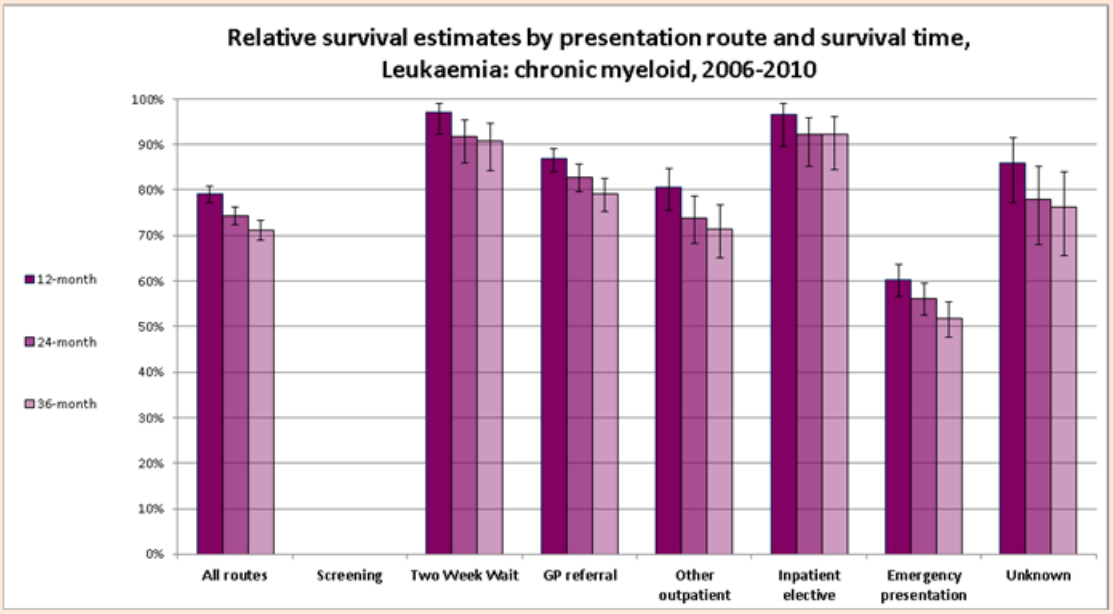
Figure 42 shows relative survival estimates by route to diagnosis for CML. Those individuals diagnosed via the emergency route have significantly poorer relative survival than all other routes to diagnosis. Patients who came in via the two week wait, and the inpatient elective route had significantly better one, two and three year relative survival than all routes combined.

Figure 42: Relative survival estimates by route to diagnosis for CML



B.9 Myeloma

Myeloma is predominantly a disease of older people, with low incidence before the age of 50 years; the incidence is greater in men at all ages.

B.9.1 Incidence

Over the reported period the age-standardised incidence of the disease rose significantly in both males and females, from 6.0 in 2001-03 to 7.0 per 100,000 in 2008-10 in males, and from 3.9 to 4.5 per 100,000 in females over the same time period (Table 26). The rising registration rates for myeloma may in part be due to greater ascertainment of cases, particularly in the elderly.

Table 26: Incidence - Multiple myeloma, by sex, England 2001-2003 to 2008-2010. Three year averages

	Male Incidence				Female incidence			
Year	Cases	ASR	95% CI		Cases	ASR	95% CI	
2001-2003	1728	6.0	5.9	6.2	1496	3.9	3.8	4.1
2002-2004	1794	6.2	6.0	6.3	1513	4.0	3.9	4.1
2003-2005	1857	6.3	6.1	6.5	1567	4.1	4.0	4.2
2004-2006	1901	6.3	6.2	6.5	1595	4.2	4.0	4.3
2005-2007	1949	6.4	6.2	6.6	1638	4.2	4.1	4.4
2006-2008	2057	6.6	6.4	6.8	1703	4.4	4.3	4.5
2007-2009	2183	6.9	6.7	7.1	1759	4.5	4.3	4.6
2008-2010	2242	7.0	6.8	7.1	1792	4.5	4.4	4.6

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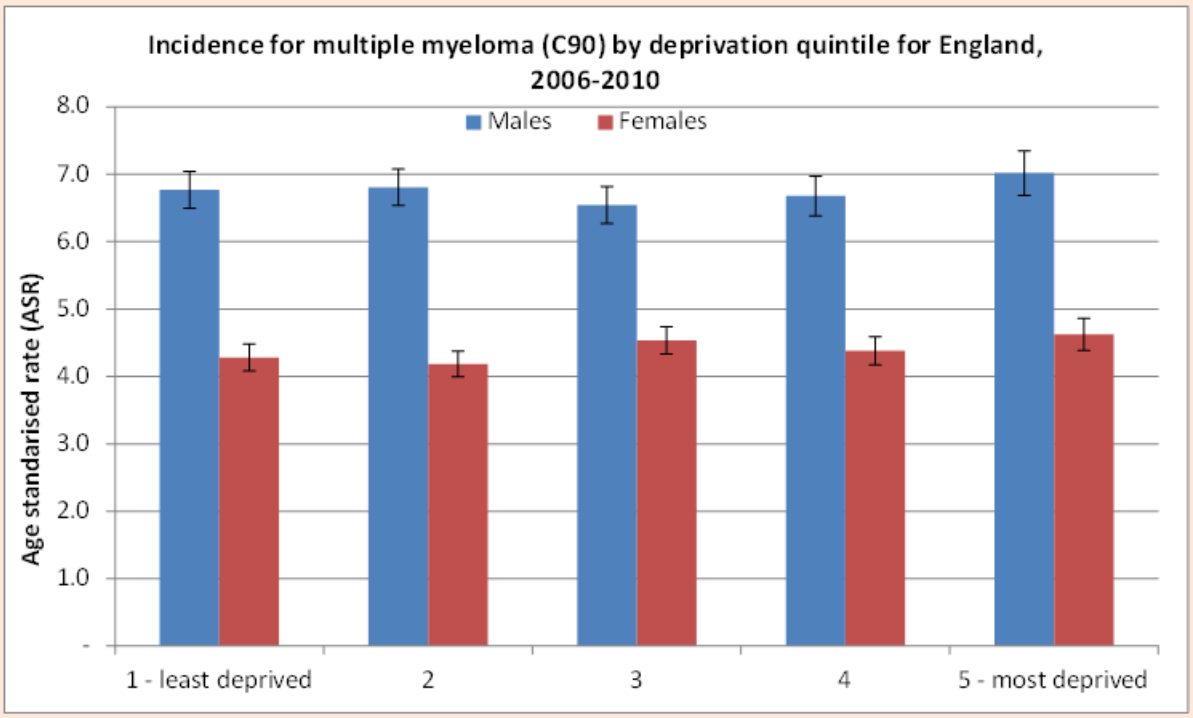
Figure 43 shows incidence of myeloma by quintile of deprivation. There is no relationship seen between deprivation and incidence of myeloma.

Figure 43: Incidence of myeloma by quintile of deprivation



B.9.2 Mortality

Table 27 shows trends in the age-standardised mortality rate from myeloma. It shows that mortality for males and females fell slightly over this time, this was significant for males (3.7 to 3.4 per 100,000) but not for females (2.5 to 2.3 per 100,000).

Table 27: Mortality- Multiple myeloma, by sex, England 2001-2003 to 2008-2010. Three year averages

	Male mortality				Female mortality			
Year	Deaths	ASR	95% CI		Deaths	ASR	95% CI	
2001-2003	1102	3.7	3.6	3.9	1043	2.5	2.4	2.6
2002-2004	1121	3.7	3.6	3.9	1031	2.5	2.4	2.6
2003-2005	1102	3.6	3.5	3.7	1024	2.4	2.3	2.5
2004-2006	1111	3.6	3.4	3.7	1006	2.4	2.3	2.5
2005-2007	1125	3.5	3.4	3.7	1044	2.4	2.4	2.5
2006-2008	1167	3.6	3.5	3.7	1045	2.4	2.3	2.5
2007-2009	1162	3.5	3.4	3.6	1039	2.3	2.2	2.4
2008-2010	1161	3.4	3.3	3.5	1031	2.3	2.2	2.4

Figure 44 shows age-standardised mortality rates for myeloma by quintile of deprivation. It shows that there is no significant difference in mortality rates between the most and least deprived quintiles for either males or females.

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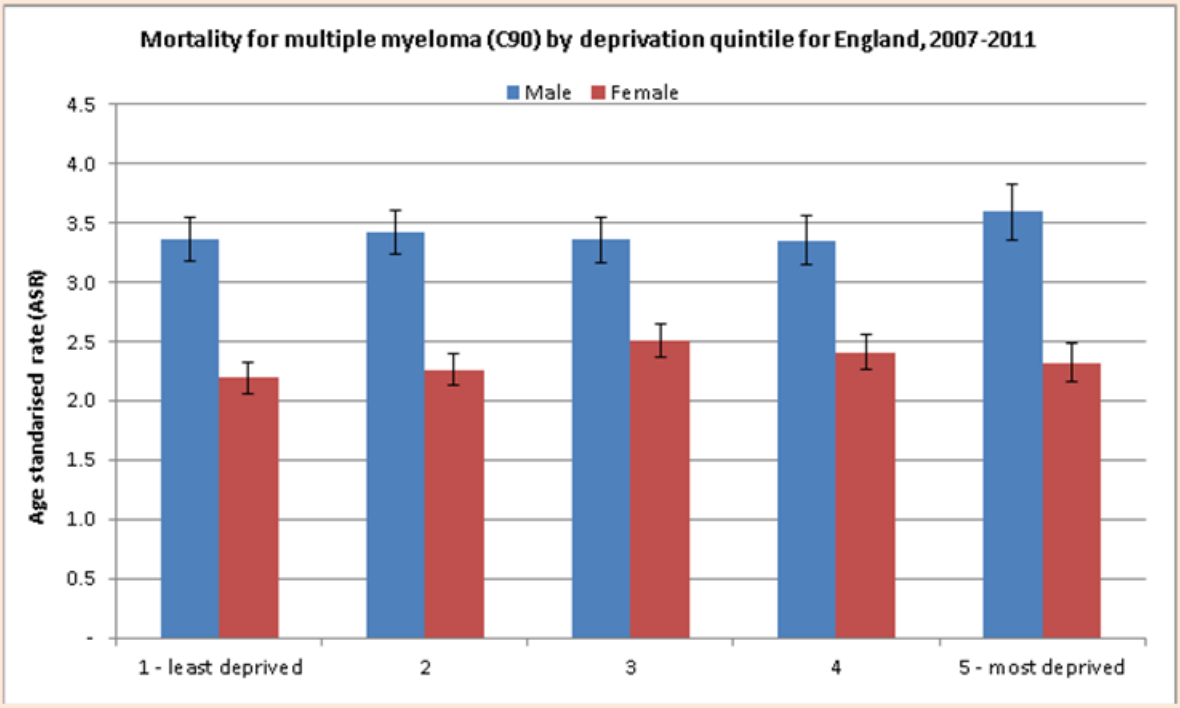
Figure 44: Age-standardised mortality rates for myeloma by quintile of deprivation



B.9.3 Survival

The time period covered in this report shows an improvement in relative survival in patients with myeloma. There was an increase in relative survival at 5 years among males (all ages) from 30% (95% CI: 29-31%) for individuals diagnosed in 2000-03 to 43% (95% CI: 41-44%) for those diagnosed in 2008-10. Among female patients (all ages) with myeloma there was an increase in relative survival at 5 years from 28% (95% CI: 27-30%) for individuals diagnosed in 2000-03 to 39% (95% CI: 37-40%) for those diagnosed in 2008-10 (Figure 45).

Update 2016

Figure 45: Relative 1 and 5 year survival - Multiple myeloma, by sex , diagnosed in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010 in England

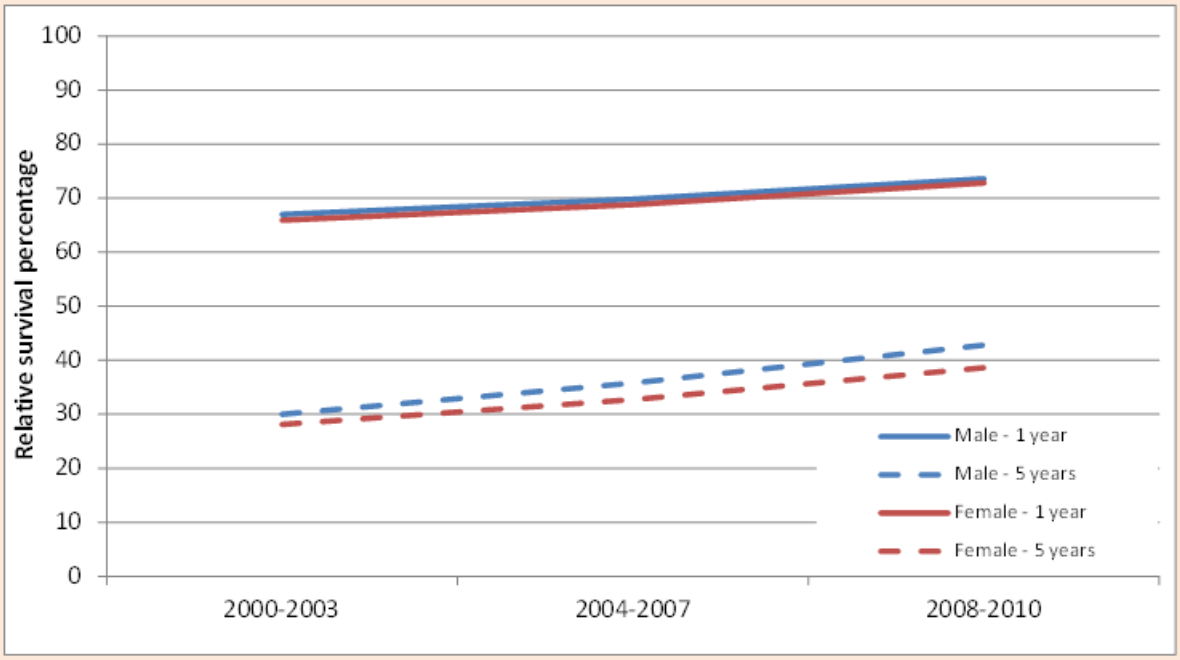


Figure 46 shows one- and five-year relative survival by age group for myeloma. It shows that there have been significant increases in one and five-year relative survival for both the 15-64 year age group, and the 65+ age group.

Figure 46: Trends in relative survival rates for myeloma diagnosed in persons in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010, by age group in England

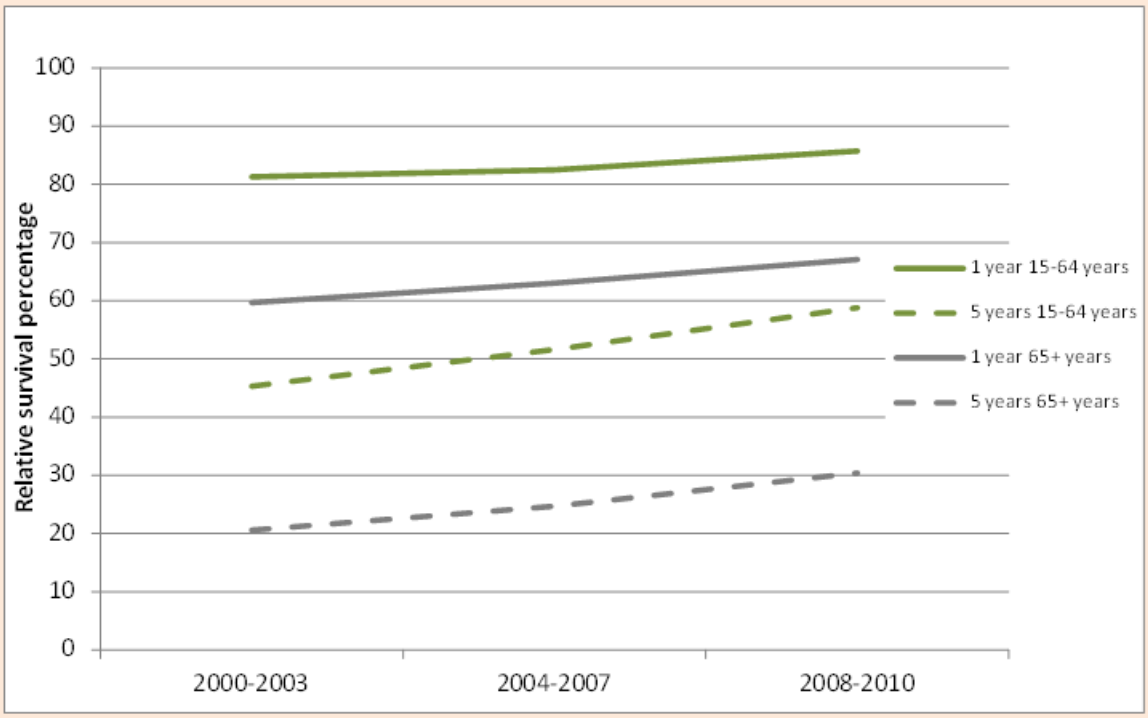


Figure 47 shows one and five-year relative survival of patients diagnosed with myeloma by quintile of deprivation. Despite the lack of any observable relationship between incidence of myeloma and deprivation, relative survival shows significant variation by quintile of deprivation, with significantly poorer one-year and five-year relative survival in the most deprived quintile (66.1% one-year relative survival in the most deprived quintile compared to 71.4% in the least, and 30.5% five-year in the most deprived quintile compared to 35.5%).

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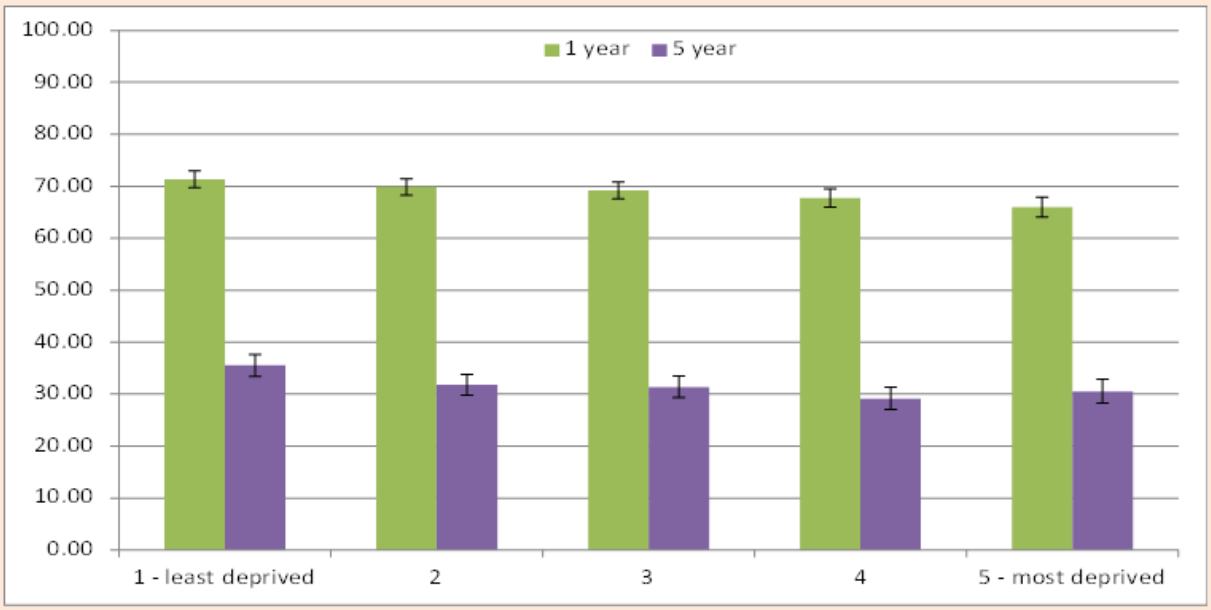
Figure 47: One and five-year relative survival of patients diagnosed with myeloma by quintile of deprivation



B.9.4 Routes to diagnosis

Figure 48 shows a breakdown of the routes to diagnosis for myeloma. The highest proportion of diagnoses occur via emergency admission (35.3%), followed by GP referral (33.8%). The proportion of emergency admissions for myeloma is significantly higher than for all malignancies combined (35.3% compared to 22.9%).

