Time-to-diagnosis and symptoms of myeloma, lymphomas and leukaemias: a report from the Haematological Malignancy Research Network

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Abstract

Background: Prior to diagnosis, patients with haematological cancers often have multiple primary care consultations, resulting in diagnostic delay. They are less likely to be referred urgently to hospital and often present as emergencies. The aim of this study was to examine patient perspectives on time to help-seeking and diagnosis, as well as associated symptoms and experiences.

Methods: Within the UK’s Haematological Malignancy Research Network (population 3.6 million) patients are routinely asked if they would like to participate in an on-going survey; and 3329 patients newly diagnosed with myeloma, lymphoma or leukaemia in 2004-2011 completed a questionnaire describing the circumstances leading their diagnosis. The information requested included whether or not they had symptoms, and if so the date(s) of symptom onset, when medical advice was first sought (help-seeking), details of type/frequency of symptoms and brief summaries of the pathways leading to their diagnosis. The duration of the total interval (symptom onset to diagnosis), patient interval (symptom onset to help-seeking) and diagnostic interval (help-seeking to diagnosis) was examined by patient characteristics and diagnosis. Type and frequency of symptoms were examined and compared with UK Referral Guidelines and diagnosis.

Results: Around one-third of patients were asymptomatic at diagnosis. In those with symptoms, the patient interval tended to be shorter than the diagnostic interval across most diseases. Intervals varied markedly by diagnosis: acute myeloid leukaemia being 41 days (Interquartile range 17-85), diffuse large B-cell lymphoma 98 days (IQR 53-192) and myeloma 163 days (IQR 84-306). Many symptoms corresponded to those cited in UK Referral Guidelines, but some were rarely reported (e.g. pain on drinking alcohol). By contrast others, absent from the guidance, were more frequent (e.g. stomach and bowel problems). Symptoms such as tiredness and pain were common across all diseases, although some specificity was evident by sub-type, such as lymphadenopathy in lymphoma and bleeding and bruising in acute leukaemia.

Conclusions: Pathways to diagnosis are varied and can be unacceptably prolonged, particularly for myeloma and some lymphomas. More evidence is needed, along with interventions to reduce time-to-diagnosis, such as public education campaigns and GP decision-making aids, as well as refinement of existing Referral Guidelines.
Introduction

The pathway to diagnosis for haematological malignancies (leukaemias, lymphomas and myeloma) can be fraught with difficulty and is often associated with excessive time between symptom onset and help-seeking; multiple primary care consultations before referral to secondary care; and an increased chance of being diagnosed after emergency admission (1–14). Diagnostic delay is known to increase complications in patients with some haematological malignancies (8), and a recent review specifically identified these as diseases for which early diagnosis could improve outcome (13). In this regard, delayed diagnosis is considered to be one of the factors contributing to poorer survival in Great Britain (15), where it has recently been estimated that around 3500 deaths occurring within five years of diagnosis of a haematological malignancy could be avoided if survival matched that of the rest of Europe (16).

Haematological malignancies comprise a heterogeneous group of over 60 cancer sub-types, many of which have unique clinical pathways and outcomes (17). As a group these cancers are relatively common, accounting for around one in ten of all new cancer diagnoses in the developed world (18,19). However, unlike some cancers, their clinical presentation is recognised as being broad and ill-defined, particularly in terms of initial symptoms; which may be non-specific, difficult to differentiate from those of benign, self-limiting conditions, and associated with a long prodrome (2). Early diagnosis of haematological malignancies therefore poses exacting challenges for patients and clinicians; patients must determine when to seek help and, when they do, practitioners must identify the symptoms of potential malignancy and make appropriate and timely referrals to secondary care.

Ensuring early diagnosis of all cancers, including haematological malignancies, has been a key priority for the UK Department of Health for over a decade (21–24). Initiatives such as the production of Referral Guidelines for Suspected Cancer to help general practitioners (GPs) identify cancer symptoms early, and waiting-time targets to ensure rapid diagnosis and treatment, are now firmly embedded in primary and secondary health care systems (25). In terms of haematological malignancies, a single list of symptoms has been developed to guide GPs in their identification of patients with constellations of these, which may indicate potential disease. Existing evidence about symptoms of haematological malignancies, however, has been largely derived from expert committee reports (25) or from studies that have focused on pre-determined symptoms or clinical parameters (blood and other diagnostic test results) (9,26–29); although several smaller studies do exist that have examined complete symptom profiles (7,8,30–35). The aim of this study was to examine time to help-seeking and diagnosis of haematological malignancies, as well as associated symptoms from the patient perspective.

Methods and materials

Covering a population of 3.6 million that is broadly representative of the UK as a whole, this study was conducted within the robust infrastructure of the Haematological Malignancy Research Network’s (www.hmrn.org) on-going patient cohort (36,37). Established in 2004, HMRN is a collaboration between the clinical haematology network, researchers at the University of York and the Haematological Malignancy Diagnostic Service (www.hmds.info), which diagnoses all haematological malignancies in the area coding to the latest WHO classification scheme (38). More
than 2000 patients are registered annually and demographic, prognostic, and treatment information are routinely abstracted from their medical records. HMRN has full ethical approval and Section 251 exemption to collect data for audit and research purposes.

With permission from their clinical teams, patients are asked to consent to their data being used for research purposes. Reflecting the diversity of disease sub-types, different consenting strategies are used (face-to-face for in-patients, postal for out-patients etc.). At this time, patients (≥ 18 years) are also given an information leaflet inviting them to take part in our on-going survey about symptoms and help seeking. Those that agree are sent a questionnaire asking if any symptom(s) were experienced before diagnosis; if the response is ‘yes’, the patient is asked to provide a list of their symptoms, including the date of onset and the date medical advice was first sought (help-seeking). To avoid leading questions, patients’ report in free-text using their own words and phrases. Importantly, the questionnaire also contains a text box in which patients can tell us anything else they consider important in relation to their disease pathway or past medical history.

This report summarises information on time to help-seeking and diagnosis, as well as symptoms, collected over seven years, 2004-11. Three time intervals were examined in symptomatic patients; the total interval (from symptom onset to diagnosis); the patient interval (from symptom onset to first help-seeking); and the diagnostic interval (from first help-seeking to diagnosis and including the time when the patient’s care is being managed in primary and/or secondary care) (39). These data are examined by patient characteristics and diagnosis and are presented as medians and interquartile ranges (IQRs). Symptoms are examined in total and by diagnostic group and findings compared to those cited in the UK Referral Guidelines (25). All analyses were conducted using Stata version 12 (40) and standard descriptive methods were applied.

Results

During the seven year period September 2004 to August 2011, 5038 (57%) of the 8858 patients contacted provided written consent and 3329 (66%) of these requested and returned a questionnaire (Table 1). No marked demographic or diagnostic differences were observed between subjects who agreed to complete a questionnaire and those who did not.

Just over two-thirds (2336) of the 3329 patients who returned a completed questionnaire reported that they had one or more symptoms before diagnosis, and the diagnostic categories listed in Table 1 are ordered according to the absolute numbers of patients reporting symptoms; ranging from 451 with diffuse large B-cell lymphoma through to six with Burkitt lymphoma. As can be seen from Table 1, the likelihood of experiencing symptoms varied markedly by disease sub-type, moving from less than half for slowly progressing conditions such as chronic lymphocytic leukaemia (47.2%) through to nearly all for more aggressive diseases such as diffuse large B-cell (89.7%) and Hodgkin (86.5%) lymphomas. Indeed, many asymptomatic patients with chronic lymphocytic leukaemia reported being diagnosed incidentally via blood tests at routine health checks, or check-ups for other comorbidities, rather than presenting with symptomatic disease.