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Figure 48: Routes to diagnosis for myeloma

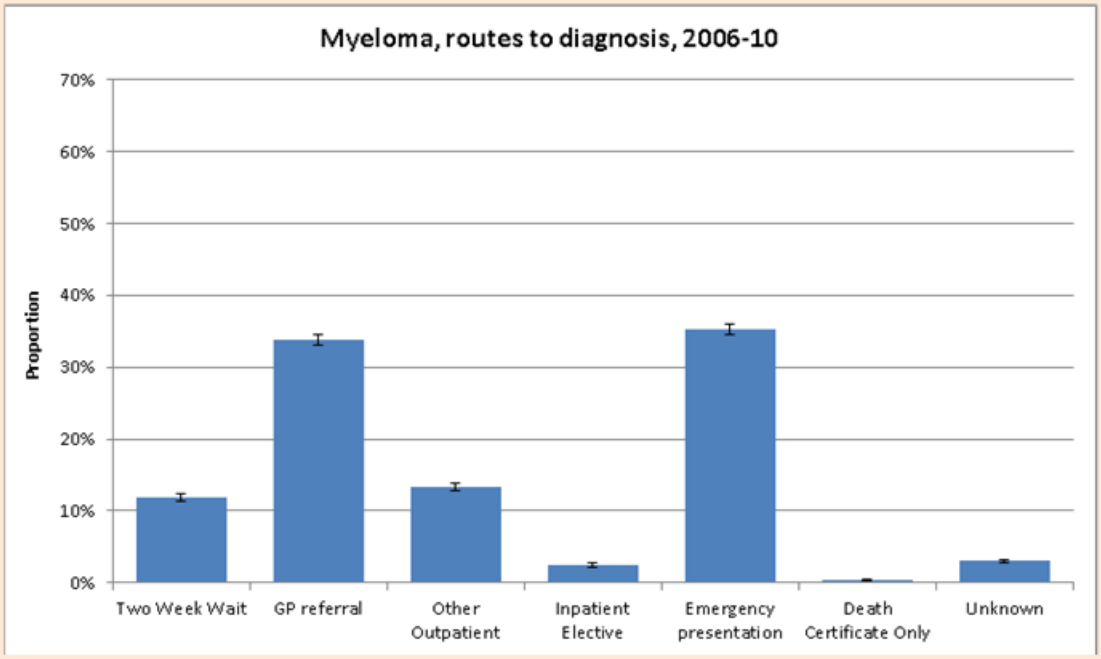


Figure 49 shows one-, two- and three-year relative survival by presentation route for myeloma. It shows that similarly to other sites, emergency presentations with myeloma had significantly poorer one-, two- and three-year relative survival than all other routes.

Figure 49: One-, two- and three-year relative survival by presentation route for myeloma

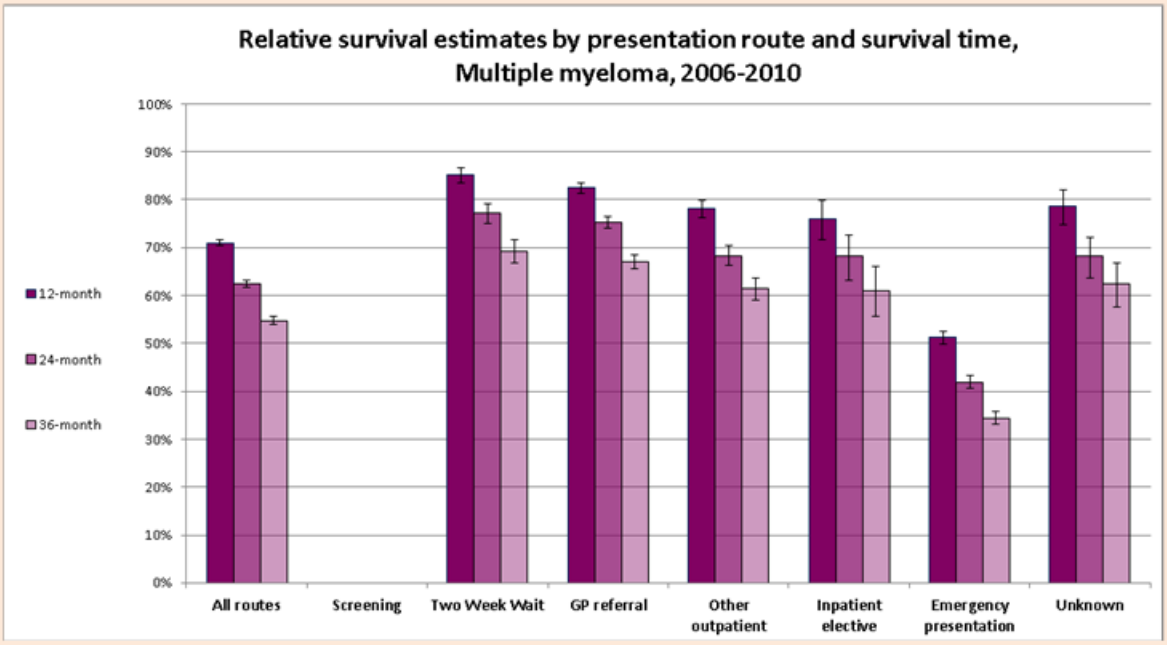
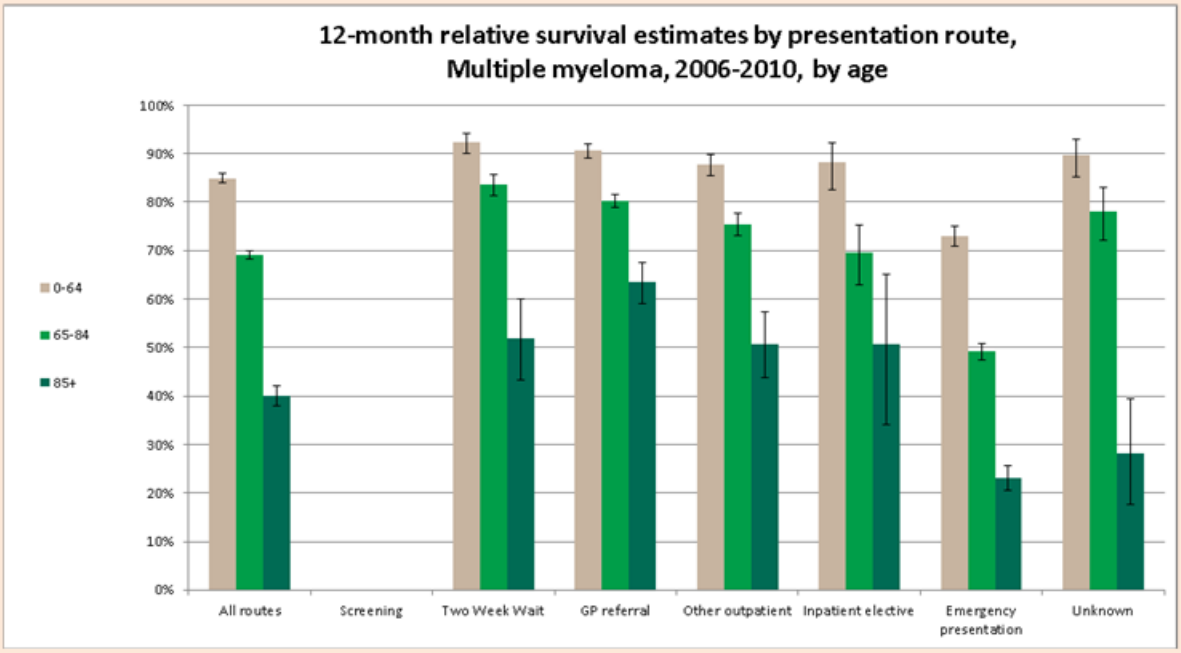


Figure 50 shows one-year relative survival estimates for myeloma by age and route to diagnosis. It shows that one-year relative survival for emergency presentations is significantly lower than all routes for each age band respectively.

Figure 50: One-year relative survival estimates for myeloma by age and route to diagnosis



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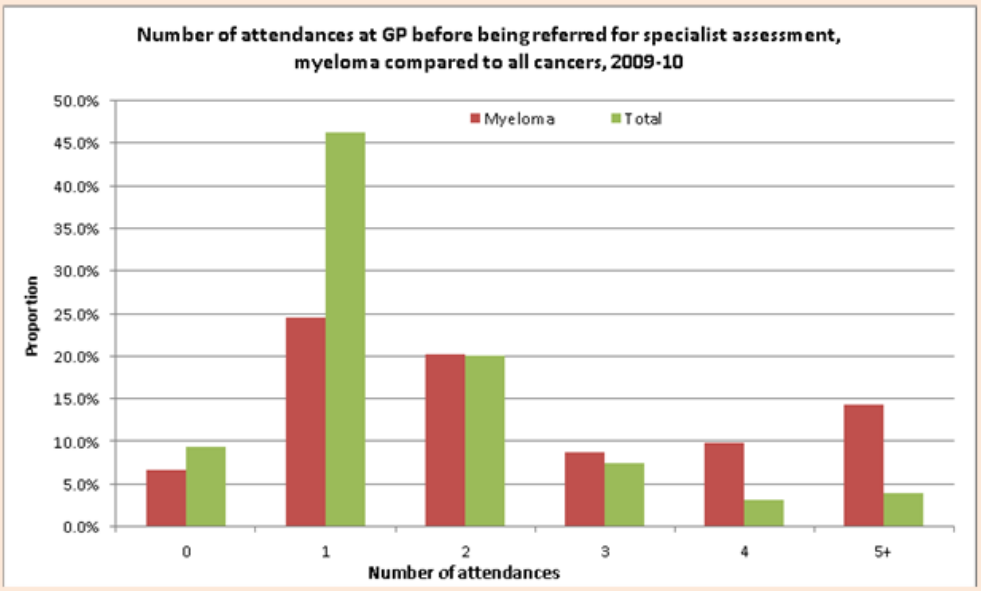
B.9.5 Primary care consultations

As part of the National Audit of Cancer Diagnosis in Primary Care (Royal College of General Practitioners, 2011), participating practices were asked to count all consultations relating to the presenting problem that was associated with the patient's cancer. The majority of patients included in the audit had consulted their GP once or twice (66%), however a third of

myeloma patients (33%) had consulted their GP three or more times, and 14% had consulted their GP five or more times (Figure 51).

Figure 51: Number of attendances at GP before being referred for specialist assessment



B.10 Hodgkin lymphoma

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B.10.1 Incidence

The age distribution for Hodgkin lymphoma has two peaks, the first in young adults and the second in old age. In the age range 15-24 years the incidence of disease is higher in females, but at all other ages the disease is more common in males (Figure 52). Over the period reported, incidence has risen significantly in both males and females (Table 28).

Figure 52: Age-specific incidence rates by age group for Hodgkin lymphoma in males and females between 2006-2008 in England

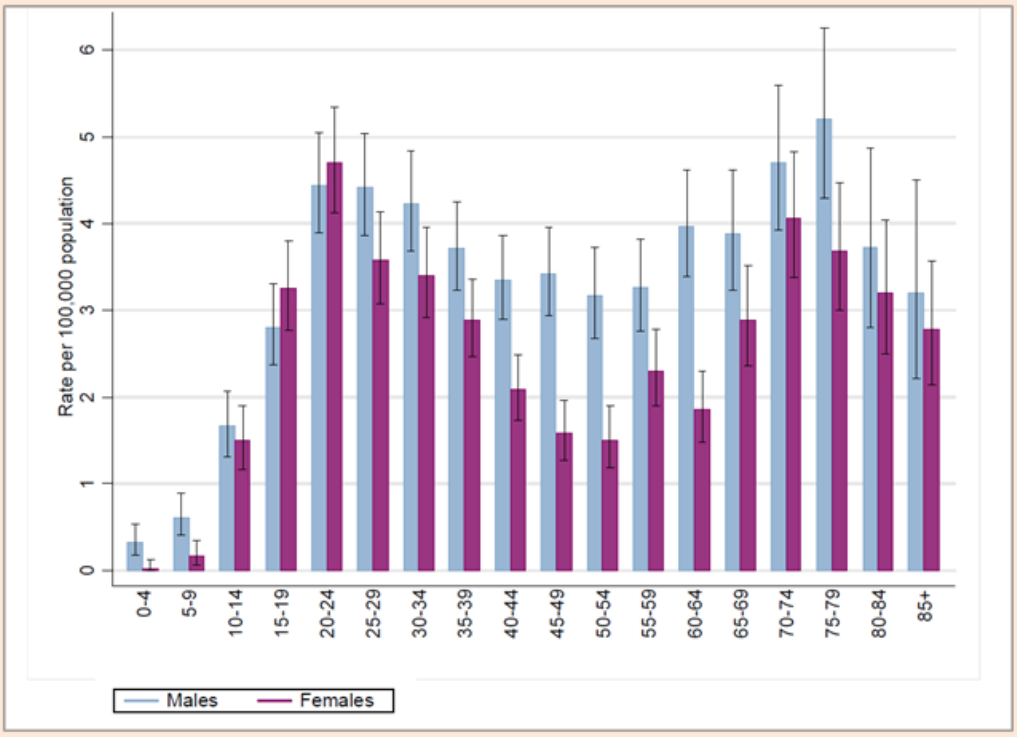


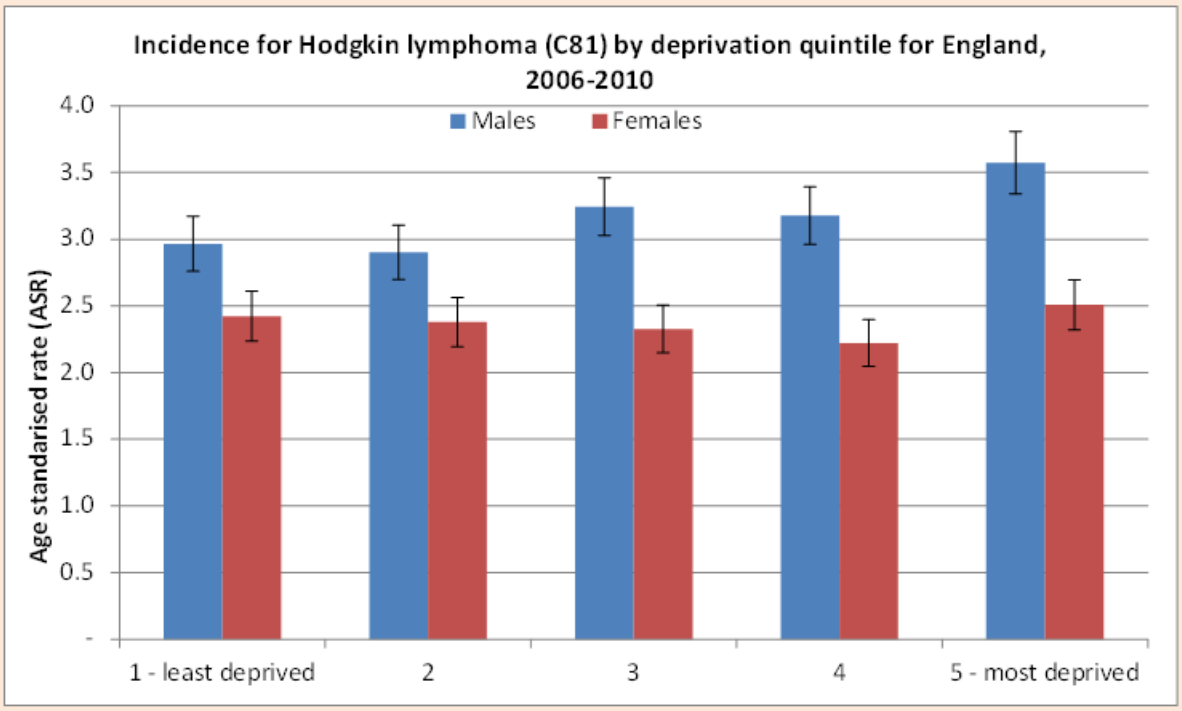
Table 28: Incidence - Hodgkin lymphoma by sex, England 2001-2003 to 2008-2010. Three year averages

	Male Incidence				Female incidence			
Year	Cases	ASR	95% CI		Cases	ASR	95% CI	
2001-2003	707	2.8	2.7	3.0	509	1.9	1.8	2.0
2002-2004	714	2.8	2.7	2.9	521	2.0	1.9	2.1
2003-2005	715	2.8	2.7	2.9	552	2.1	2.0	2.2
2004-2006	758	2.9	2.8	3.1	592	2.2	2.1	2.3
2005-2007	790	3.0	2.9	3.2	602	2.2	2.1	2.3
2006-2008	800	3.1	2.9	3.2	627	2.3	2.2	2.4
2007-2009	839	3.2	3.0	3.3	646	2.4	2.2	2.5
2008-2010	860	3.2	3.1	3.3	669	2.4	2.3	2.5

Figure 53 shows incidence of Hodgkin lymphoma by quintile of deprivation; incidence of Hodgkin lymphoma in males is significantly higher in the most deprived quintile (3.6 per 100,000 population) than in the least deprived quintile (3.0 per 100,000). There was no significant difference in incidence by deprivation for females.

Update 2016

Figure 53: Incidence of Hodgkin lymphoma by quintile of deprivation



B.10.2 Mortality

Table 29 shows trends in age-standardised mortality rates from Hodgkin lymphoma; mortality from Hodgkin lymphoma did not change significantly between 2001 and 2010 for either males or females.

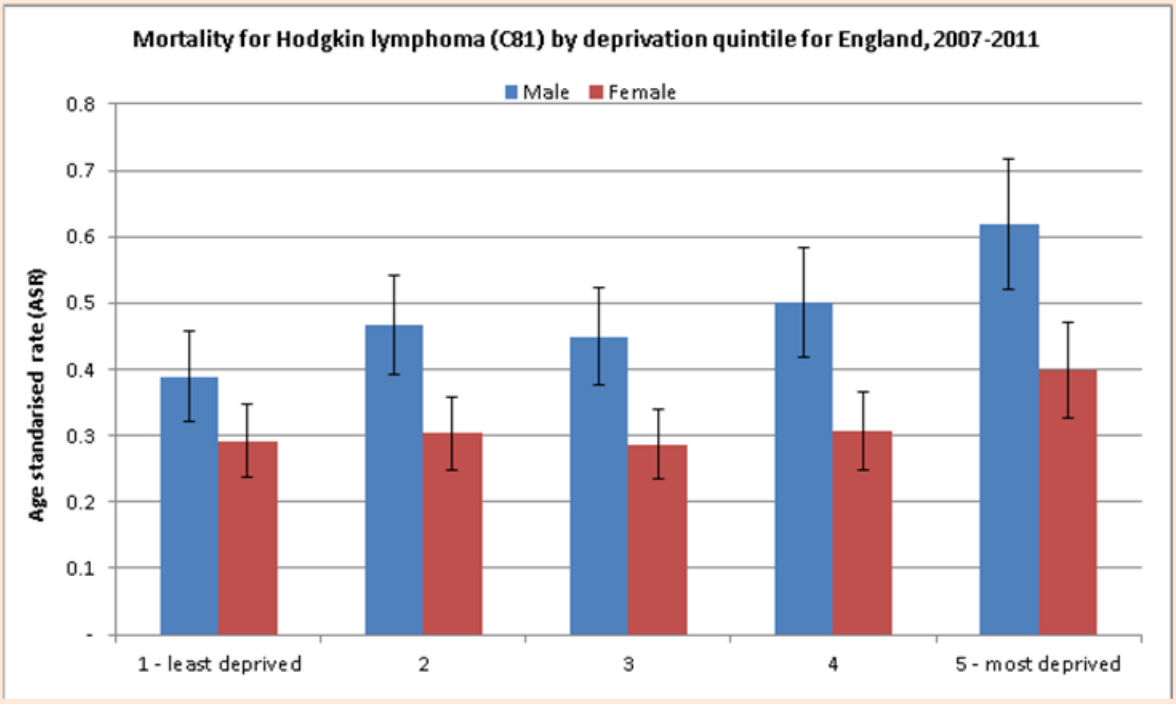
Update 2016

Table 29: Mortality- Hodgkin lymphoma by sex, England 2001-2003 to 2008-2010. Three year averages

	Male mortality				Female mortality			
Year	Deaths	ASR	95% CI		Deaths	ASR	95% CI	
2001-2003	135	0.5	0.4	0.5	103	0.3	0.3	0.4
2002-2004	147	0.5	0.5	0.6	108	0.3	0.3	0.4
2003-2005	146	0.5	0.5	0.6	107	0.3	0.3	0.4
2004-2006	148	0.5	0.5	0.6	111	0.3	0.3	0.4
2005-2007	140	0.5	0.4	0.5	120	0.4	0.3	0.4
2006-2008	144	0.5	0.4	0.5	125	0.4	0.3	0.4
2007-2009	142	0.5	0.4	0.5	117	0.3	0.3	0.4
2008-2010	146	0.5	0.4	0.5	111	0.3	0.3	0.3

Figure 54 shows age-standardised mortality rates by quintile of deprivation for Hodgkin lymphoma. It shows that the mortality rate for males in the most deprived quintile (0.62 per 100,000) is significantly higher than that in the least deprived (0.39 per 100,000). There is no significant difference in mortality rates by deprivation for females

Figure 54: Age-standardised mortality rates by quintile of deprivation for Hodgkin lymphoma



B.10.3 Survival

Relative survival did not change for females or males in any age group over this time period. Survival is good in children and young adults, but a poorer outcome is seen for elderly patients (Figures 55 and 56).

Figure 55: Relative 1 and 5 year survival - Hodgkin lymphoma, by sex , diagnosed in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010 in England

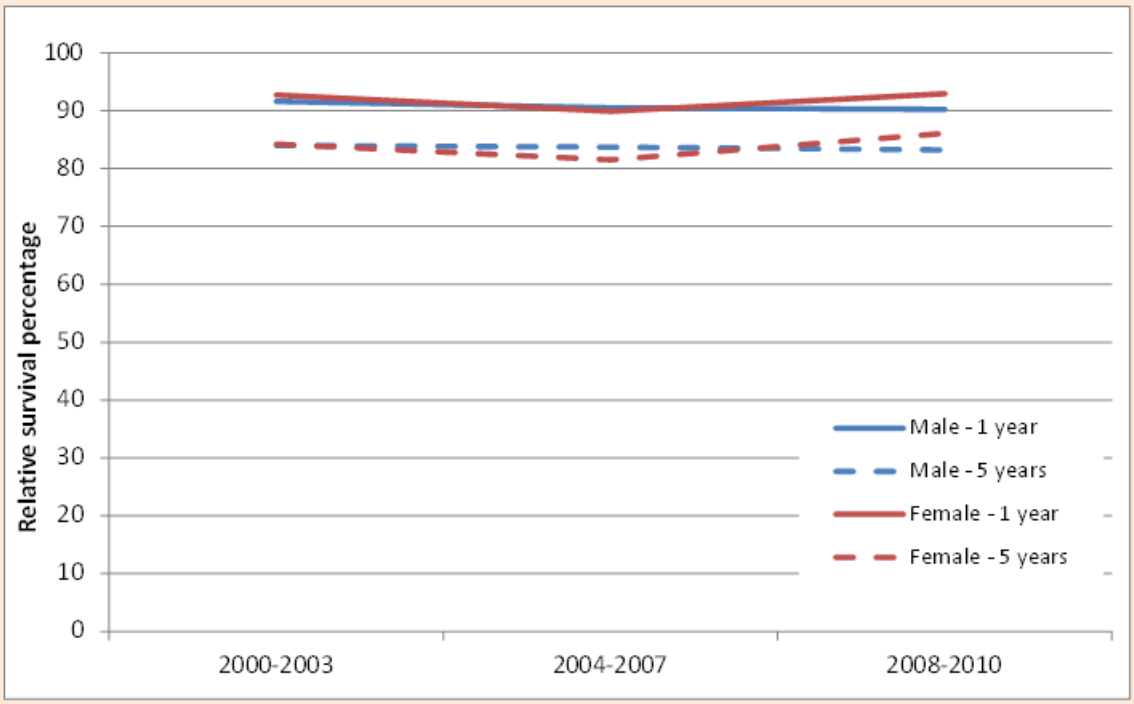


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Figure 56: Trends in relative survival rates for Hodgkin lymphoma diagnosed in persons in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010, by age group in England

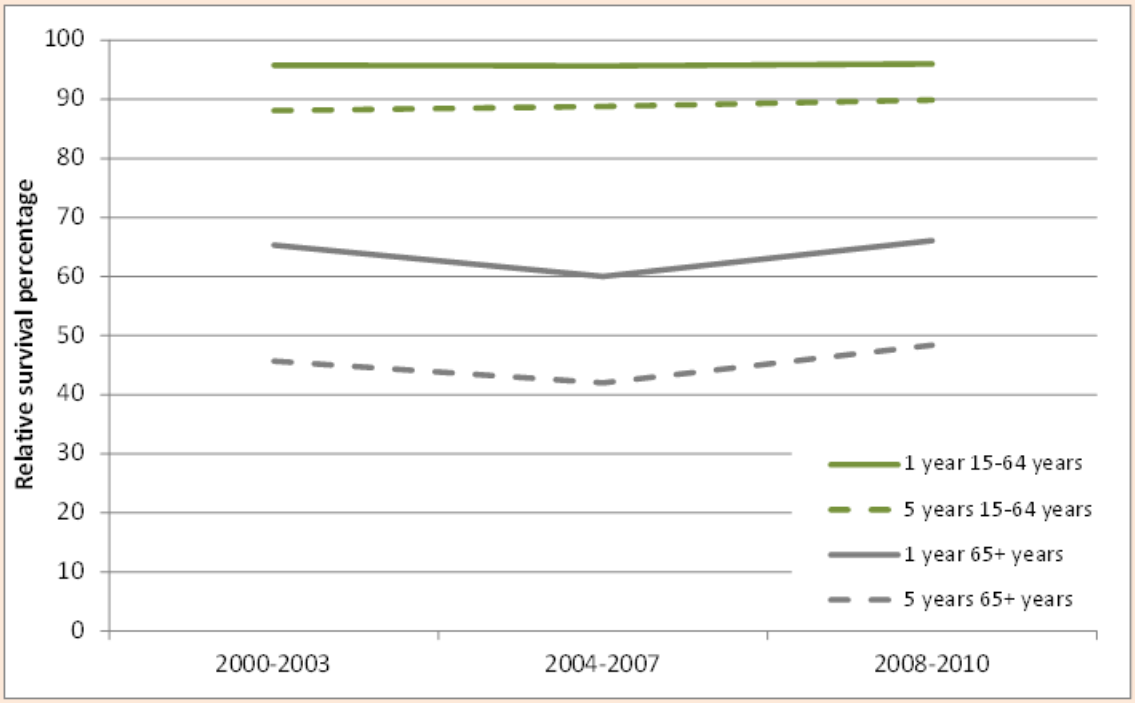

Figure 52 shows one- and five-year relative survival by quintile of deprivation for Hodgkin lymphoma; it shows that five-year relative survival is significantly poorer in the most deprived quintile (80.3%) compared to the least deprived (86.9%), although there is not a clear gradient across deprivation quintiles.

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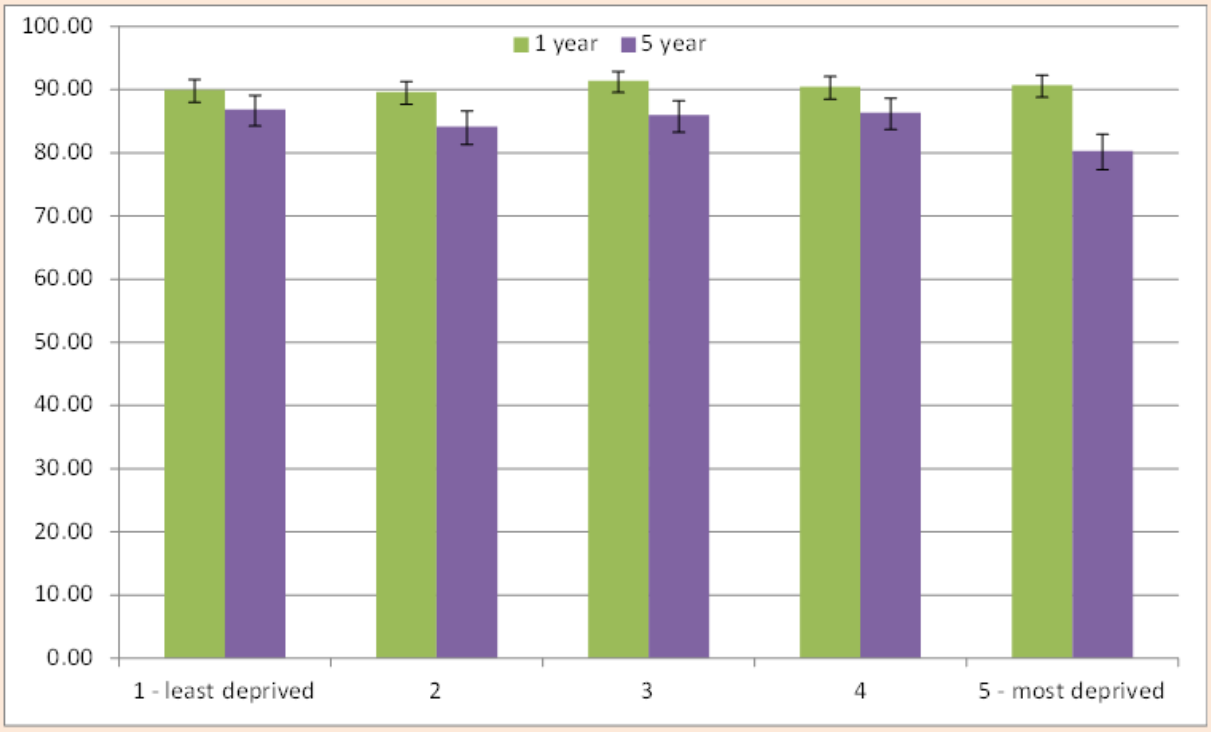
Figure 57: 1 and 5-year survival of patients (persons) diagnosed with Hodgkin lymphoma in England, 2000-2007 by deprivation (IMD2004)



B.10.4 Routes to diagnosis

Figure 58 shows the breakdown of routes to diagnosis for Hodgkin lymphoma. It shows that the majority of patients were diagnosed via GP referral (34.9%) and the two week wait route (27.8%). Only 16.4% of patients were diagnosed via an emergency presentation, the lowest of any of the haematological cancers discussed in this report, and significantly lower than for all malignancies combined (22.9%).

Figure 58: Routes to diagnosis for Hodgkin lymphoma

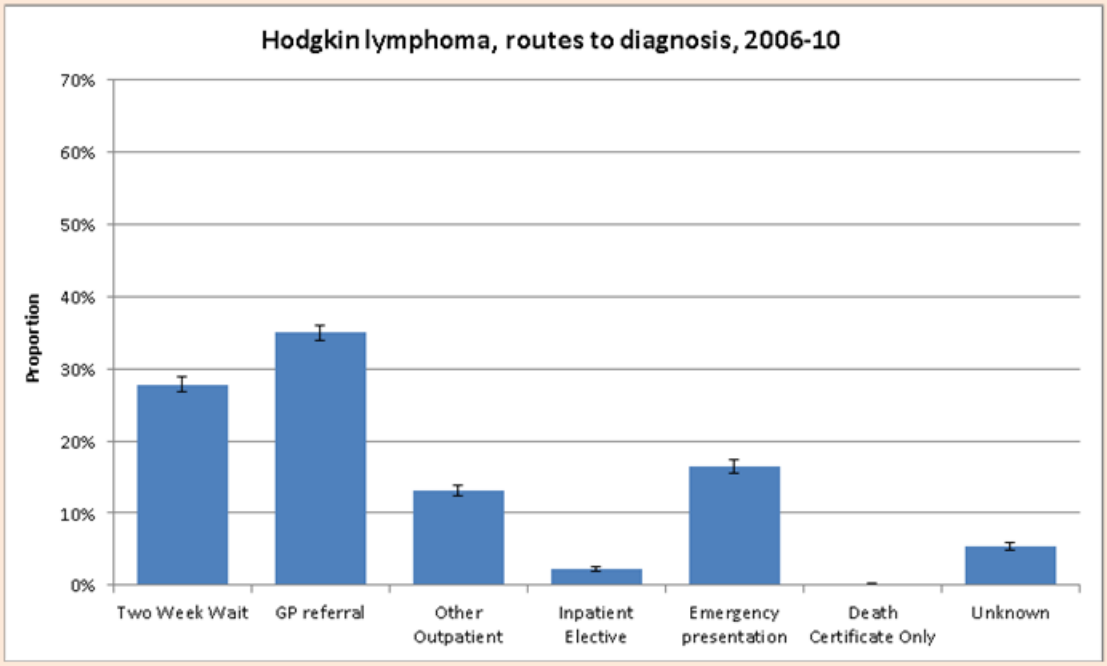


Figure 59 shows one, two and 3 year relative survival estimates by presentation route for Hodgkin lymphoma. It shows that in common with other tumour sites, patients with emergency presentations have significantly lower relative survival at all intervals than other routes to diagnosis.

Figure 59: One, two and 3 year relative survival estimates by presentation route for Hodgkin lymphoma

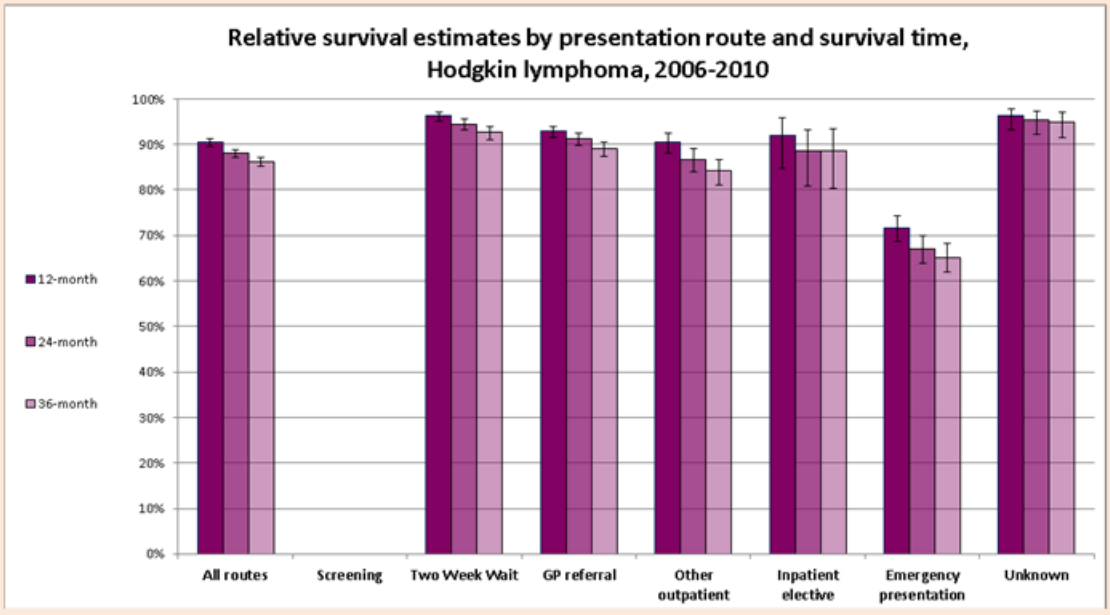


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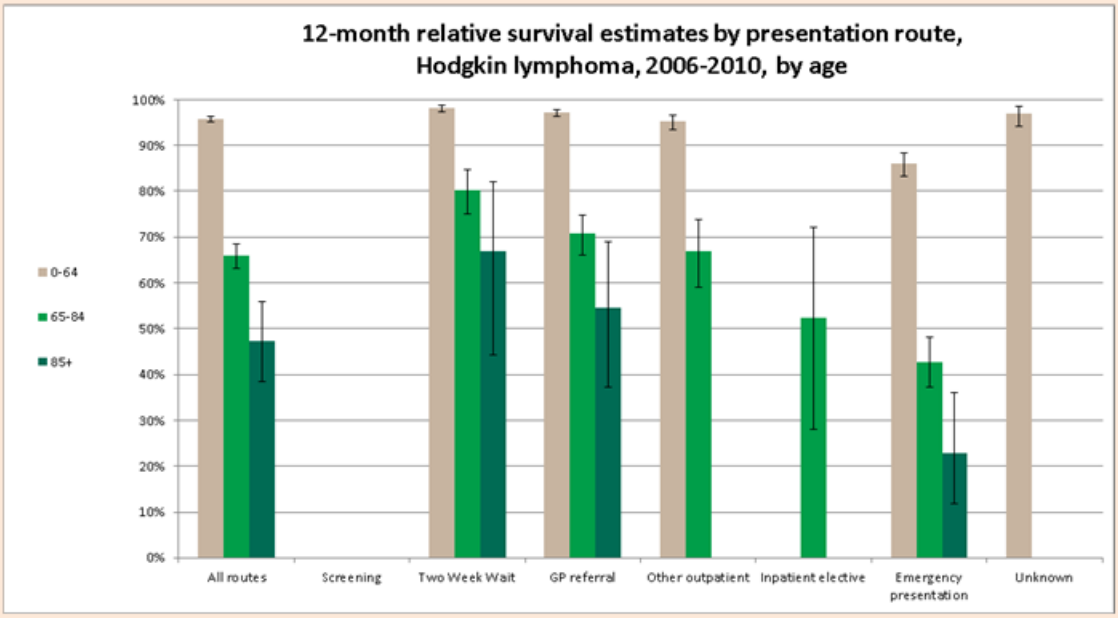
Figure 60 shows one-year relative survival estimates for Hodgkin lymphoma by age and route to diagnosis. It shows that one-year relative survival was significantly worse in the emergency presentation group for all age groups when compared to all routes combined.

Figure 60: One-year relative survival estimates for Hodgkin lymphoma by age and route to diagnosis



B.11 Non Hodgkin Lymphoma (NHL)

Non-Hodgkin lymphoma (NHL) is not one but several diseases. For the majority of this report they have been analysed together, but each of the different NHLs has different behaviour, prognosis and treatment, and observed changes in incidence or outcome are unlikely to apply to all forms of NHL.

As discussed in the first section of this report, the quality of coding of the large and varied group of conditions grouped together as NHL, is not currently sufficient to allow disaggregation to the component diseases. However, for some of these analyse we can use HMRN data to give an indication of the breakdown of these individual diseases.

B.11.1 Incidence

The incidence of NHL increases with age, with most cases occurring in the elderly, incidence rates are higher in men at all ages (Figure 61).

Age-standardised incidence rates rose over the period reported in men and women (Table 30). Registration rates for NHL have been rising since the 1970's; it is not clear exactly what the determinants of this apparent increase in incidence are. But it is important to recognise that improvements in the ascertainment of these cancers, with changing thresholds for diagnosis and greater access to diagnostic testing particularly in the elderly, is likely to contribute at least in part to this trend.

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Figure 61: Age-specific incidence rates by age group for Non-Hodgkin lymphoma in males and females between 2006-2008 in England

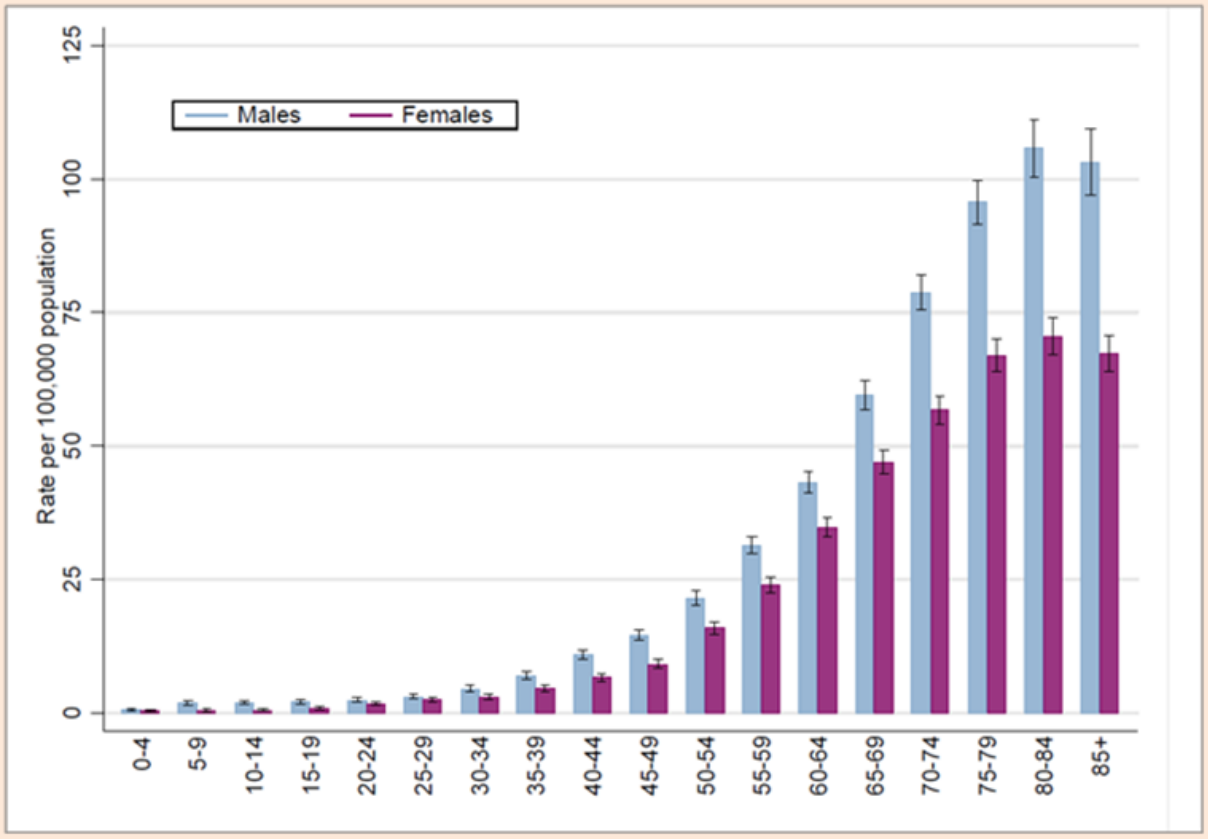

Table 30: Incidence - Non Hodgkin lymphoma by sex, England 2001-2003 to 2008-2010. Three year averages

	Male Incidence				Female incidence			
Year	Cases	ASR	95% CI		Cases	ASR	95% CI	
2001-2003	4361	15.9	15.6	16.1	3874	11.4	11.2	11.6
2002-2004	4447	15.9	15.7	16.2	3950	11.6	11.3	11.8
2003-2005	4597	16.3	16.0	16.5	4034	11.7	11.5	12.0
2004-2006	4772	16.7	16.4	16.9	4105	11.9	11.7	12.1
2005-2007	4936	17.0	16.7	17.3	4184	12.0	11.8	12.3
2006-2008	5132	17.4	17.1	17.7	4379	12.4	12.2	12.6
2007-2009	5343	17.7	17.5	18.0	4549	12.7	12.5	12.9
2008-2010	5499	17.9	17.7	18.2	4680	12.9	12.7	13.2

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B.11.2 HMRN incidence for NHL

Table 31 shows the expected UK incidence of the individual diseases which make up NHL, and the age-standardised rates for males, females and persons. It shows that two thirds of all NHL consists of diffuse large B-cell lymphoma (48.5%) and follicular lymphoma (18.1%). HMRN estimate just over 10,000 cases of NHL per year in the UK.