In symptomatic patients, differences in time to help-seeking and diagnosis were observed by sex and age. Among those with symptoms, women had, on average, longer intervals than men, and those
aged ≥80 years tended to longer total intervals (symptom onset to diagnosis) than younger patients; largely driven by the length of the diagnostic interval (help-seeking to diagnosis). As with the occurrence of symptoms, there is marked variation in the duration of intervals by diagnosis (Table 1). As might be expected, the total interval was shortest for acute myeloid leukaemia at 41 days (interquartile range (IQR) 17-85). The lymphomas tended to have longer intervals with the more aggressive diffuse large B-cell lymphoma being diagnosed soonest at 98 days (IQR 53-192) and marginal zone (generally the most indolent) having the greatest delay at 172 days (IQR 77-385). The total interval for myeloma was also prolonged at 163 days (IQR 84-306) and myeloproliferative neoplasms, again being particularly indolent, were found to have the longest overall time-to-diagnosis at 215 days (IQR 84-539). For the vast majority of conditions the average patient interval (symptom onset to help-seeking) was considerably shorter than the diagnostic interval. The main exceptions to this were chronic myeloid leukaemia, where the patient and diagnostic intervals were 33.5 days (IQR 4.5-127.5) and 9 days (IQR 5-52) respectively and acute myeloid leukaemia, being 13 days (IQR 1-47) and 10 days (IQR 5-32) respectively. In contrast, for diffuse large B-cell lymphoma, the most common of the lymphomas, the diagnostic interval accounted for an extremely large proportion of the time-to-diagnosis, having a patient interval of 9 days (IQR 1-42) and diagnostic interval of 69 days (IQR 37-134).

Information on symptom frequency across all haematological malignancies combined is presented in Figure 1. In line with UK Referral Guidelines (blue bars), symptoms most frequently reported were tiredness, pain, lump, shortness of breath/cough, skin problems, abnormal sweating and infections. However, certain listed symptoms were mentioned comparatively infrequently, most notably pain when drinking alcohol, which was only reported by five patients – all with lymphoma. By contrast, as can be seen from Figure 1 (red bars), patients identified a range of other symptoms, including for example, stomach/bowel problems, joint problems and fractures, cardiovascular problems, dizziness and loss of appetite. We were unable to match any of the reported symptoms with any of those in the Referral Guidelines in 10% of patients, and this was most common in myeloproliferative neoplasms. No differences were detected in time-to-diagnosis between those that reported having symptoms cited in the UK Referral Guidelines and those that did not (data not shown).

A number of the reported symptoms, such as tiredness and pain, occurred across all diseases (Figure 2). The type of pain reported varied, however, by diagnosis, with musculoskeletal pain being particularly pronounced in myeloma, abdominal pain being common in the non-Hodgkin lymphomas and chest pain in patients with acute leukaemia and myelodysplastic syndrome (data not shown). Furthermore, in contrast to traditional perceptions of painless lymphadenopathy, some patients reported otherwise, particularly for Hodgkin lymphoma. For other symptoms there was greater specificity by sub-type: bruising/bleeding and shortness of breath/cough in acute myeloid leukaemia and myelodysplastic syndromes; lymphadenopathy (usually reported as a lump) in lymphoma; joint problems and fractures in myeloma; and skin problems and headaches in myeloproliferative neoplasms. However, with around half of all patients only reporting one symptom, there were no obvious constellations by diagnostic group (data not shown).

The challenges and variations associated with diagnosing haematological cancers, particularly myeloma and lymphoma, are clearly illustrated in the self-reported statements shown in Box 1. These accounts range from patients acknowledging that they were diagnosed incidentally after a routine blood test, without experiencing any symptoms, to those reporting particularly poor
experiences in terms of multiple symptoms, repeated consultations, emergency presentation and prolonged time-to-diagnosis. A wide variety of reasons for delayed help-seeking are highlighted in these excerpts including: musculoskeletal pain on a background of existing bone/joint problems; having an abnormal lump but not feeling ill at all; having a lump with no pain; having symptoms which were intermittent; and presuming symptoms were normal for their age or sex. However poorer experiences did not always correlate with longer time-to-diagnosis; and some patients were diagnosed quickly, but reported being acutely ill and repeatedly consulting GPs or presenting in emergency departments during this time.