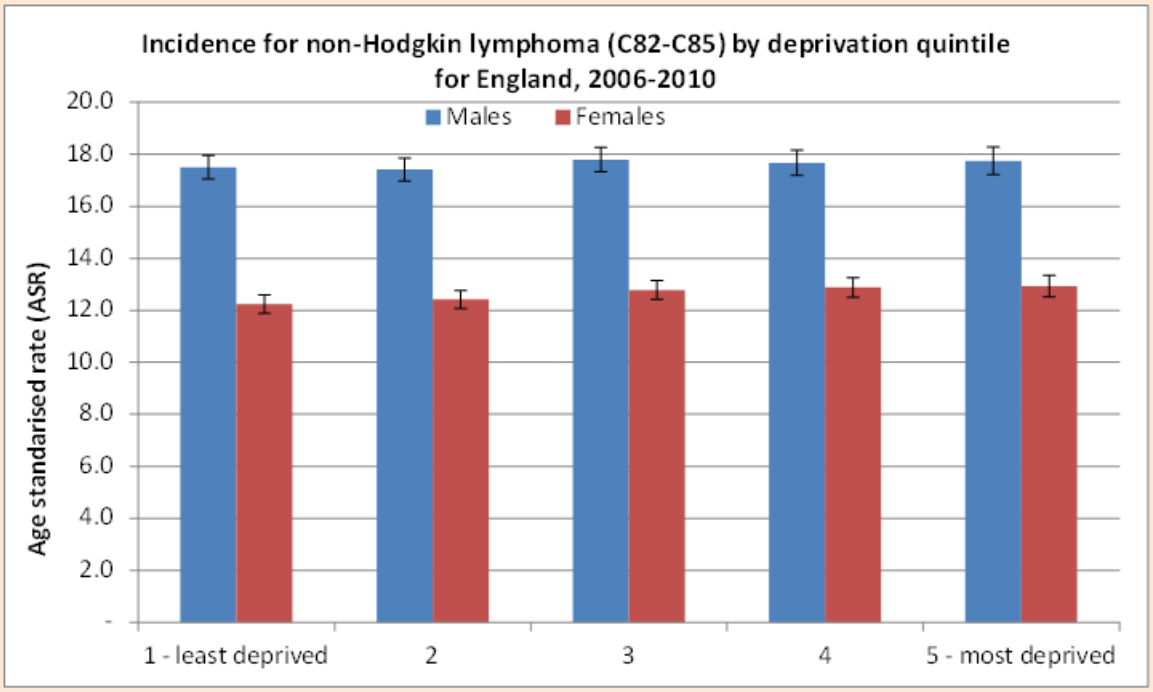
Table 31: Expected incidence of Non-Hodgkin lymphoma (HMRN data)

	Expected UK cases per year	ASR per 100,000	ASR per 100,000	ASR per 100,000
		Total	Male	Female
Non-Hodgkin Lymphoma (all)	**10280**	**14.2**	**16.8**	**12.1**
Diffuse large B-cell lymphoma	4990	6.8	8	5.8
Follicular lymphoma	1860	2.8	2.7	2.8
Marginal zone lymphoma	2050	2.7	3.4	2.1
T-Cell lymphoma	650	0.9	1.2	0.7
Mantle cell lymphoma	510	0.7	1	0.4
Burkitt lymphoma	210	0.4	0.6	0.2

Source: Haematological Malignancies Research Network (HMRN)

Figure 62 shows incidence of NHL by quintile of deprivation in English national data from NCRS, there is no significant difference in incidence of NHL by quintile of deprivation for either males or females.

Figure 62: Incidence of NHL by quintile of deprivation



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B.11.3 Mortality

Table 32 shows trends in age-standardised mortality from NHL; age-standardised mortality fell significantly between 2001-03 and 2008-10 for both males and females.

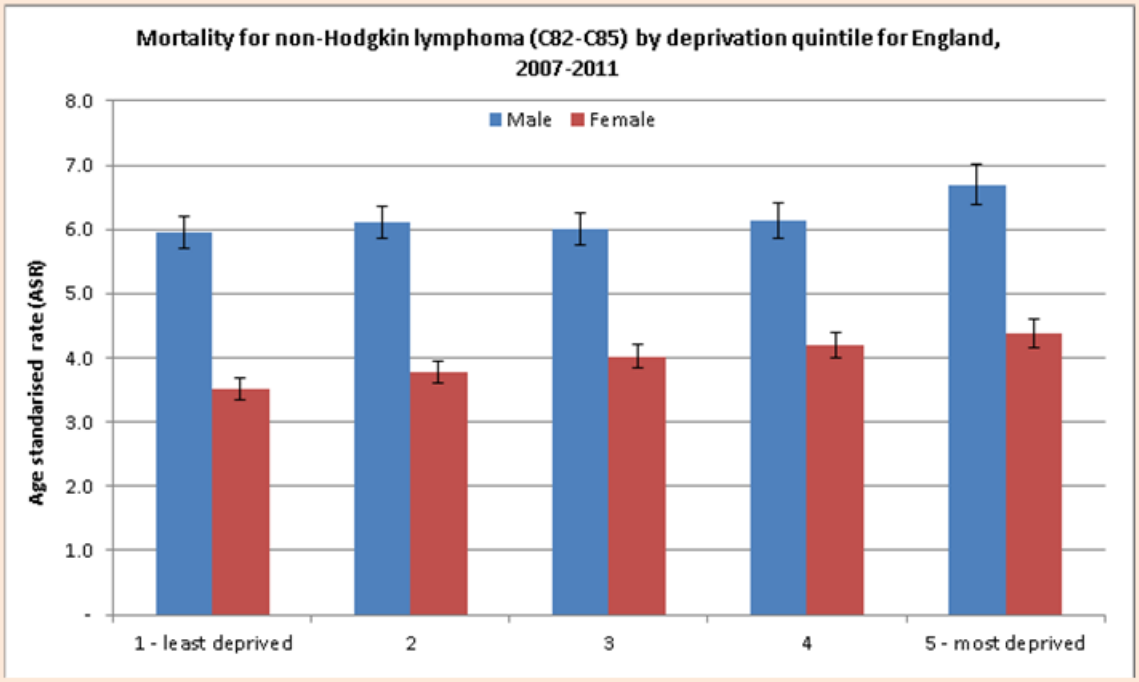
Table 32: Mortality – Non Hodgkin lymphoma by sex, England 2001-2003 to 2008-2010. Three year averages.

	Male mortality				Female mortality			
Year	Deaths	ASR	95% CI		Deaths	ASR	95% CI	
2001-2003	2073	7.3	7.1	7.4	1818	4.7	4.5	4.8
2002-2004	2056	7.1	6.9	7.3	1796	4.5	4.4	4.6
2003-2005	2011	6.8	6.6	7.0	1767	4.4	4.3	4.5

	Male mortality				Female mortality			
2004-2006	1983	6.6	6.4	6.7	1748	4.3	4.2	4.4
2005-2007	2010	6.5	6.3	6.7	1742	4.2	4.1	4.3
2006-2008	2012	6.3	6.2	6.5	1724	4.0	3.9	4.2
2007-2009	2030	6.2	6.1	6.4	1713	4.0	3.9	4.1
2008-2010	2024	6.1	5.9	6.2	1706	3.9	3.8	4.0

Figure 63 presents age-standardised mortality rates for NHL by quintile of deprivation, whilst there is no relationship between deprivation and incidence of NHL, the mortality rate from NHL is significantly higher in the most deprived quintile compared to the least deprived for both males and females (6.7 per 100,000 in the most deprived quintile compared to 6.0 in the least for males, and 4.4 per 100,000 in the most deprived quintile compared to 3.5 in the least for females).

Figure 63: Age-standardised mortality rates for NHL by quintile of deprivation



B.11.4 Survival

Table 33 shows five-year relative survival for NHL as a whole, and the various conditions that are grouped together as NHL from the Haematological Malignancies Research Network (HMRN).

Table 33: 5-year relative survival (%) (HMRN data)

	5 Year Relative Survival (%)
Non-Hodgkin Lymphoma (all)	67.3
Marginal zone lymphoma	78
Follicular lymphoma	87.4
Mantle cell lymphoma	36.2
Diffuse large B-cell lymphoma	59.9
Burkitt lymphoma	57.1
T-Cell lymphoma	49.4

Source: Haematological Malignancies Research Network (HMRN)

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Figures 64 and 65 show trends in relative survival for all NHL combined in English national data from NCRS. There was an increase in relative survival at 5 years among males (all ages) from 54% (95% CI: 53-55%) for individuals diagnosed in 2000-03 to 65% (95% CI: 64-66%) for those diagnosed in 2008-10. Among female patients (all ages) with NHL there was an increase in relative survival at 5 years from 56% (95% CI: 55-56%) for individuals diagnosed in 2000-03 to 67% (95% CI: 66-68%) for those diagnosed in 2008-10.

Figure 64: Relative 1 and 5 year survival - Non Hodgkin lymphoma, by sex , diagnosed in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010 in England

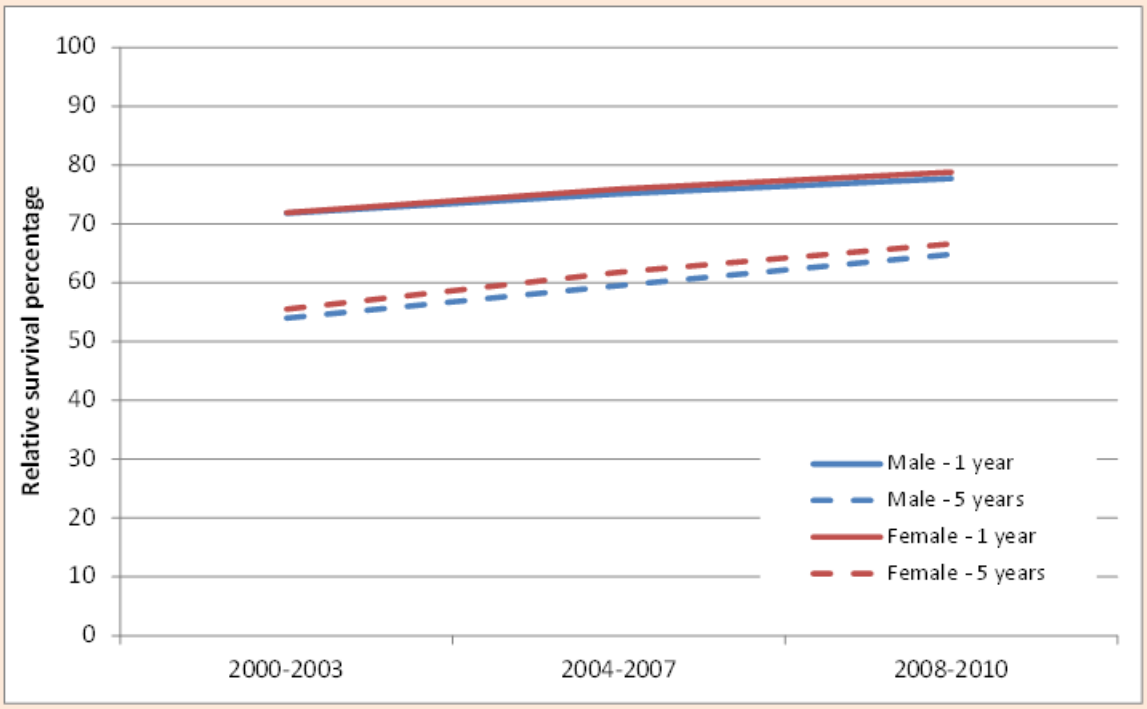

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Figure 65: Trends in relative survival rates for Non-Hodgkin lymphoma diagnosed in persons in the periods 2000-2003, 2004-2007 and 2008-2010 followed up to end of 2010, by age group in England

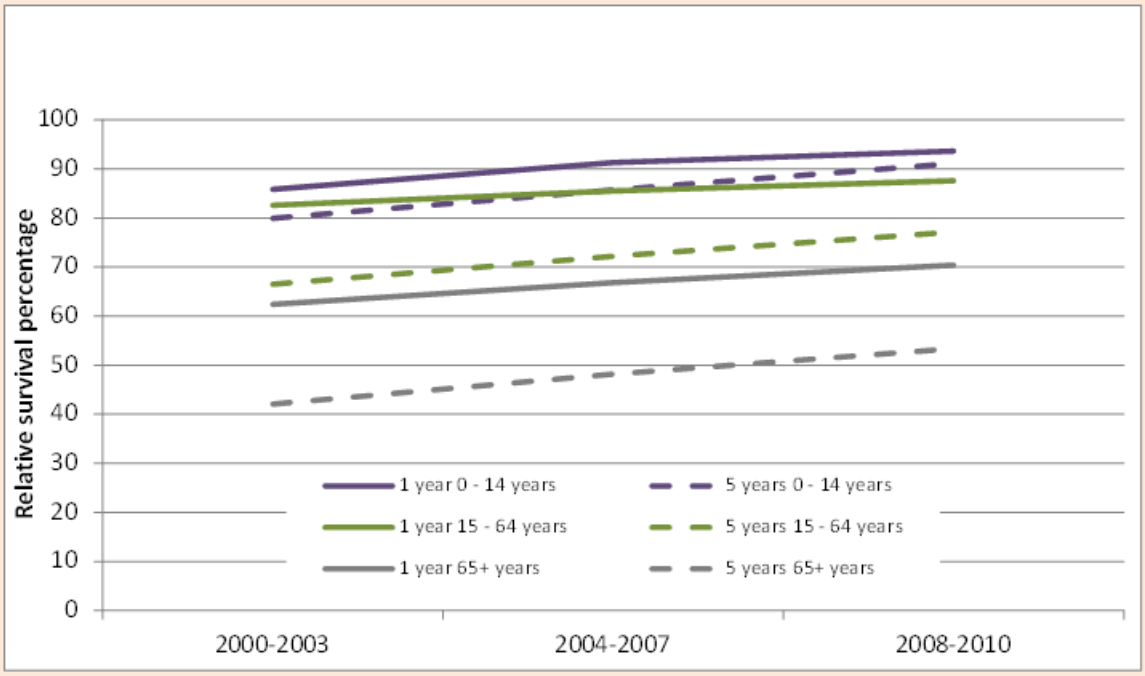

Figure 66 shows one- and five-year relative survival of patients with NHL by quintile of deprivation, relative survival is significantly lower in the most deprived quintile compared to the least deprived quintile, at both one (72.4% compared to 78.9%) and five years (54.3% compared to 61.3%).

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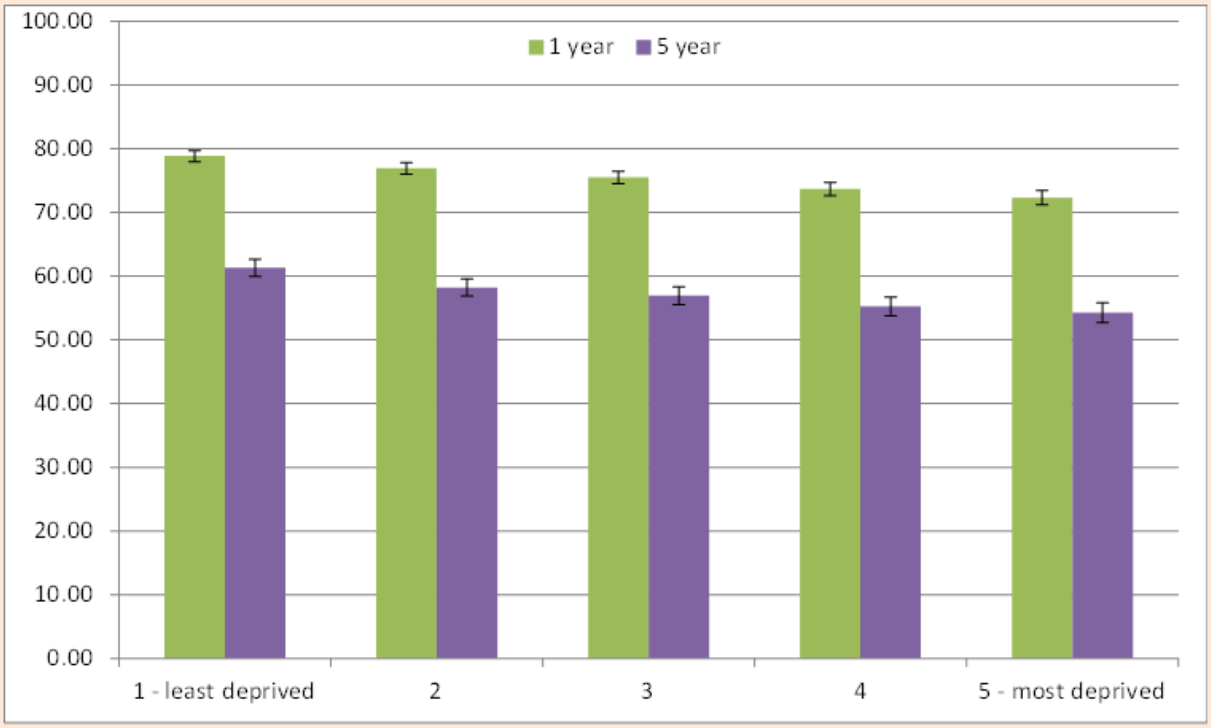
Figure 66: 1 and 5-year survival of patients (persons) diagnosed with Non-Hodgkin lymphoma in England, 2000-2007 by deprivation (IMD2004)



B.11.5 Routes to diagnosis

Figure 67 shows a breakdown of referrals for NHL by presentation route. It shows that the highest proportion of referrals came to diagnosis via a GP referral (34.2%), followed by emergency admissions (26.9%). The proportion of emergency admissions for NHL is significantly higher than all malignancies combined (22.9%).

Figure 67: Referrals for NHL by presentation route

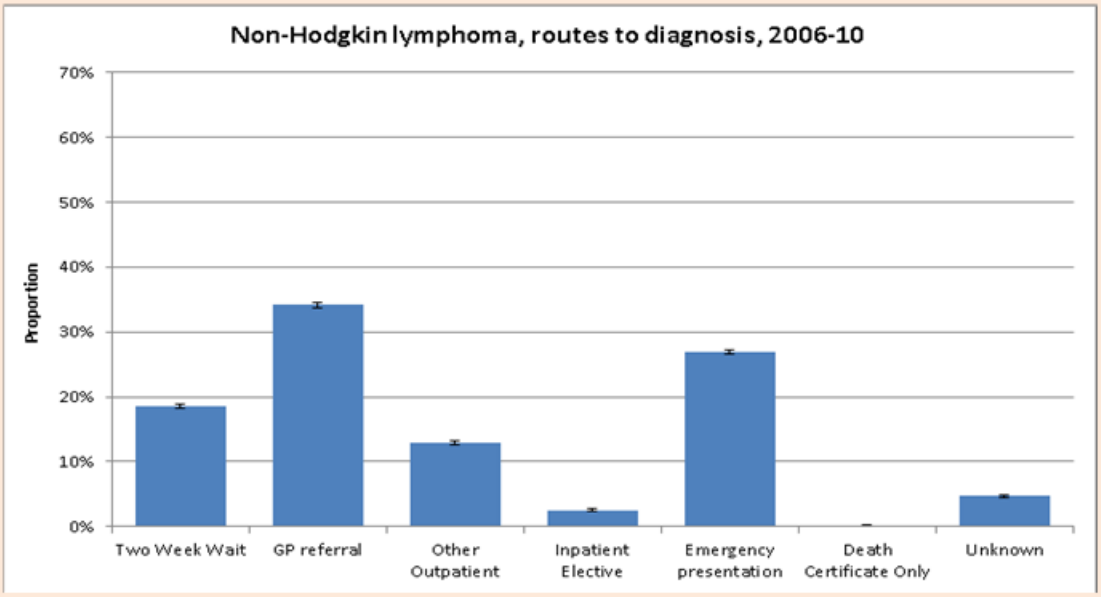


Figure 68 shows one-, two- and three-year relative survival estimates for NHL by presentation route. In common with other haematological malignancies emergency presentations had significantly poorer relative survival at all time intervals, compared to all other presentation routes.

Figure 68: One-, two- and three-year relative survival estimates for NHL by presentation route

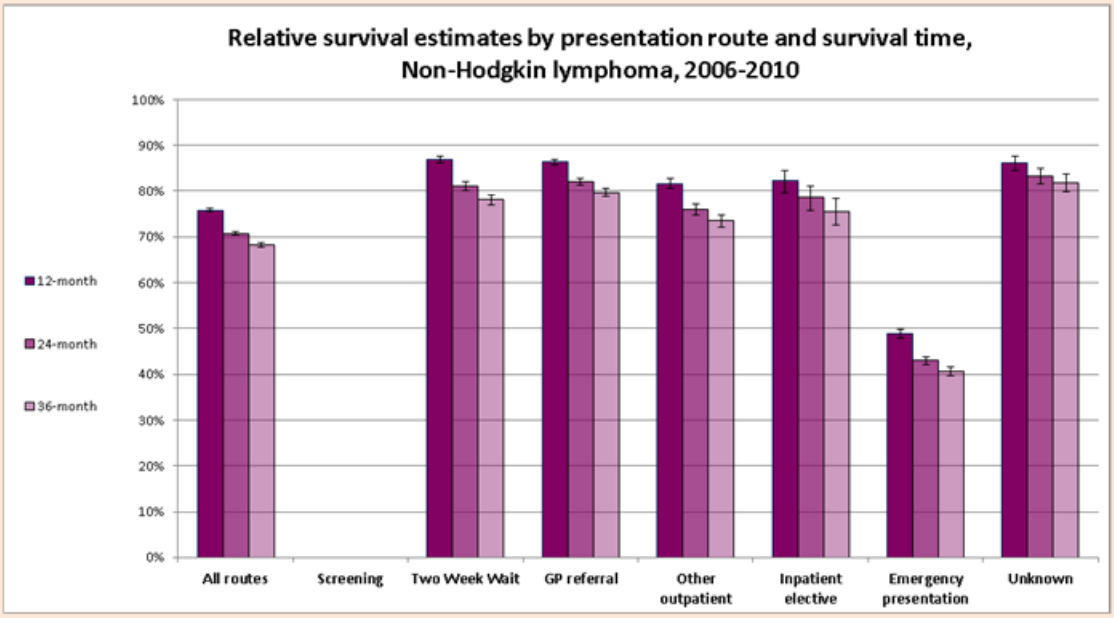


Figure 69 shows one-year relative survival estimates for NHL by age and presentation route. Tere is significantly lower one-year relative survival amongst patients presenting as an emergency for all age groups when compared to all routes as a whole. The effect of the

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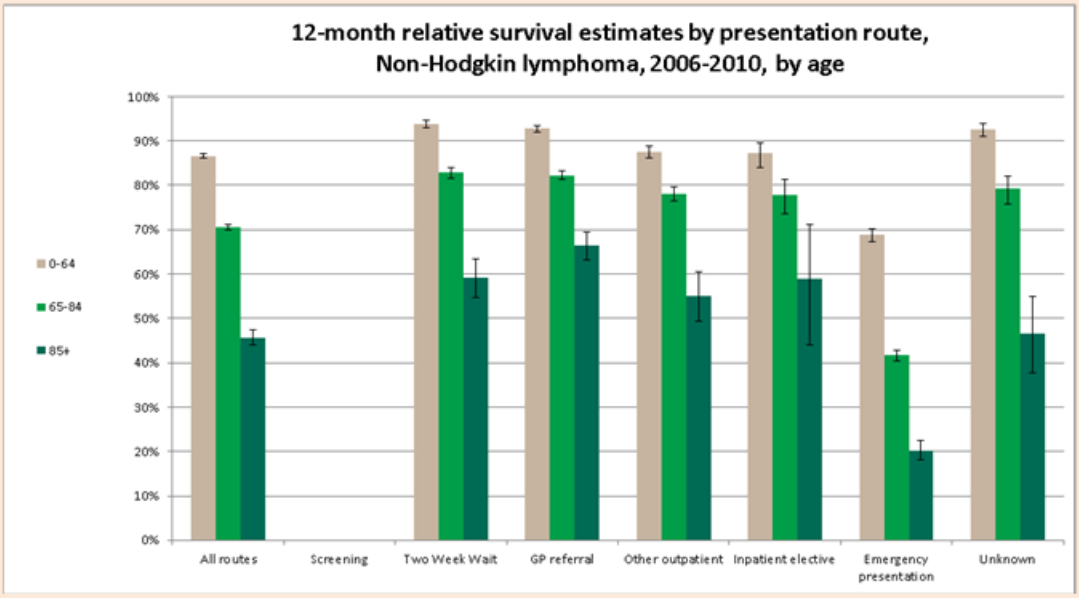
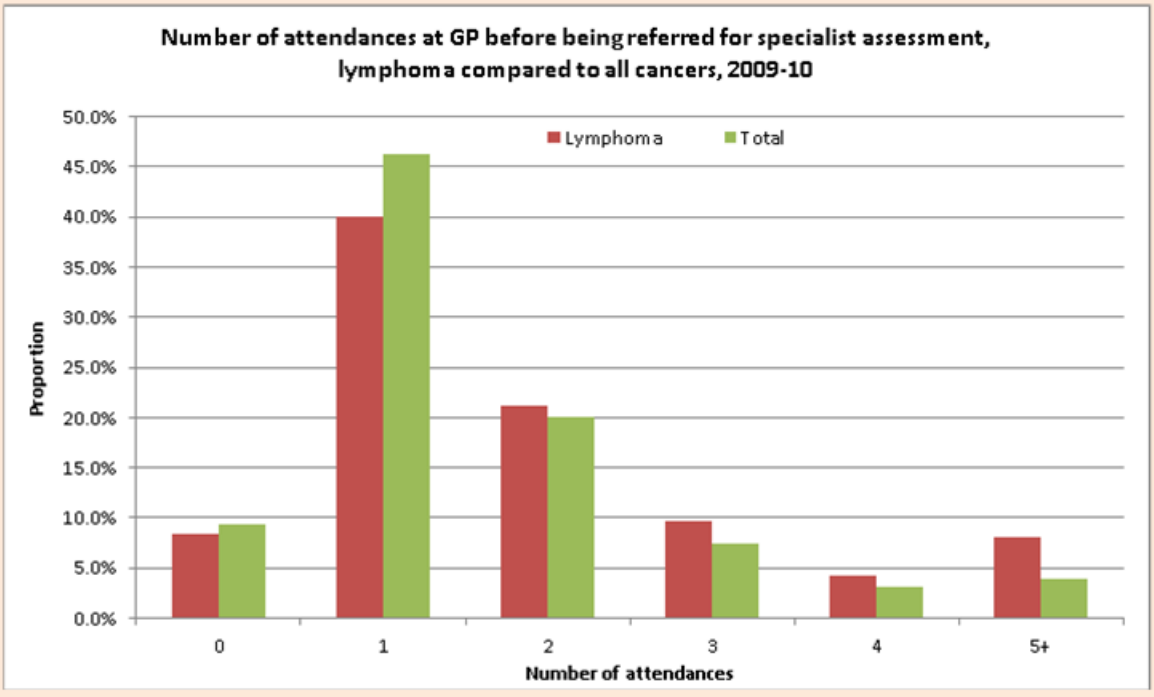
emergency presentation on relative survival seems particularly acute in the older age group, with one-year relative survival in the 85+ emergency presentations group (20%), being less than half that for 85+ patients in all groups combined (46%).

Figure 69: One-year relative survival estimates for NHL by age and presentation route



As part of the National Audit of Cancer Diagnosis in Primary Care (Royal College of General Practitioners, 2011), participating practices were asked to count all consultations relating to the presenting problem that was associated with the patient's cancer. The majority of patients included in the audit had consulted their GP once or twice (66%), and only 15% had consulted their GP three or more times. For lymphoma patients 22% of patients had consulted their GP three times or more, and 8% more than five times (Figure 70).

Figure 70: Number of attendances at GP before being referred for specialist assessment



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References

L Elliss-Brookes, S McPhail, A Ives, M Greenslade, J Shelton, S Hiom and M Richards (2012) Routes to diagnosis for cancer – determining the patient journey using multiple routine data sets. British Journal of Cancer 107: 1220-1226. Doi:10.1038/bjc.2012.408 www.bjcancer.com

National Institute for Clinical Excellence: Guidance on Cancer Services – Improving Outcomes in Haematological Cancers – The Manual 2003

NCIN (2010) Blood Cancers Data Quality Report National Cancer Data Repository (NCDR)

NCIN (2013) Registration for Blood Cancers in England: comparison of routine data with a specialist population-based register - http://www.ncin.org.uk/view?rid=2166

Royal College of General Practitioners (2011) National Audit of cancer diagnosis in primary care

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Appendix C: Guideline Scope

C.1 Topic

This guideline will update the NICE cancer service guidance on 'Improving Outcomes in Haematological Cancers' as set out in the update decision.

Who the guideline is for

- Healthcare professionals in secondary care.
- Managed clinical networks.
- Commissioners of haematological cancer diagnostic and treatment services (including Clinical Commissioning Groups and NHS England Specialised Commissioning).

It may also be relevant for:

- Healthcare professionals in primary care.
- People using haematological cancer services, their family members and carers, and the public.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive.

C.1.1 Equality considerations

NICE has carried out an equality impact assessment during scoping. The assessment:

- lists equality issues identified, and how they have been addressed
- explains why any groups are excluded from the scope, if this was done.

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C.2 What the guideline is about

C.2.1 Who is the focus?

Group that will be covered

- All healthcare professionals that provide diagnostic and treatment services to the patient groups below, including clinical and scientific staff in secondary care
- Adults (over 24 years), young people (16 to 24 years) and children (under 16 years) who are referred to secondary care with suspected haematological cancer.
- The staffing and facilities (levels of care) needed to treat haematological cancers in adults and young people.

No specific subgroups of people have been identified as needing specific consideration.

In this guideline, haematological cancer also includes myelodysplastic syndromes, myeloproliferative neoplasms and histocytic and dendritic cell neoplasms.

Borderline conditions such as aplastic anaemia and other non-malignant bone marrow failure syndromes (which overlap with hypoplastic myelodysplastic syndrome), monoclonal gammopathy of uncertain significance (MGUS) or monoclonal B-cell lymphocytosis will only be considered in the diagnostic pathway.

Groups that will not be covered

- The staffing and facilities (levels of care) needed to treat haematological cancers in children (under 16 years).

C.2.2 Settings

Settings that will be covered

- All secondary and tertiary care services that provide NHS care to people with suspected or diagnosed haematological cancers.

C.2.3 Activities, services or aspects of care

Key areas that will be covered

Areas from the published guideline that will be updated

- Chapter 3: Diagnosis and evaluation
- Chapter 4: Organisation of specialist services
- Chapter 5: Treatment (excluding high-dose therapy) – Facilities necessary for provision of intensive chemotherapy

Areas from the published guideline that will not be updated

- Chapter 1: Access to care
- Chapter 2: Patient-centred care
- Chapter 7: Continuing management
- Chapter 8: Palliative care
- Chapter 9: Clinical trials and use of protocols

Recommendations in areas that are not being updated may be edited to ensure that they meet current editorial standards, and reflect the current policy and practice context.

Areas from the published guideline that will be removed

- Chapter 5:Treatment (excluding high-dose therapy) – Treatment for specific forms of haematological cancer and Management of complications of chemotherapy
- Chapter 6: High-dose therapy

C.2.4 Economic aspects

We will take economic aspects into account when making recommendations. We will develop an economic plan that states for each review question (or key area in the scope) whether economic considerations are relevant, and if so, whether this is an area that should be prioritised for economic modelling and analysis. We will review the economic evidence and carry out economic analyses, using an NHS and PSS perspective, as appropriate.

C.2.5 Key issues and questions

While writing this scope, we have identified the following key issues, and review questions related to them:

Key Issues

1. Providing a diagnostic service for diagnosing and managing haematological cancers for adults, young people and children:

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- Should centralised, integrated diagnostic reporting via Specialist Integrated Haematological Malignancy Diagnostic Services [SIHMDS] be the standard of care for diagnosing haematological cancers in all age groups?
- What is the most effective way of providing an integrated diagnostic service (for example, co-located laboratory facilities that solely provide haematological cancer diagnosis or networked geographically separate facilities that may also provide other services)?

2. The staffing and facilities (levels of care) needed to treat haematological cancers and support adults and young people who are having intensive non-transplant chemotherapy.

- How should level of care be defined and categorised for people with haematological cancers who are having intensive (non-transplant) chemotherapy, considering:
  - diagnosis
  - comorbidities
  - medicine regimens
  - the management of medicine administration and toxicities?
- What support facilities are needed at the different levels of care for people with haematological cancers who are having intensive (non-transplant) chemotherapy?

Main outcomes

The main outcomes that will be considered when searching for and assessing the evidence are:

- Mortality
- Treatment-related morbidity and mortality
- Reliability, error rates and adverse events
- Time to definitive diagnosis and treatment
- Diagnostic accuracy
- Patient and staff satisfaction
- Health-related quality of life
- Resource use and costs

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C.3 Links with other NICE guidance and NICE pathways

C.3.1 NICE guidance

C.3.1.1 NICE guidance that will be updated by this guideline

Improving Outcomes in Haematological Cancers (2003) NICE cancer service guidance. Recommendations in sections 3, 4 and 5.

C.3.1.2 NICE guidance about the experience of people using NHS services

NICE has produced the following guidance on the experience of people using the NHS. This guideline will not include additional recommendations on these topics unless there are specific issues related to haematological cancers:

- Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes (2015) NICE guidelines [NG5]
- Patient experience in adult NHS services (2012) NICE guideline CG138
- Service user experience in adult mental health (2011) NICE guideline CG136
- Medicines adherence (2009) NICE guideline CG76

- Improving outcomes in children and young people with cancer (2005) NICE guideline CSGCYP

C.3.1.3 NICE guidance in development that is closely related to this guideline

NICE is currently developing the following guidance that is closely related to this guideline:

- Non-Hodgkin's lymphoma. NICE guideline. Publication expected July 2016.
- Myeloma. NICE guideline. Publication expected January 2016.
- Brentuximab vedotin for treating CD30-positive Hodgkin's lymphoma after autologous stem cell transplant NICE technology appraisal. Publication expected July 2016.
- Lenalidomide for the treatment of newly diagnosed multiple myeloma. NICE technology appraisal. Publication expected April 2016.
- Ibrutinib for treating relapsed or refractory mantle cell lymphoma. NICE technology appraisal. Publication expected February 2016.
- Bortezomib for previously untreated mantle cell lymphoma. NICE technology appraisal. Publication expected February 2016
- Panobinostat for treating multiple myeloma in people who have received at least 1 prior therapy. NICE technology appraisal. Publication expected January 2016.
- Idelalisib for relapsed chronic lymphocytic leukaemia. NICE technology appraisal. Publication expected October 2015.
- Ofatumumab for the maintenance treatment of relapsed chronic lymphocytic leukaemia. NICE technology appraisal. Publication expected September 2015.
- Suspected cancer. NICE guideline. Publication expected May 2015.
- Obinutuzumab in combination with chlorambucil for previously untreated chronic lymphocytic leukaemia. NICE technology appraisal. Publication expected May 2015.
- Ofatumumab in combination with chlorambucil or bendamustine for previously untreated chronic lymphocytic leukaemia. NICE technology appraisal. Publication expected May 2015.
- Bendamustine in combination with rituximab for the first-line treatment of mantle cell lymphoma. NICE technology appraisal. Publication date to be confirmed.
- Ibrutinib for treating relapsed or refractory chronic lymphocytic leukaemia and small lymphocytic leukaemia. NICE technology appraisal. Publication date to be confirmed.
- Bortezomib for the treatment of relapsed or refractory follicular non-Hodgkin's lymphoma. NICE technology appraisal. Publication date to be confirmed.
- Bendamustine in combination with rituximab for the first-line treatment of mantle cell lymphoma. NICE technology appraisal. Publication date to be confirmed.
- Bendamustine in combination with rituximab for the first-line treatment of indolent non-Hodgkin's lymphoma. NICE technology appraisal. Publication date to be confirmed.
- Pralatrexate for the treatment of relapsed or refractory peripheral T-cell lymphoma. NICE technology appraisal. Publication date to be confirmed.
- Lenalidomide as maintenance treatment of multiple myeloma after autologous stem cell transplantation. NICE technology appraisal. Publication date to be confirmed.
- Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy with bortezomib (partial review of TA171). NICE technology appraisal. Publication date to be confirmed
- Lenalidomide for treating relapsed or refractory mantle cell lymphoma. NICE technology appraisal. Publication date to be confirmed.
- Vorinostat in combination with bortezomib for the treatment of multiple myeloma in people who have received at least one prior therapy. NICE technology appraisal. Publication date to be confirmed.

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- Romidepsin for the treatment of relapsed or refractory peripheral T-cell lymphoma. NICE technology appraisal. Publication date to be confirmed.

C.3.1.4 NICE Pathways

When this guideline is published, the recommendations will be added to NICE Pathways. NICE Pathways bring together all related NICE guidance and associated products on a topic in an interactive topic-based flow chart.

The recommendations will be added to a new 'haematological cancer services' path in the blood and bone marrow cancers pathway, replacing the current 'service organisation' node. A draft path outline on haematological cancer services, based on the draft scope, is included below. It will be adapted and more detail added as the recommendations are written during guideline development.