Discussion

This paper presents results from a study examining self-reported time to help-seeking and diagnosis, as well as symptoms in a large cohort of patients with haematological cancers. Substantial variation was noted in the experiences reported by patients and this was largely driven by diagnostic sub-type. This is because sub-type generally determines disease aggressiveness, the manifestation of symptom(s) and the speed with which these exacerbate. Thus time-to-diagnosis was shortest for acute myeloid leukaemia which is generally perceived as the most aggressive, acute and progressive disease, longer for the lymphomas and particularly prolonged for myeloma. The large number of patients (30%) without any symptoms often reported that had been diagnosed incidentally when blood tests were taken to monitor other comorbidities or at routine health checks carried out at GP surgeries. In this respect, the diagnostic sub-types of those less likely to experience symptoms in our study correspond with the diseases that can be identified by blood testing alone (e.g. chronic lymphocytic leukaemia).

A myriad of different symptoms were reported and although some, such as tiredness and pain, were common across diseases, there was some specificity by sub-type. Tiredness, perhaps occurring as a consequence of anaemia, was expected, however, the frequency with which pain was reported was surprising and it is possible that pain may have been previously underestimated. Although many of the symptoms reported corresponded to those cited in UK Referral Guidelines for Suspected Cancer (25) a number of were rarely mentioned by patients while others were frequently reported, but absent from the Guidelines. Interestingly, only five lymphoma patients reported pain after drinking alcohol.

Strengths and weaknesses

As far as we can identify, this is the largest and most comprehensive study asking patients across all sub-types of haematological cancers to report their symptoms and help-seeking experiences before diagnosis. In order to limit recall bias, data were collected soon after diagnosis, with questionnaires generally being dispatched within 6 weeks of diagnosis. HMRN was established in order to facilitate research with patients and as our study was predicated on this infrastructure, we had access to a large population-based cohort of patients that had already consented to being approached for research purposes. HMRN includes patients of all ages and with all haematological malignancies, classified according to WHO schema, meaning that we were able to examine and compare symptoms and time-to-diagnosis across all disease sub-types, some of which had not previously been examined. Patients are approached to consent to inclusion in HMRN with permission from their clinical team; unfortunately, some patients are deemed too ill to be approached, and others die
soon after diagnosis. Consequently, the experiences of patients with very acute/aggressive or advanced stage disease (perhaps as a consequence of longer time-to-diagnosis) may not have been included in our study.

It was our intention to capture the breadth of symptoms patients considered to be related to their diagnosis; however, there are always uncertainties inherent in using self-reported data and variation may have occurred in the completeness with which patients reported their symptoms – some recording them all and others only reporting those most troublesome or painful. Use of self-reported data may also be limited by the patient’s ability to distinguish symptoms of haematological cancer from those that are unrelated; but it is nonetheless important to take account of the patients’ interpretation of their own experiences. We are currently building on these data, however, by examining symptoms, symptom management, visit frequency and referral pathways in primary and secondary medical records, with funding from the National Awareness and Early Diagnosis Initiative. Although using data from medical records has its own disadvantages, it will provide further evidence and also enable us to explore the diagnostic interval in greater detail.

Comparison of findings with previous literature

Few studies, with the exception of those that are qualitative, have previously collected self-reported symptom-data, and ours is the largest to do this. Using this approach meant that patients could tell us their interpretation of events leading to diagnosis, and the symptoms they considered to be related to their disease. Comparing findings about time-to-diagnosis is always difficult due to different methods of data collection (self-reported survey, medical records, medical insurance claim dates), use of different summary measures (mean or median) and variation in the time-periods measured (39). Existing studies vary in size, with larger North American studies using SEER/Medicare data based on claims for specific symptoms (9,26). However, average time-to-diagnosis of lymphoma (multiple types) in existing studies was reported at between 2.5 months and around a year (1,4,5,41,42); myeloma was between 3 and 5.5 and a half months (9,27); chronic lymphocytic leukaemia 3 months (26); and chronic myeloid leukaemia 5 months (30). Findings from our study are similar to these, with the exception of chronic myeloid leukaemia, which we found to be somewhat shorter at around 3 months.