The guideline will overlap with the NICE guidelines on myeloma and non-Hodgkin's lymphoma, which will be published in January and July 2016 respectively. The NICE Pathway will integrate the recommendations from all 3 guidelines, showing clearly how they fit together. Other relevant NICE guidance is already in the blood and bone marrow cancers pathway, including:

- Improving supportive and palliative care for adults with cancer (2004) NICE cancer service guidance
- Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and bortezomib (2015) NICE technology appraisal guidance 338
- Idelalisib for treating follicular lymphoma that is refractory to 2 prior treatments (terminated appraisal) (2014) NICE technology appraisal guidance 328
- Lenalidomide for treating myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality (2014) NICE technology appraisal guidance 322
- Bortezomib for induction therapy in multiple myeloma before high-dose chemotherapy and autologous stem cell transplantation (2014) NICE technology appraisal guidance 311
- Pixantrone monotherapy for treating multiply relapsed or refractory aggressive non-Hodgkin's B cell lymphoma (2014) NICE technology appraisal guidance 306
- Bosutinib for previously treated chronic myeloid leukaemia (2013) NICE technology appraisal guidance 299
- Decitabine for the treatment of acute myeloid leukaemia (terminated appraisal) (2012) NICE technology appraisal guidance 270
- Denosumab for the prevention of skeletal-related events in adults with bone metastases from solid tumours (2012). NICE technology appraisal guidance 265
- Dasatinib, nilotinib and standard-dose imatinib for the first-line treatment of chronic myeloid leukaemia (part review of technology appraisal guidance 70) (2012) NICE technology appraisal guidance 251
- Rituximab for the first-line treatment of stage III-IV follicular lymphoma (2012) NICE technology appraisal guidance 243
- Dasatinib, high-dose imatinib and nilotinib for the treatment of imatinib-resistant chronic myeloid leukaemia (CML) (part review of NICE technology appraisal guidance 70), and dasatinib and nilotinib for people with CML for whom treatment with imatinib has failed because of intolerance (2012) NICE technology appraisal guidance 241
- Bortezomib and thalidomide for the first line treatment of multiple myeloma (2011) NICE technology appraisal guidance 228
- Rituximab for the first-line maintenance treatment of follicular non-Hodgkin's lymphoma (2011) NICE technology appraisal guidance 226

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- Azacitidine for the treatment of myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia (2011) NICE technology appraisal guidance 218
- Bendamustine for the first-line treatment of chronic lymphocytic leukaemia (2011) NICE technology appraisal guidance 216
- Temsirolimus for the treatment of relapsed or refractory mantle cell lymphoma (terminated appraisal) (2010) NICE technology appraisal guidance 207
- Bendamustine for the treatment of indolent (low grade) non-Hodgkin's lymphoma that is refractory to rituximab (2010) NICE technology appraisal guidance 206
- Ofatumumab for the treatment of chronic lymphocytic leukaemia refractory to fludarabine and alemtuzumab (2010) NICE technology appraisal guidance 202
- Rituximab for the treatment of relapsed or refractory chronic lymphocytic leukaemia (2010) NICE technology appraisal guidance 193
- Rituximab for the first-line treatment of chronic lymphocytic leukaemia (2009) NICE technology appraisal guidance 174
- Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy (2009) NICE technology appraisal guidance 171
- Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma: Review of technology appraisal guidance 37 (2008) NICE technology appraisal guidance 137
- Bortezomib monotherapy for relapsed multiple myeloma (2007) NICE technology appraisal guidance 129
- Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia (2007) NICE technology appraisal guidance 119
- Guidance on the use of imatinib for chronic myeloid leukaemia (2013) NICE technology appraisal guidance 70
- Rituximab for aggressive non-Hodgkin's lymphoma (2003) NICE technology appraisal guidance 65
- Guidance on the use of fludarabine for B-cell chronic lymphocytic leukaemia (2011) NICE technology appraisal guidance 29

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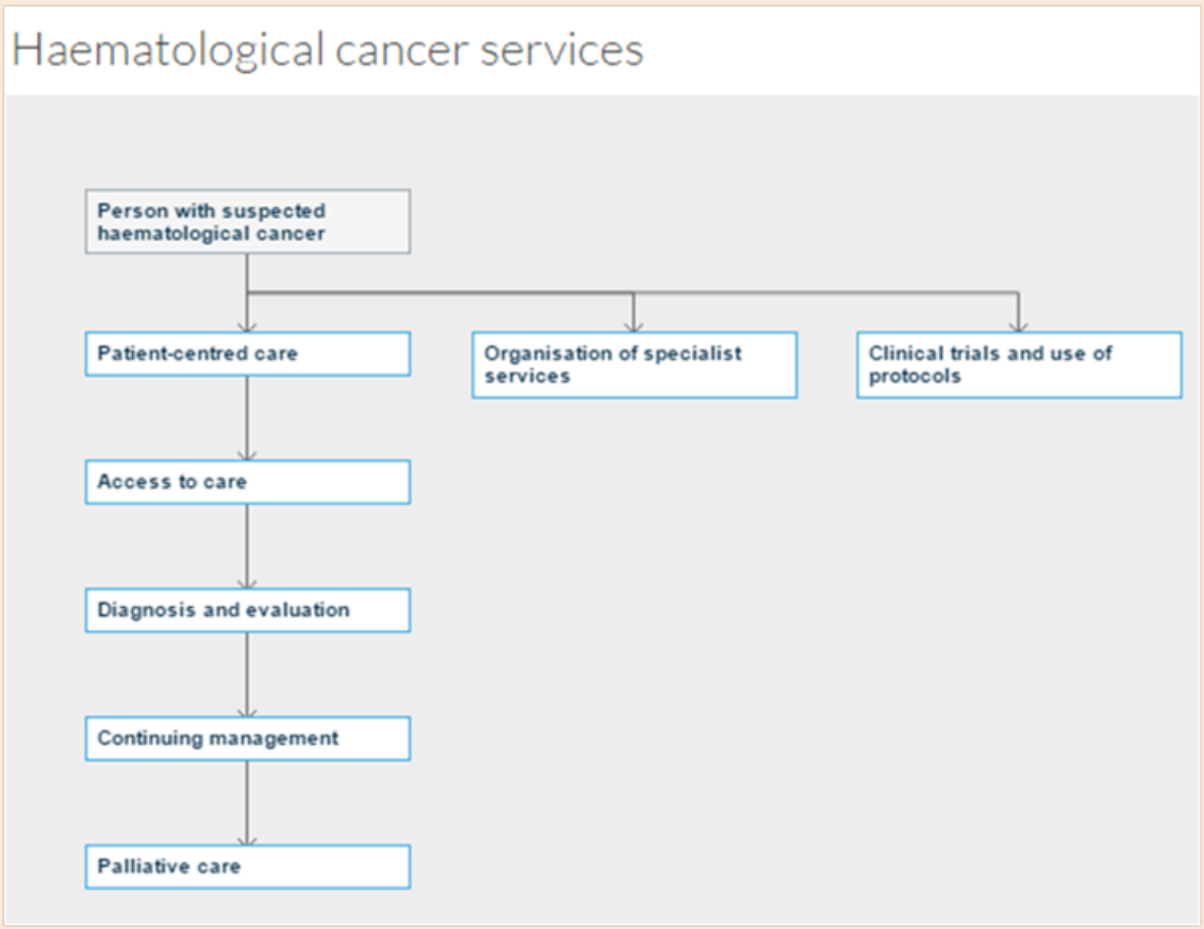

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C.4 Context

C.4.1 Key facts and figures

Haematological malignancies are a diverse group of cancers that affect the blood, bone marrow, and lymphatic systems. Some forms are highly aggressive, and others are so benign that they are often only discovered by chance. Symptoms may include:

- lumps caused by enlarged lymph nodes, which are characteristic of lymphomas
- bone fractures and kidney problems, which are characteristic of myeloma
- fatigue and vulnerability to infection and bleeding, which can be caused by most types of haematological cancer but are particularly severe in acute leukaemia.

The main categories of haematological cancer are lymphoma, myeloma, leukaemia, myelodysplastic syndromes and myeloproliferative neoplasms. These categories vary in prevalence, incidence and survival rates. In addition, there are subtypes of lymphoma and leukaemia, as well as rarer haematological cancers that have their own categories.

Haematological cancers accounted for 8.4% of all cancers (excluding non-melanoma skin cancer) diagnosed in England between 2001 and 2010 (National Cancer Intelligence Network). Based on data from the UK in 2011 (Cancer Research UK), there were approximately:

- 12,800 new cases of non-Hodgkin's lymphoma
- 8,600 new cases of leukaemia
- 4,800 new cases of myeloma
- 1,845 new cases of Hodgkin's lymphoma.

Non-Hodgkin's lymphoma is the sixth most common cancer in the UK and the most common type of haematological cancer, accounting for over 40% of all cases in both men and women (National Cancer Intelligence Network).

Myeloma is the seventeenth most common cancer in the UK and the second most commonly registered haematological cancer, accounting for 17% of all new haematological cancers annually (National Cancer Intelligence Network).

Hodgkin's lymphoma is an uncommon cancer in the UK and accounts for less than 1% of all cancer diagnoses.

Leukaemia accounts for 3% of all cancer diagnoses in the UK (Cancer Research UK). There are 4 main subtypes of leukaemia: acute myeloid leukaemia, acute lymphoblastic leukaemia, chronic lymphocytic leukaemia and chronic myeloid leukaemia.

There are also borderline conditions such as aplastic anaemia and other non-malignant bone marrow failure syndromes (which overlap with hypoplastic myelodysplastic syndrome), and suspected cutaneous lymphomas that need specialised facilities for diagnosis and treatment.

The age-standardised incidence of haematological cancers in the UK has risen from 2001–2010 in both men and women. This is partly because of improved diagnosis, particularly from 2008 onwards. Conversely, age-standardised mortality rates have fallen over this period because of improvements in management (National Cancer Intelligence Network).

The 5-year relative survival rate was 67.7% for all haematological cancers as a whole (Haematological Malignancy Research Network).

Different levels of service are needed to manage haematological cancers, depending on the particular cancer in question.

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The original 2003 guidance on improving outcomes in haematological cancers made recommendations on the structure of services. Since then there have been significant clinical, therapeutic and diagnostic developments, as well as a major reorganisation of the NHS in England. Cancer services have also learned from peer review and other NHS quality initiatives. Bodies such as the National Cancer Research Institute and National Cancer Survivorship Initiative have been created, and data collection through the National Cancer Intelligence Network has become routine. There have also been major developments in cancer services for teenagers and young adults, and in palliative care services. The FACT-JACIE accreditation system has become established for blood and marrow transplant services, and is now a policy requirement within the NHS England National Specialised Commissioning Clinical Reference Group for blood and marrow transplants. In addition, a number of relevant disease-specific guidelines and technology appraisals have been published or are in development by NICE.

The development of new diagnostic techniques has made it necessary to update the diagnostic and evaluation sections in the original guidance. In addition, changes in the levels of care provided to people with haematological cancers mean an update to the section on organisation of specialist services is needed.

C.4.2 Current practice

Specialist Integrated Haematological Malignancy Diagnostic Services (SIHMDS) were recommended in the original NICE guidance on improving outcomes in haematological cancers, and were specified in the Cancer Peer Review Measures for England. Because of slow implementation, additional guidance was issued by the Department of Health in 2012. These recommendations have still not been implemented fully.

Levels of hospital care for people with haematological cancers were specified in the original NICE guidance. Because of the increased complexity of care, the British Committee for Standards in Haematology published new recommendations for levels of care in 2010.

There has been progressive and variable adoption of SIHMDS, aimed at improving diagnostic accuracy and expertise. Integrated diagnostic reports are well established in some centres but not everywhere. The models of SIHMDS provision vary, with 2 broad types:

- co-located' models, in which haematological cancer diagnosis is provided in dedicated, purpose-built and localised laboratories.
- 'networked' models, in which established laboratories work on the same information network, but are geographically separate and not dedicated solely to haematological cancer diagnosis
- Both approaches offer potential advantages and disadvantages. Networked SIHMDS models use the experience of established laboratories, and also potentially avoid the capital, staffing and other developmental costs needed for a co-located service. However, individual laboratories may deliver other services outside of haematological diagnosis, and so may be less focussed on haemato-oncology.

Although there are common areas in the diagnosis of both adult and paediatric haematological cancers, there has been no directive for integrated diagnostics for children under 16, for whom considerations of accuracy, central review and integration are similar.

Although FACT-JACIE is now well established for high-dose therapy and blood and marrow transplantation, the provision of non-transplant intensive chemotherapy needs to be reviewed. In this guideline the definition of 'intensive chemotherapy' will be based on the anticipated level of neutropenia being less than or equal to 0.5x109/litre for more than 7 days, in addition to other potential organ toxicities, comorbidities and frailty. This update will therefore only consider the staffing and facilities (levels of care) needed to provide intensive (non-transplant) chemotherapy regimens for:

- acute myeloid leukaemia
- myelodysplastic syndrome and other myeloid cancers
- acute lymphoblastic leukaemia
- lymphoblastic lymphoma
- Burkitt lymphoma
- diffuse large-cell non-Hodgkin's lymphoma
- Hodgkin's lymphoma
- multiple myeloma and other lymphoproliferative disorders.

As in the original guidance, service delivery has a focus on inpatient facilities, but this update will also include ambulatory care.

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C.4.3 Policy, legislation, regulation and commissioning

C.4.3.1 Policy

Department of Health (2013) Helping more people survive cancer

Department of Health (2012) Commissioning cancer services

Department of Health (2011) The National cancer strategy

C.4.3.2 Legislation, regulation and guidance

The following guidance from professional bodies will be taken into account when developing this guideline:

British Committee for Standards in Haematology (2010) Facilities for the Treatment of Adults with Haematological Malignancies – 'Levels of Care'

Joint Accreditation Committee ISCT-EBMT (2015) International standards for cellular therapy product collection, processing and administration

World Health Organization (2008) Classification of Tumours of Haematopoietic and Lymphoid Tissues 4th Edition

C.4.3.3 Commissioning

Commissioning of cancer diagnostic services falls within the remit of the Clinical Commissioning Groups in England. Treatment of haematological cancers is commissioned by NHS England Specialised Commissioning.

C.5 Further information

This is the final scope, incorporating comments from registered stakeholders during consultation.

The guideline is expected to be published in May 2016.

You can follow progress of the guideline.

Our website has information about how NICE guidelines are developed.

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Appendix D: Abbreviations

ALL	Acute lymphoblastic leukaemia
AML	Acute myeloid leukaemia
APML	Acute promyelocytic leukaemia
BCSH	British Committee for Standardisation in Haematology
BMT	Blood and marrow transplantation
BSBMT	British Society for Bone Marrow Transplantation
CLL	Chronic lymphocytic leukaemia
CML	Chronic myeloid leukaemia
CMV	Cytomegalovirus
CNS	Clinical Nurse Specialist
CT	Computed tomography
DLBCL	Diffuse large B-cell lymphoma
FACT	Foundation for the Accreditation of Cellular Therapy
G-CSF	Granulocyte-colony-stimulating factor
GC	Guideline committee
HEPA	High efficiency particulate air
HSCT	Haematopoietic Stem Cell Transplantation
JACIE	Joint Accreditation Committee
MDT	Multi-disciplinary team
MDS	Myelodysplastic syndromes
MGUS	Monoclonal gammopathy of uncertain significance
MPN	Myeloproliferative neoplasms
NCRN	National Cancer Research Network
NHL	Non-Hodgkin lymphoma
PET	Positron emission tomography
PET-CT	Positron emission tomography-computed tomography
RT	Radiotherapy
SIHMDS	Specialist Integrated Haematological Malignancy Diagnostic Services
WHO	World Health Organisation

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Appendix E: Glossary

Acute leukaemia

Progressive, malignant disease of the blood-forming tissue in the bone marrow, usually characterised by the production of abnormal white blood cells, which may be present in the bone marrow and blood.

Acute lymphoblastic leukaemia (ALL)

A type of acute leukaemia in which the white blood cells produced in excess are immature lymphocytes (white blood cells formed from lymphoid stem cells).

Acute myeloid leukaemia (AML)

A type of acute leukaemia in which the white blood cells produced in excess are immature granulocytes or monocytes (types of white blood cells formed from myeloid stem cells).

Acute promyelocytic leukaemia (APML)

A distinct sub-type of AML where patients present with a higher frequency of life-threatening complications (typically bleeding, thrombosis and renal failure) and require specific chemotherapy treatment. Patients whose conditions are stabilised sufficient to achieve remission subsequently have a high rate of cure.

Allogeneic haematopoietic stem cell transplantation (AlloHSCT)

A complex procedure involving administration of high-dose cytotoxic therapy (chemotherapy with or without radiotherapy) followed by transplant of peripheral blood or bone marrow stem cells (or occasionally cord blood) from a sibling or unrelated donor, and usually followed by immunosuppressive drugs to prevent graft rejection and graft-versus-host disease.

Ambulatory care

A planned care system in which patients at risk of prolonged neutropenia are based at home or in other specified accommodation. There should be specific safeguards to minimise the risk from potentially life-threatening complications of chemotherapy.

Asymptomatic

Without obvious signs or symptoms of disease. Cancer may cause symptoms and warning signs, but, especially in its early stages, cancer may develop and grow without producing any symptoms.

Autologous haematopoietic stem cell transplantation (Auto HSCT)

A procedure involving administration of high-dose high-dose cytotoxic therapy (chemotherapy with or without radiotherapy) followed by transplant of peripheral blood or bone marrow stem cells previously harvested from the patient

Biopsy

Removal of a sample of tissue from the body to assist in diagnosis or inform the choice of treatment of a disease.

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Blood and marrow transplantation (BMT)

Another term for allogeneic and autologous HSCT. The term 'Bone Marrow Transplantation' is now obsolete as most transplants use haematopoietic stem cells collected from peripheral blood as opposed to bone marrow.

Chemotherapy

The use of medication (drugs) that is toxic to cancer cells, given with the aim of killing the cells or preventing or slowing their growth.

Chronic leukaemia

Generally a slowly progressing cancer of the blood, usually of gradual onset, where the white blood cells present in excess are more mature than those in acute leukaemia. In some types of chronic leukaemia the blood cells are not over-produced but fail to die when they should do.

Chronic lymphocytic leukaemia (CLL)

A type of chronic leukaemia in which the white blood cells present in excess are lymphocytes (white blood cells formed from lymphoid stem cells).

Chronic myeloid leukaemia (CML)

A type of chronic leukaemia in which the white blood cells present in excess are granulocytes (white blood cells formed from myeloid stem cells).

Computed tomography (CT)

Imaging technique in which the person lies on a table within an x-ray gantry. The images are acquired using a spiral (helical) path and banks of detectors, allowing presentation of the internal organs and blood vessels in different projections including 3-D views.

Co-located

Service models in which haematological cancer diagnosis is provided in dedicated, purpose-built and localised laboratories.

Consolidation chemotherapy

Chemotherapy treatment given when remission has been achieved, aimed at eliminating low levels of malignant cells.

Cytogenetics

A branch of genetics that is concerned with the study of the structure and function of the genetic material in a cell, especially the chromosomes. It includes routine analysis of chromosomes, as well as molecular cytogenetics such as fluorescent in situ hybridization (FISH) and other molecular techniques.

Flow cytometry (also known as immunophenotyping)

A technique for the detection of specific proteins expressed by cells using one or multiple monoclonal antibodies labelled with fluorescent tags. The labelled cells are processed in a flow cytometer, a laser-based instrument capable of analyzing thousands of cells per second. The whole procedure can be performed on cells from the fluid specimens in a matter of a few

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hours. The overall pattern of expression of proteins on tumour cells usually gives a diagnosis. This is a core technique in the investigation of suspected leukaemia and lymphoma and in follow up after treatment. It is usually performed on liquid specimens, such as blood or bone marrow and, less frequently, on cerebrospinal, pleural, pericardial or ascitic fluid. Specimens of lymph node and other solid tissues can also be broken down into a form that can be analysed in this way.

Fluorescence in situ hybridisation (FISH)

A molecular test carried out on biopsy or cytology samples to show whether extra or abnormal copies of specific genes or genetic material are present or absent.

Granulocyte Colony Stimulating Factor (GCSF)

A type of protein that stimulates the bone marrow to make white blood cells (granulocytes).

Haematological cancers

Cancers of the blood and blood-forming tissues.

Haematologist

A doctor who specialises in disorders of the blood and blood-forming tissues.

Haematology

A branch of medicine concerned with the study and treatment of disorders of the blood and blood-forming tissues.

Haemato-oncology

A branch of medicine concerned with the study and treatment of cancers of the blood and blood-forming tissues.

Haemato-oncologist

A doctor who specialises in treating blood, bone marrow and lymphatic cancers.

Haemato-pathologist

A doctor, usually a histopathologist but on occasions a haematologist with appropriate additional training, who specialises in the diagnosis of haemato-oncological disease.

Health economics

The study of the allocation of scarce resources among alternative health care treatments. Health economists are concerned with both increasing the average level of health in the population and improving the distribution of health.

High dose therapy

Previous term used interchangeably with Bone Marrow Transplantation. Now both terms have been replaced with either Haematopoietic Stem Cell Transplantation (HSCT) and Blood and Marrow Transplantation (BMT) in order to reflect current clinical and scientific practice.

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High grade lymphomas

Faster growing, clinically aggressive lymphomas.

Histopathologist

A doctor who specialises in the diagnosis of disease primarily through the microscopic examination of tissues

Hodgkin lymphoma

A type of cancer in which the cells of the lymph tissue are produced in excess and result in the progressive, painless enlargement of lymph nodes, the spleen and general lymph tissue. A particular abnormal cell, known as the Reed-Sternberg cell is found in Hodgkin lymphoma disease.

Indolent lymphomas

Lymphomas that grow and spread slowly (also called low grade lymphomas).

Induction chemotherapy

The first phase of chemotherapy treatment designed to induce remission.

Immunohistochemistry

The process of detecting antigens (e.g., proteins) in the cells of a tissue section, by using antibodies binding specifically to antigens in biological tissues.

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Immunophenotyping

A technique used to study the protein expressed by cells. It is usually done on liquid specimens and involves the labelling of white blood cells with antibodies directed against surface proteins on their membrane. The labelled cells are processed in a flow cytometry, a laser-based instrument capable of analyzing thousands of cells per second. The whole procedure can be performed on cells from the blood, bone marrow or spinal fluid in a matter of a few hours.

Integrated report

A single report summarising all elements of laboratory diagnosis for a specific patient episode i.e. based on available haematological cytology, histopathology, immunophenotyping by flow cytometry, cytogenetics, FISH and molecular genetics and in accordance with the current WHO diagnostic classification.

Integration

The process of producing an integrated report.

Lymphoma

Cancer of the lymphatic system. There are two main types of lymphoma - Hodgkin lymphoma and Non-Hodgkin lymphoma.

Monoclonal gammopathy of undetermined significance (MGUS)

A common plasma cell disorder characterised by a low level monoclonal protein (<30g/L), less than 10% bone marrow plasma cells and the absence of myeloma related organ disease.

Morphology

The shape, size and general appearance of cells under a microscope.

Monoclonal protein (paraprotein)

Monoclonal protein or paraprotein is a single immunoglobulin molecule produced in excess indicating a plasma cell disorder

Multi disciplinary team (MDT)

A team with members from different health care professions and specialties (e.g. urology, haematology, oncology, pathology, radiology, nursing). Cancer care in the NHS uses this system to ensure that all relevant health professionals are engaged to discuss the best possible care for that patient.

Myelodysplasia

Another term for Myelodysplastic Syndrome.

Myelodysplastic syndromes (MDS)

A group of diseases in which the bone marrow functions abnormally and fails to produce enough normal blood cells. It may progress to acute myeloid leukaemia. Sometimes referred to as myelodysplasia.

Myeloid leukaemia

A type of leukaemia in which the white blood cells produced in excess are those produced by myeloid stem cells. Also see acute myeloid leukaemia and chronic myeloid leukaemia.

Myeloproliferative neoplasms (MPN)

Disorders in which too many blood cells are made by the bone marrow with increased numbers of red cells, white cells or platelets in the blood. Main types are polycythemia vera, essential thrombocythaemia and primary myelofibrosis.

Networked

Service models in which established laboratories work on the same information network, but are geographically separate and not dedicated solely to haematological cancer diagnosis.

Neutropenia

An abnormally low number of neutrophils, the most important type of white blood cell to fight off bacterial infections.

Non-Hodgkin lymphoma (NHL)

Any cancer of lymphocytes other than Hodgkin lymphoma. There are two main groups – high grade which are aggressive and fast growing and low grade which are slow growing (also

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known as indolent lymphomas). High grade lymphomas include: diffuse large B-cell lymphoma (DLBCL), peripheral T-cell lymphoma, Burkitt lymphoma, and AIDS-related lymphoma. Low grade or indolent lymphomas include: follicular lymphomas, mantle cell lymphoma, lymphoplasmacytic lymphoma and marginal zone lymphomas. Extra-nodal lymphomas are those that develop outside lymph nodes such as those affecting the skin or intestine.

Positron emission tomography CT (PET-CT)

A medical imaging technique using a device which combines a (PET) scanner (which utilises a radioactive tracer to show functional activity) with an x-ray computed tomography (CT) scanner. Images acquired from both devices can be taken sequentially, in the same session, and combined into a single superposed image.

Rare

A disease or a cancer that affects fewer than 1 in 2000 people

Relapse

Where cancer starts to grow again after treatment.

Re-induction chemotherapy

The first phase of chemotherapy treatment in the treatment of relapsed disease aiming to induce remission again. Sometimes referred to as salvage chemotherapy.

Remission

A period when cancer has responded to treatment and there are no signs of cancer or cancer-related symptoms. In haematological cancers, there are specific criteria for remission depending on the condition, depending on blood and bone marrow and/or radiological assessments.

Specialist Centre

A healthcare facility which has been designated by an approved national process for the treatment of patients (in the present context) with cancer, leukaemia or lymphoma.

Symptoms

The feelings and problems experienced by a patient relating to their illness.

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Appendix F:People and organisations involved in the production of this guideline

F.1 Members of the Guideline Committee

GC Chair	
Dr Fergus Macbeth	Clinical adviser, Wales Cancer Trials Unit, Cardiff University
GC Lead Clinician	
Professor John Snowden	Consultant Haematologist and Director of Blood and Marrow Transplantation. Sheffield Teaching Hospitals NHS Foundation Trust
Group Members	
Dr Clare Rowntree	Consultant Haematologist, Cardiff and Vale University Health Board
Dr Christopher Dalley	Consultant Haematologist, Brighton and Sussex University Hospital Trust
Dr Deepak Mannari	Consultant Haematologist, Musgrove Park Hospital, Taunton
Dr Geoff Shenton	Consultant & Associate Clinical Lecturer in Paediatric and Adolescent Haematology & BMT, Great North Children's Hospital, Newcastle upon Tyne
Dr Elizabeth Soilleux	Consultant Haematopathologist, Oxford University Hospital NHS Trust and honorary senior clinical lecturer, Oxford University
Dr Andrew Jack	Consultant Haematopathologist, Leeds Cancer Centre
Mrs Sarah Steele	Senior Quality Improvement Lead, East of England Strategic Network
Dr Bhuey Sharma	Consultant Radiologist, The Royal Marsden Hospital NHS Foundation Trust, Department of Diagnostic Imaging, Surrey
Dr Christopher McNamara	Consultant Haematologist, The Royal Free London NHS Foundation Trust
Dr Mike Scott	Consultant Clinical Scientist and Clinical Lead, Cambridge University Hospital NHS Trust
Dr Nia Evans	Lead Haematology Pharmacist, Cardiff & Vale University Health Board
Ms Barbara von Barsewisch	Macmillan Lymphoma and CLL Clinical Nurse Specialist
Ms Marie Waller	Trainee Advanced Nurse Practitioner, Manchester Royal Infirmary
John Reeve	Patient and Carer Member
Alan Chant	Patient and Carer Member
Jonathan Pearce	Patient and Carer Member

F.2 Declarations of interest

Name	Interest declared	Type of interest	Decision taken
Fergus Macbeth	Chief investigator of a CRUK funded trial supported by Pfizer with free drug and unrestricted educational grant.	Non-personal financial non specific	Declare and participate in discussions on all topics as lung cancer is not being covered by the guideline.
Fergus Macbeth	Received reimbursement of travel and subsistence expenses for attending the World lung cancer	Personal financial non-specific	Declare and participate in discussions on all topics as lung cancer is not being covered by the

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Name	Interest declared	Type of interest	Decision taken
	conference.		guideline.
John Snowden	Received an honorarium from MSD for chairing a meeting on antifungal drugs.	Personal financial Specific	Declare and must withdraw from topics which include antifungal drugs as an intervention until October 2014
John Snowden	Received an honorarium from Celgene for chairing a meeting on myeloma drugs.	Personal financial Specific	Declare and participate in discussions on all topics as myeloma drugs are not being covered by the guideline.
John Snowden	Received an honorarium from MSD for attending an advisory board on Posoconazole	Personal financial Specific	Declare and participate in discussions on all topics as Posoconazole is not being covered by the guideline.
John Snowden	Received reimbursement of accommodation, travel, subsistence and registration fee from MSD, to attend the American Society for Hematology conference in New Orleans	Personal financial Non-specific	Declare and can participate in discussion of all topics as expenses not beyond reasonable amounts.
John Snowden	Co-applicant on a research grant from Pfizer to investigate characterisation of central brain processing of chemotherapy-induced peripheral neuropathy	Non-personal financial Specific	Declare and participate in discussions on all topics as characterisation of central brain processing of chemotherapy-induced peripheral neuropathy is not being covered by the guideline.
John Snowden	Local principal investigator for the Myeloma XI trial (Randomised comparisons in myeloma patients of all ages of thalidomide, lenalidomide and bortezomib combinations and maintenance lenalidomide). Funded by CTAAC	Non-personal financial Specific	Declare and participate in discussions on all topics as no Randomised comparisons in myeloma patients of all ages of thalidomide, lenalidomide and bortezomib combinations and maintenance lenalidomide is not being covered by the guideline.
John Snowden	Local principal investigator for the RIC UCBT trial (Transplantation of umbilical cord blood from unrelated donors in patients with haematological diseases using a reduced intensity conditioning regimen). Funded by The Sue Harris Bone Marrow Trust.	Non-personal financial Non-specific	Declare and participate in discussion of all topics as transplantation of umbilical cord blood is not being investigated by the guideline and has no supervisory responsibility on trials.

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Name	Interest declared	Type of interest	Decision taken
John Snowden	Local principal investigator for the MAC UCBT trial (Transplantation of umbilical cord blood from unrelated donors in patients with haematological diseases using a myeloablative conditioning regimen). Funded by The Sue Harris Bone Marrow Trust.	Non-personal financial Non-specific	Declare and participate in discussion of all topics as transplantation of umbilical cord blood is not being investigated by the guideline and has no supervisory responsibility on trials.
John Snowden	Local principal investigator for the LenaRIC trial (Phase II study of the adjuvant use of lenalidomide in patients undergoing reduced intensity conditioning allogeneic transplantation for multiple myeloma). Funded by CTAAC.	Non-personal financial Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
John Snowden	Local principal investigator for the ProT-4 trial (Phase II study to evaluate the efficacy of prophylactic transfer of CD4 lymphocytes after T-cell depleted reduced intensity HLA-identical sibling transplantation for haematological cancers). Funded by Leukaemia and Lymphoma Research.	Non-personal financial Non-specific	Declare and participate in discussion of all topics as transfer of lymphocytes after transplantation is not being investigated by the guideline and has no supervisory responsibility on trials.
John Snowden	Local principal investigator for the Myeloma IX trial (A randomised trial comparing second generation vs third generation bisphosphonates, induction chemotherapy regimens (CVAD vs CTD, and MP vs CTDa) and thalidomide maintenance vs no maintenance therapy). Funded by MRC	Non-personal financial Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials
John Snowden	Local principal investigator for the Myeloma X relapse (intensive) trial (to determine whether a high-dose procedure with autologous transplant is superior to low-dose consolidation therapy following re-induction chemotherapy in patients with relapsed myeloma). Funded by CRUK	Non-personal financial Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
John Snowden	Local principal investigator for the RICAZA trial (Phase II study of the tolerability of adjunctive azacitidine in patients undergoing reduced intensity allogeneic stem cell	Non-personal financial Non-specific	Declare and participate in discussion of all topics as transplantation for acute myeloid leukaemia is not being investigated by the

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Name	Interest declared	Type of interest	Decision taken
	transplantation for acute myeloid leukaemia). Funded by Celgene.		guideline and has no supervisory responsibility on trials.
John Snowden	Local principal investigator for the Living with advanced relapsed myeloma study (cross sectional observational study to identify preventable and manageable late effects). Funded by Myeloma UK.	Non-personal financial Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
John Snowden	Local principal investigator for a Phase 2, Multi-centre, Randomised, Open-Label, Parallel Group Study to Evaluate the Effect of VELCADE on Myeloma related Bone Disease. Funded by Janssen-Cilag Ltd.	Non-personal financial Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
John Snowden	Local principal investigator for the UK Haplo Trial (A UK multicentre phase II study of haploidentical stem cell transplantation in patients with haematological malignancies). Funded by Leukaemia Lymphoma Research.	Non-personal financial Non-specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
John Snowden	Local principal investigator for the UK Haplo Trial (A UK multicentre phase II study of haploidentical stem cell transplantation in patients with haematological malignancies). Funded by Leukaemia Lymphoma Research.	Non-personal financial Non-specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
John Snowden	Local principal investigator for the HLA Epitope trial (HLA epitope matched platelet transfusion in aplastic anaemia, MDS and AML patients) Funded by NHS Blood and Transplant (NHSBT)	Non-personal financial Non-specific	Declare and participate in discussions on all topics as aplastic anaemia, myelodysplastic syndrome and acute myeloid leukaemia are not being investigated by the guideline and no supervisory responsibility on trials.
John Snowden	Principal investigator of a charitable grant from Royal Hallamshire Hospital Leukaemia and Research Fund, for a bolt-on study to Myeloma X, relating to supportive care in myeloma.	Non-personal financial Specific	Declare and can participate in discussion of all topics as research not funded by the healthcare industry.
John Snowden	Co-investigator on the MUK5 trial (A phase II randomised	Non-personal financial	Declare and participate in discussions on all

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Name	Interest declared	Type of interest	Decision taken
	trial of carfilzomib, cyclophosphamide and dexamethasone (CCD) vs cyclophosphamide, velcade and dexamethasone (CVD) for first relapse or primary refractory multiple myeloma). Funded by Myeloma UK	Non-specific	topics as no supervisory responsibility on trials.
John Snowden	Co-investigator on the TEAMM trial (trial assessing the benefit of antibiotic prophylaxis with levofloxacin, and its effect on health care associated infections in patients with newly diagnosed symptomatic myeloma). Funded by NIHR Health Technology Assessment.	Non-personal financial Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
John Snowden	Co-investigator on the AML 17 trial (Working parties on leukaemia in adults and children trial in AML or high risk MDS 17). Funded by CRUK	Non-personal financial Non-specific	Declare and participate in discussions on all topics as leukaemia, AML and MDS are not being investigated by the guideline no supervisory responsibility on trial.
John Snowden	Co-investigator on the FiTT study (Investigating the effectiveness of co-morbidity assessment in male patients with myeloma and prostate cancer). Funded by Weston Park Hospital Cancer Charity and Sheffield Teaching Hospitals NHS Foundation trust.	Non-personal financial Non-specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
John Snowden	Co-investigator on the AML 15 trial (Working parties on leukaemia in adults and children AML trial 15). Funded by MRC.	Non-personal financial Non-specific	Declare and participate in discussions on all topics as leukaemia is not being investigated by the guideline no supervisory responsibility on trial.
John Snowden	Co-investigator on the AML 16 trial (A programme of development for older patients with AML and high risk MDS). Funded by CRUK	Non-personal financial Non-specific	Declare and participate in discussions on all topics as AML and MDS are not being investigated by the guideline no supervisory responsibility on trial.
John Snowden	Co-investigator on the MCL MiniAllo trial (Phase II study of low intensity allogeneic transplantation in Mantle Cell Lymphoma). Funded by CRUK, Genzyme Therapeutics, National	Non-personal financial Non-specific	Declare and participate in discussions on all topics as mantle cell lymphoma is not being investigated by the guideline no supervisory responsibility on trial.

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Name	Interest declared	Type of interest	Decision taken
	Institute for Health Research Cancer Network (NRCN).		
John Snowden	Co-investigator on the ORCHARRD trial (Ofatumumab rituximab chemoimmunotherapy ASCT relapsed refractory DLBCL). Funded by GlaxoSmithKline.	Non-personal financial Non-specific	Declare and participate in discussions on all topics as diffuse large B cell lymphoma is not being investigated by the guideline no supervisory responsibility on trial.
John Snowden	Co-investigator on the FIGARO trial (A randomised trial of the FLAMSA-BU conditioning regimen in patients with AML and MDS undergoing allogeneic stem cell transplantation). Funded by Leukaemia and Lymphoma Research.	Non-personal financial Non-specific	Declare and participate in discussions on all topics as AML and MDS are not being investigated by the guideline no supervisory responsibility on trial.
John Snowden	Co-investigator on the MUK 4 trial (phase II trial of combination treatment with Vorinostat, bortezomib and dexamethasone in patients with relapsed multiple myeloma). Funded by Myeloma UK	Non-personal financial Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
John Snowden	Co-investigator on the SarCaBon trial (A randomised phase II trial of Saracatinib versus placebo for cancer-induced bone pain). Funded by MRC	Non-personal financial Non-specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
John Snowden	Member of the UK Myeloma Forum. Involved in writing the evidence-based position statement: 'The use of consolidation and maintenance treatment in myeloma'	Personal non-financial	Declare and participate in discussion on all topics as conclusions of the paper were based on a review of the published evidence and the guideline will not be investigating maintenance and consolidation therapy for myeloma.
John Snowden	Member of the UK Myeloma Forum has been involved in writing the evidence-based position statement: 'The use of bendamustine in myeloma'	Personal non-financial	Declare and participate in discussion on all topics as conclusions of the paper were based on a review of the published evidence.
John Snowden	Executive member of the UK Myeloma Forum, a non-profit organisation for the support of UK health professionals and scientists in the myeloma field	Personal non-financial	Declare and participate in discussion on all topics as interest does not impact on content of the guideline.
John Snowden	Co-author on the following abstract, which were	Personal non-	Declare and participate in discussion on all

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Name	Interest declared	Type of interest	Decision taken
	prepared by BresMed on behalf of Celgene: Stradwick S, Freemantle N, Snowden J, Rodrigues F, Brereton N. 2012. Comparative Effectiveness of Lenalidomide plus Dexamethasone for the Treatment of Refractory/Relapsed Multiple Myeloma: A Systematic Review and Mixed Treatment Comparison. Blood (ASH Annual Meeting Abstracts); 120 (21): A4076	financial	topics as Comparative Effectiveness of Lenalidomide plus Dexamethasone for the Treatment of Refractory/Relapsed Multiple Myeloma is not being investigated by the guideline.
John Snowden	Co-author on the following abstract, which were prepared by BresMed on behalf of Celgene: Stradwick S, Freemantle N, Vickers A, Rodrigues F, Monzini M, Brereton N, Snowden. 2013. Comparative Effectiveness of Lenalidomide Plus Dexamethasone Versus Bortezomib Subcutaneous for the Treatment of RRMM. Presented at the 14th International Myeloma Workshop (IMW); Kyoto, Japan; April 3–7.	Personal non-financial	Declare and participate in discussion on all topics as Comparative Effectiveness of Lenalidomide Plus Dexamethasone Versus Bortezomib Subcutaneous for the Treatment of RRMM is not being investigated by the guideline.
John Snowden	Received reimbursement of travel expenses from the organisers for speaking on quality in transplantation at the Joint Accreditation Committee in Autoimmune Diseases meeting	Personal financial Non-specific	Declare and participate in discussion on all guideline topics as expenses not beyond reasonable amounts.
John Snowden	Received an honorarium for from Sanofi for attending an advisory board on the mobilising agent plerixafor and possibly some future currently unlicensed drugs	Personal financial Non-specific	Declare and participate in discussion of all guideline topics as plerixafor is not being investigated by the guideline.
Clare Rowntree	Received an honorarium from Roche for attending an advisory board on GA101 in CLL.	Personal financial Non specific	Declare and participate in discussions on all topics as expenses not beyond a reasonable amount.
Clare Rowntree	Received an honorarium from Amgen for attending an advisory board on Blimatumomab in ALL	Personal financial Non specific	Declare and participate in discussions on all topics as expenses not beyond a reasonable amount.
Clare Rowntree	Received an honorarium from Amgen for giving a lecture on ALL in the elderly	Personal financial Non specific	Declare and participate in discussions on all topics as expenses not

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Name	Interest declared	Type of interest	Decision taken
	at the British Society for Haematology.		beyond a reasonable amount.
Clare Rowntree	Local PI on MABCUTE trial (randomized study comparing maintenance therapy with subcutaneous rituximab continued until progression with observation only in patients with relapsed or refractory, indolent non-Hodgkin's lymphoma who completed and responded to rituximab-based immunochemotherapy induction and initial 2-year rituximab maintenance therapy administered subcutaneously). Funded by Roche. Trial is closed and in follow-up. No involvement in designing trial protocol.	Non-personal financial Specific	Declare and participate in discussions on all topics as individual has no supervisory responsibility for the trial.
Clare Rowntree	Local PI on ECHELON-1 trial (A Randomized, Open-label, Phase 3 Trial of A+AVD Versus ABVD as Frontline Therapy in Patients With Advanced Classical Hodgkin Lymphoma). Funded by Millenium Pharmaceuticals Ltd. No involvement in designing trial protocol	Non-personal financial Specific	Declare and participate in discussions on all topics as individual has no supervisory responsibility for the trial.
Clare Rowntree	Member of the trial management group for the UKALL 14 (A randomized trial for adults with newly diagnosed acute lymphoblastic leukaemia). Funded by CTAAC. Involved in designing the trial protocol.	Non-personal financial Specific	Declare and participate in discussion on all topics because not industry funded.
Clare Rowntree	Member of the trial management group for the UKALL 2011 (United Kingdom National Randomised Trial for Children and Young Adults with Acute Lymphoblastic Leukaemia and Lymphoma 2011). Funded by Leukaemia & Lymphoma Research. Involved in designing the trial protocol.	Non-personal financial Specific	Declare and participate in discussion on all topics because not industry funded.
Clare Rowntree	Member of the trial management group for the UKALL 60+ (A Phase 2 study for older adults with Acute Lymphoblastic Leukaemia). Funded by CRUK. Involved in designing the trial protocol	Non-personal financial Specific	Declare and participate in discussion on all topics because not industry funded.