Unlike existing studies, we collected information about all symptoms, rather than pre-defining the categories which would be included. Close correlation was, however, identified between the major symptoms we reported and those in existing research studies of lymphoma (7,31,35), myeloma (8,33,34), chronic myeloid leukaemia (30,32) and chronic lymphocytic leukaemia (26), although we were able to identify a far wider range.

Implications of the study

This study provides clear evidence that time-to-diagnosis of haematological malignancies, particularly myeloma and some lymphomas, can be unacceptably prolonged. This reflects the difficulties previously reported in relation to the pathways to diagnosis of these diseases, including: repeated GP consultations (14), which are associated with a prolonged interval before hospital
referral (12); infrequent use of the urgent referral route (suggesting that malignancy is not suspected at referral) and frequent emergency presentation prior to diagnosis (13). Previous studies of lymphoma also indicate that patients are rarely referred directly to haematology by GPs (6).

Diagnosing these diseases is, however, undoubtedly fraught with difficulty. Symptoms are often vague and frequently seen in primary care in patients with non-malignant illness, making it difficult to differentiate patients that need urgent hospital referral from those that do not. Lack of knowledge about the symptoms of lymphoma among patients, as well as the particular characteristics of these symptoms (e.g. potentially painless, intermittent lumps) have also been reported as factors acting as barriers to help-seeking (7). Importantly, unlike many other cancers (e.g. breast, testicular, prostate, melanoma) the symptom signature for these diseases is relatively poor; there is no single, specific symptom to prompt early help-seeking and referral. Although certain sub-types can be identified by means of a routine blood test, a specific screening test does not exist. In terms of UK Referral Guidelines, we have shown that these are not as useful in the context of haematological malignancy as they may be for other cancers. These factors are combined with a lack of knowledge about the impact of delayed diagnosis on outcome in these diseases, although it is recognised that patients presenting as emergencies have poorer survival than those presenting via other routes (13).

However, despite the difficulties described above, it is important that haematological cancers are diagnosed as soon as possible, in order both to improve the patient experience and avoid increasing complications at diagnosis (such as anaemia, bone disease and renal failure in myeloma) (8). Recent initiatives such as the UK’s ‘Be Clear on Cancer’ campaign have been introduced to increase knowledge of the symptoms of certain cancers among the general public. Similar approaches could be effective in the context of haematological cancers, describing for example some of the more disease specific symptoms such as the characteristics of lymphadenopathy and drenching sweats in lymphoma and bleeding and bruising in leukaemia. Further refinement of the UK Referral Guidelines for Suspected Cancer (at the very least distinguishing between myeloma, lymphoma, and the acute and chronic leukaemias) could assist GPs to identify these diseases earlier and make more timely referrals. The introduction of decision aid tools, combining information on symptoms with that of visit frequency, particularly with the same or related symptoms, may also facilitate GP decision-making.

Unfortunately, haematological malignancies are often overlooked in the context of introducing measures to promote early diagnosis. However, the findings presented in this report provide evidence that time-to-diagnosis can be unacceptably prolonged in these diseases and interventions are urgently needed to address this issue.

**Conclusion**

Pathways to diagnosis are varied and can be unacceptably prolonged, particularly for myeloma and some of the lymphomas. More evidence is needed, along with interventions to reduce time-to-diagnosis, such as public education campaigns and GP decision-making aids, as well as refinement of existing Referral Guidelines.
Acknowledgments

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Details of contributors

DH, AS, ER, AJ and RP planned the study. EM conducted the pilot study and the initial literature review. DH, ER and AS implemented the study, coded symptoms and wrote the first draft of the manuscript. AS managed and analysed the data and produced the figures. RP, AJ and UM gave clinical advice. All authors contributed to the final draft of the paper.
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<th>Diagnostic Group</th>
<th>Contacted N (%)</th>
<th>Consent N (%)</th>
<th>Questionnaire N (%)</th>
<th>Symptoms N (%)</th>
<th>Interval - Median Days (25-75 percentile – interquartile range)</th>
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<td></td>
<td></td>
<td></td>
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<td>Total</td>
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<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td>No</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Total</td>
<td>8858 (100)</td>
<td>5038 (100)</td>
<td>3329 (100)</td>
<td>2336 (29.8)</td>
<td>993 (70.2)</td>
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<td>617 (33.1)</td>
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<td>2198 (43.6)</td>
<td>1464 (44)</td>
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<td>Median Age (Range)</td>
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<td>67.7 (18.1-96.8)</td>
<td>66.4 (18.1-95.2)</td>
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<td>&lt;40</td>
<td>664 (7.5)</td>
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<td>702 (13.9)</td>
<td>401 (12)</td>
<td>256 (63.8)</td>
<td>145 (36.2)</td>
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*Note: N (%): Number (% of total)*