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Name	Interest declared	Type of interest	Decision taken
Clare Rowntree	Member of the Teenage Cancer Trust advisory board. Advises on how to invest in research.	Personal Non-financial Specific	Chair persons action to declare and participate in discussions on all topics.
Christopher Dalley	Attending an advisory board organised by Novartis for Iron chelation therapy in low risk MDS	Personal financial Non-Specific	Declare and participate in discussion on all topics as Iron chelation therapy in low risk MDS is not being investigated by the guideline.
Christopher Dalley	Co-signatory for the departmental budget for training and education of department staff. Income is primarily from patient donations (but not Pharma)	Non-personal financial Non-specific	Declare and participate in discussion on all topics because not industry funded.
Christopher Dalley	Member of the BMT clinical reference group.	Personal Non-financial Non-specific	Chair persons action to declare and participate in discussions on all topics.
Christopher Dalley	Member of the UK MDS executive.	Personal Non-financial Non-specific	Chair persons action to declare and participate in discussions on all topics.
Christopher Dalley	Member of the UK NEQAS Executive for Leukocyte and immunophenotyping.	Personal Non-financial Non-specific	Chair persons action to declare and participate in discussions on all topics
Christopher Dalley	Member of the MDS, NCRI group for clinical trials.	Personal Non-financial Non-specific	Chair persons action to declare and participate in discussions on all topics.
Christopher Dalley	Was lead author on a published article for the Journal of Clinical Pathology on Specialist Integrated haematological malignancy diagnostic services: an Activity Based Cost (ABC) analysis of a networked laboratory service model.	Personal Non-financial Specific	Chair person's action to declare and participate in discussions on all topics.
Deepak Mannari	Received an honorarium from Celgene for chairing a meeting on the management of myeloma and myelodysplasia.	Personal financial Non specific	Declare and participate in discussion on all topics as management of myeloma and myelodysplasia is not being investigated by the guideline.
Deepak Mannari	Received an honorarium from Amgen for chairing a meeting on the management of immunothrobocytopenia.	Personal financial Non specific	Declare and participate in discussion on all topics as management of immunothrobocytopenia is not being investigated by the guideline.
Geoff Shenton	Principal investigator and member of the trial	Non-personal financial	Declare and participate in discussion on all

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Name	Interest declared	Type of interest	Decision taken
	management group for MyeChild 01: Induction: daunoxome v mitoxantrone, Consolidation: Fludarabine/Cytarbine v high dose cyosine arabinoside, SCT conditioning. Funded by the University of Birmingham and the NCRI.	Specific	topics because not industry funded.
Geoff Shenton	Principal Investigator and Co-investigator for the UK for the InteReALL Sr and HR trial for relapsed acute lymphoblastic leukaemia. Funded by the University of Birmingham and the NCRI.	Non-personal financial Specific	Declare and participate in discussion on all topics because not industry funded.
Geoff Shenton	Principal Investigator for Blinotunomab for relapsed leukaemia trial. Funded by Amgen.	Non-personal financial Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
Geoff Shenton	Member of the I=BFM resistant disease working party.	Personal Non-financial Non-specific	Chair persons action to declare and participate in discussions on all topics
Geoff Shenton	Member of the UKCCSG (UK Children's Cancer Study Group now Children's Cancer and Leukaemia Group (CCLG) Bone Marrow Transplant Committee.	Personal Non-financial Non-specific	Chair persons action to declare and participate in discussions on all topics
Geoff Shenton	Member of the Medical Research Council (MRC) Childhood Leukaemia Working Group (now CCLG Leukaemia Group)	Personal Non-financial Non-specific	Chair persons action to declare and participate in discussions on all topics
Geoff Shenton	Member of the Yorkshire and Humber Bone Marrow Transplant Executive	Personal Non-financial Non-specific	Chair persons action to declare and participate in discussions on all topics
Geoff Shenton	Member of the NCRI Paediatric Leukaemia CSG (ALL and AML subgroups)	Personal Non-financial Non-specific	Chair persons action to declare and participate in discussions on all topics
Andrew Jack	Member of a the trial management group for a Phase III randomised clinical trial comparing rituximab given every 14 days with CHOP given every 21 days (R-CHOP 14 vs21) for patients with newly diagnosed diffuse large B Cell non Hodgkins Lymphoma. Funded by Cancer Research UK and Chugai Pharma Europe Ltd.	Non-personal financial Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
Andrew Jack	Principal investigator for a	Non-personal	Declare and participate

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Name	Interest declared	Type of interest	Decision taken
	randomised evaluation of molecular targeted therapy with bortezomib in diffuse large B-cell lymphoma (REMoDL-B). Funded by Janssen-Cilag.	financial Specific	in discussions on all topics as no supervisory responsibility on trials.
Andrew Jack	Principal investigator for biomarker development and monoclonal antibodies for the treatment of lymphoma. Funded by Genentech Ltd.	Non-personal financial Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
Andrew Jack	Principal investigator on a trial to compare remission rates of low grade non Hodgkin's lymphoma with GA101 vrs rituximab. Funded by Experimental Cancer Medicine (ECMC), Genentech Ltd, NCRN and Roche.	Non-personal financial Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
Andrew Jack	Principal investigator on the stratification of treatment by molecular and genetic sub-typing for diffuse large B-cell lymphoma. Funded by Leukaemia and lymphoma research.	Non-personal financial Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
Andrew Jack	Represents the NCRI on the Lunenburg lymphoma biomarker consortium, the European and North American initiative for the development of biomarkers in clinical trials.	Personal Non-financial	Chair person's action to declare and participate in discussions on all topics as the interest is not specific to the content of the guideline.
Andrew Jack	Host Trust is contracted to provide diagnostic services for the GALLIUM trial to Roche. Responsible for supervising staff and ensuring the work is carried out to the required quality in line with the contract.	Non-personal financial Specific	Declare and participate in discussions on all topics as individual has no responsibility for the contract and does not provide any advice or opinion to Roche.
Andrew Jack	As head of department was involved in a joint project between Host trust, 14M Genomics and University of York to develop new diagnostics in genomics, ceased involvement when no longer head of department in October 2014.	Personal financial Non-Specific	Declare and participate in discussion on all topics as develop new diagnostics in genomics not being investigated by the guideline.
Andrew Jack	Received reimbursement of travelling and subsistence expenses from Roche for attending the American Society of Haematologists (ASH) meeting in December 2013.	Personal financial interest Specific	Declare and participate in discussions on all topics as expenses not beyond a reasonable amount

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Name	Interest declared	Type of interest	Decision taken
Andrew Jack	Member of a the trial management group for a Phase III randomised clinical trial comparing rituximab given every 14 days with CHOP given every 21 days (R-CHOP 14 vs21) for patients with newly diagnosed diffuse large B Cell non Hodgkins Lymphoma. Funded by Cancer Research UK and Chugai Pharma Europe Ltd.	Non-personal financial Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials
Andrew Jack	Principal investigator for a randomised evaluation of molecular targeted therapy with bortezomib in diffuse large B-cell lymphoma (REMoDL-B). Funded by Janssen-Cilag.	Non-personal financial interest Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials
Andrew Jack	Principal investigator for biomarker development and monoclonal antibodies for the treatment of lymphoma. Funded by Genentech Ltd.	Non-personal financial interest Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
Andrew Jack	Principal investigator on a trial to compare remission rates of low grade non Hodgkin's lymphoma with GA101 vrs rituximab. Funded by Experimental Cancer Medicine (ECMC), Genentech Ltd, NCRN and Roche.	Non-personal financial interest Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
Andrew Jack	Principal investigator on the stratification of treatment by molecular and genetic sub-typing for diffuse large B-cell lymphoma. Funded by Leukaemia and lymphoma research.	Non-personal financial interest Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
Andrew Jack	Represents the NCRI on the Lunenburg lymphoma biomarker consortium, the European and North American initiative for the development of biomarkers in clinical trials.	Personal non-financial interest Specific	Chair person's action to declare and participate in discussions on all topics as the interest is not specific to the content of the guideline.
Andrew Jack	Host Trust is contracted to provide diagnostic services for the GALLIUM trial to Roche. Responsible for supervising staff and ensuring the work is carried out to the required quality in line with the contract.	Non-personal financial Specific	Declare and participate in discussions on all topics as individual has no responsibility for the contract and does not provide any advice or opinion to Roche.
Andrew Jack	Has supervisory responsibility for a	Non-personal financial	Declare and participate in discussions on all

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Name	Interest declared	Type of interest	Decision taken
	collaborative research project to identify targets for therapeutic antibody development. Funded by Genetech.	Non-Specific	topics as therapeutic antibody development is not the focus of the guideline.
Sarah Steele	Volunteers as Treasurer for the Friends of West Suffolk Hospital. Responsible for keeping the books and part of the committee that decides how to spend the fund. Fund only used to support patients and staff of the hospital.	Non-personal financial Non-Specific	Chair person's action to declare and participate in discussions on all topics as the interest is not specific to the content of the guideline.
Bhuey Sharma	Received an honorarium from Roche Products Ltd for giving a lecture on "Metastatic breast cancer: future positive. Navigating the HER 2+ journey: Targeting and imaging invasion and metastases".	Personal financial Non-specific	Declare and participate in discussions on all topics as breast cancer is not being investigated by the guideline.
Bhuey Sharma	Co-investigator on a multicentre randomised phase II study on CHEMO-T, Cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) versus gemcitabine, cisplatin and methyl prednisolone (GEM-P) in the first line treatment of T-cell lymphoma. Funded by Royal Marsden NHS Foundation trust.	Non-personal financial interest Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials
Bhuey Sharma	Co-investigator on a multicentre randomised phase II study on LEGEND comparing Lenalidonmide plus rituximab, gemcitabine, methylprednisolone and cisplatin (RG-EMP) in second line treatment of diffuse large B-cell lymphoma. Funded by Celgene Europe Ltd.	Non-personal financial interest Specific	Declare and participate in discussions on all topics as no supervisory responsibility on trials.
Christopher McNamara	Principal investigator for the GALLIUM trial on rituximab versus GA101 in combination with chemotherapy in first-line follicular and marginal zone lymphoma. Funded by NCR and Roche. Advised on setting up the laboratory diagnostics for patients participating in the trial, when the trial protocol was being determined	Non-personal financial Specific	Declare and participate in discussions on all topics as individual has only provided advice on laboratory diagnostics components of the trial protocol.
Christopher McNamara	Local principal investigator for the PACIFICO trial	Non-personal financial	Declare and participate in discussions on all

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Name	Interest declared	Type of interest	Decision taken
	(Alkylator Combination In Follicular lymphoma Immuno-Chemotherapy for Older patients: a phase III comparison of first-line R-CVP (rituximab, cyclophosphamide, vincristine and prednisone) versus R-FC (rituximab, fludarabine and cyclophosphamide). Funded by CTAAC	Specific	topics as individual has no supervisory responsibility for the trial.
Christopher McNamara	Local principal investigator for the REMoDLB trial (A randomised evaluation to see whether adding bortezomib to standard combination chemotherapy and rituximab (RCHOP) can improve progression free survival in diffuse large B-cell lymphoma with Bortezomib). Funded by Janssen Cilag Ltd	Non-personal financial Specific	Declare and participate in discussions on all topics as individual has no supervisory responsibility for the trial.
Christopher McNamara	Local principal investigator for the RATHL trial (a multicentre randomised phase II study to assess response adapted therapy using FDG-PET imaging in patients with newly diagnosed, advanced Hodgkin's lymphoma). Funded by CRUK	Non-personal financial Non-specific	Declare and participate in discussions on all topics as Hodgkin's lymphoma is not being covered by the guideline.
Christopher McNamara	Local principal investigator for the RAPID trial (A randomised Phase III trial to determine the role of FDG-PET Imaging in Clinical Stages IA/IIA Hodgkin's Disease). Funded by Leukaemia and Lymphoma Research	Non-personal financial Non-specific	Declare and participate in discussions on all topics as Hodgkin's lymphoma is not being covered by the guideline.
Christopher McNamara	Medical advisor to the Lymphoma Association	Personal non-financial	Declare and participate in discussions on all topics as interest is not specific to the content of the guideline.
Christopher McNamara	Local principal investigator for the REMoDLB trial (A randomised evaluation to see whether adding bortezomib to standard combination chemotherapy and rituximab (RCHOP) can improve progression free survival in diffuse large B-cell lymphoma with Bortezomib). Funded by Janssen Cilag Ltd	Non-personal financial Specific	Declare and participate in discussions on all topics as individual has no supervisory responsibility for the trial.

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Name	Interest declared	Type of interest	Decision taken
Christopher McNamara	Local principal investigator for the RATHL trial (a multicentre randomised phase II study to assess response adapted therapy using FDG-PET imaging in patients with newly diagnosed, advanced Hodgkin's lymphoma). Funded by CRUK	Non-personal financial Non-specific	Declare and participate in discussion on all topics because not industry funded.
Christopher McNamara	Local principal investigator for the RAPID trial (A randomised Phase III trial to determine the role of FDG-PET Imaging in Clinical Stages IA/IIA Hodgkin's Disease). Funded by Leukaemia and Lymphoma Research	Non-personal financial Specific	Declare and participate in discussion on all topics because not industry funded.
Christopher McNamara	Principal investigator for the GALLIUM trial on rituximab versus GA101 in combination with chemotherapy in first-line follicular and marginal zone lymphoma. Funded by NCR and Roche. Advised on setting up the laboratory diagnostics for patients participating in the trial, when the trial protocol was being determined	Non-personal financial Specific	Declare and participate in discussions on all topics as individual has no supervisory responsibility for the trial.
Nia Evans	Member of British Oncology Pharmacists Association (BOPA) and UKBMT pharmacist's group	Personal Non-financial Non-specific	Chair persons action to declare and participate in discussions on all topics
Nia Evans	Lead pharmacist on a CRUK trial management group for AML18, and provides expert pharmacy input, responds to queries. Involved in checking the drug information and dosages were correct in the development of the trial protocol.	Non-personal financial Non-Specific	Declare and participate in discussion on all topics because not industry funded.
Nia Evans	Lead pharmacist and involved in developing the trial protocol for a CRUK trial management group for UKALL14.	Non-personal financial Non-Specific	Declare and participate in discussion on all topics because not industry funded.
Barbara von Barsewisch	Attending an advisory board organised by Roche on Subcutaneous administration of Mabtherea feedback from Clinical Nurse Specialists.	Personal Non-financial Non-specific	Declare and participate in discussion on all topics as Mabtherea feedback is not being investigated by the guideline.
Barbara von Barsewisch	Member of the London Haematological Oncology	Personal Non-financial	Chair persons action to declare and participate

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Name	Interest declared	Type of interest	Decision taken
	Nurses Forum	Non-specific	in discussions on all topics
Marie Waller	Received honoraria from Eusa Pharma for giving a lecture on state of the art management of post-BMT complications, psychological late effects of transplantation.	Personal financial Non specific	Declare and participate in discussion on all topics as state of the art management of post-BMT complications, psychological late effects of transplantation is not being investigated by the guideline.
Marie Waller	Received reimbursement of travelling expenses and subsistence from EBMT UK for helping with the administration of an education study day.	Personal financial Non-specific	Declare and participate in discussion on all topics as expenses not beyond a reasonable amount.
Marie Waller	Member of the EBMT UK nurses group.	Personal Non-financial Non-specific	Chair persons action to declare and participate in discussions on all topics
Marie Waller	Committee member of the trust board charity.	Personal non-financial Non-specific	Chair persons action to declare and participate in discussions on all topics

F.3 Expert advisors to the Guideline Committee

Professor David Barnett	Professor in Diagnostic Haematology & UK NEQAS LI Director, Sheffield Teaching Hospitals NHS Foundation Trust
Dr Robert Hills	Reader in Translational Statistics, Head HCTU, Department of Haematology, Cardiff University School of Medicine

F.4 Individuals carrying our literature reviews and complementary work

Overall Co-ordinators	
Dr John Graham	Director, National Collaborating Centre for Cancer, Cardiff
Dr Andrew Champion	Centre Manager, National Collaborating Centre for Cancer, Cardiff
Angela Bennett	Assistant Centre Manager, National Collaborating Centre for Cancer, Cardiff
Project Managers	
Lianne Gwillim	National Collaborating Centre for Cancer, Cardiff
Senior Researcher	
Dr Nathan Bromham	National Collaborating Centre for Cancer, Cardiff
Researchers	
Susan O'Connell	National Collaborating Centre for Cancer, Cardiff
Information Specialists	
Stephanie Arnold	National Collaborating Centre for Cancer, Cardiff
Senior Health Economist	
Matthew Prettyjohns	National Collaborating Centre for Cancer, Cardiff
Health Economist	

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Overall Co-ordinators	
James Hawkins	National Collaborating Centre for Cancer, Cardiff
Needs Assessment	
Verity Bellamy	Northern & Yorkshire Knowledge and Intelligence Team, Public Health England
Stephen Oliver	Department of Health Sciences, University of York & Hull, York Medical School

F.5 Organisations invited to comment on the guideline development

5 Boroughs Partnership NHS Foundation Trust	National Atrial Fibrillation Clinical Policy Forum
Academy for Healthcare Science	National Clinical Guideline Centre
Acorns Children's Hospice	National Collaborating Centre for Mental Health
Aintree University Hospital NHS Foundation Trust	National Collaborating Centre for Women's and Children's Health
Alder Hey Children's NHS Foundation Trust	National Deaf Children's Society
Anthony Nolan	National Institute for Health Research
Association of Anaesthetists of Great Britain and Ireland	NHS Choices
Beckman Coulter	NHS Chorley and South Ribble CCG
Belfast Health and Social Care Trust	NHS England
Blood & Marrow Transplantation Clinical Reference Group NHS England	NHS Health at Work
Boehringer Ingelheim	NHS Somerset CCG
Boehringer Ingelheim Ltd	Northern Health and Social Care Trust
British HIV Association	Nursing and Midwifery Council
British Medical Association	Nutricia Advanced Medical Nutrition
British Medical Journal	Public Health England
British Nuclear Cardiology Society	Roche Products
British Psychological Society	Royal College of Anaesthetists
British Red Cross	Royal College of General Practitioners
Cambridge University Hospitals NHS Foundation Trust	Royal College of General Practitioners in Wales
Cancer Research UK	Royal College of Midwives
Caplond Services	Royal College of Nursing
Care Quality Commission	Royal College of Obstetricians and Gynaecologists
Chartered Society of Physiotherapy	Royal College of Paediatrics and Child Health
Children's Cancer and Leukaemia Group	Royal College of Pathologists
College of Paramedics	Royal College of Physicians
County Durham and Darlington NHS Foundation Trust	Royal College of Psychiatrists
CTI Life Sciences	Royal College of Radiologists
Department of Health	Royal College of Speech and Language Therapists
Department of Health, Social Services and Public Safety - Northern Ireland	Royal College of Surgeons of England
East of England Strategic Clinical Network	Royal Pharmaceutical Society

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5 Boroughs Partnership NHS Foundation Trust	National Atrial Fibrillation Clinical Policy Forum
Faculty of Dental Surgery	Sandoz Ltd
Gilead Sciences Ltd	Scottish Intercollegiate Guidelines Network
Gloucestershire Hospitals NHS Foundation Trust	Sebia
Greenwich & Bexley Community Hospice	Sheffield Teaching Hospitals NHS Foundation Trust
Health and Care Professions Council	Social Care Institute for Excellence
Health and Social Care Information Centre	Somerset, Wiltshire, Avon and Gloucestershire Cancer Services Operational Group
Healthcare Improvement Scotland	South Eastern Health and Social Care Trust
Healthcare Quality Improvement Partnership	South Wales Cancer Network
Janssen	Southern Health & Social Care Trust
Leukaemia & Lymphoma Research	Teenagers and Young Adults with Cancer
Leukaemia CARE	The British Society for Haematology
Manchester Cancer	The Intensive Care Society
Mastercall Healthcare	The Royal Surrey County Hospital
MDS UK Patient Support Group	University Hospital Birmingham NHS Foundation Trust
Medicines and Healthcare Products Regulatory Agency	Welsh Government
Ministry of Defence	Welsh Scientific Advisory Committee
Napp Pharmaceuticals Ltd	Western Health and Social Care Trust

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