**Table 1: Characteristics of patients diagnosed with a haematological malignancy: Haematological Malignancy Research Network (HMRR), 2004-2011**
<table>
<thead>
<tr>
<th></th>
<th>Count</th>
<th>Percentage</th>
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<td>T-cell leukaemia</td>
<td>62 (0.7)</td>
<td>37 (0.7)</td>
<td>32 (1)</td>
<td>13 (40.6)</td>
<td>19 (59.4)</td>
<td>502 (75-761)</td>
<td>30 (3-153)</td>
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<td>Hairy cell leukaemia</td>
<td>65 (0.7)</td>
<td>43 (0.9)</td>
<td>26 (0.8)</td>
<td>10 (38.5)</td>
<td>16 (61.5)</td>
<td>88.5 (44-194)</td>
<td>35 (1-138)</td>
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<td>Burkitt lymphoma</td>
<td>37 (0.4)</td>
<td>18 (0.4)</td>
<td>6 (0.2)</td>
<td>0 (0.0)</td>
<td>6 (100.0)</td>
<td>67.5 (34-136)</td>
<td>19 (4.5-30.5)</td>
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</table>

*ordered by the absolute numbers of patients reporting symptoms; total interval – symptom onset to diagnosis; patient interval – symptom onset to help-seeking; diagnostic interval – help-seeking to diagnosis.
Footnote to Figure 1:

All symptoms are coded once only. **Pain:** includes musculoskeletal, abdominal, chest and other; **Infections:** include throat, chest, common cold, flu (like symptoms), mouth sores, skin infections and other; **Stomach/bowel:** nausea, vomiting, bloated, indigestion, diarrhoea and other; **Bruising/bleeding:** includes nosebleeds, bleeding from bowel/stomach, gums/mouth and other; **Cardiovascular:** includes abnormal blood pressure, abnormal heart beat, stroke, deep vein thrombosis and other.
Figure 2 Distribution of Symptoms by Diagnostic Group
Box 1 Self-reported experiences leading-up to diagnosis

Mediastinal large B-cell lymphoma, aged 30-40 years
Reported symptoms: Pains when eating, weight loss, breathlessness.
Free text: “Also had other symptoms which I saw Dr about including fatigue, severe constipation. Also chronic back pain. But other reasons were found for all the symptoms. Wasn’t till I went to A&E and later got a cancer diagnosis that it all fitted together. So all the signs were missed by GPs from (onset of symptoms) to (diagnosis).”
Interval: Patient (symptom to help-seeking) – 1 month; diagnostic (help-seeking to diagnosis) – 7 months.

Diffuse large B-cell lymphoma, aged 30-40 years
Reported symptoms: Pain in left shoulder and left side of chest, not able to lie down, tiredness, breathlessness, cough, weight loss, coughing up blood.
Free text: “Went to the doctors at least 8 times. Kept telling me it would not be anything serious as I was too young. I demanded an x-ray in (month) as symptoms kept getting worse.”
Interval: Patient – immediate; diagnostic - 5 months.

Diffuse large B-cell lymphoma, aged 50-60 years
Reported symptoms: Lots of pain and swelling in stomach, back pain, loss of weight, not eating or drinking, not sleeping.
Free text: “A&E wasn’t productive. Went there four times and sent home with just other painkillers. But not tried to find out why by then I’d lost nearly 3 stone. Was suicidal with pain and not sleeping.”
Interval: Patient - immediate; diagnostic - 1 month.

Diffuse large B-cell lymphoma, aged 50-60 years
Reported symptoms: Lump on face.
Free text: “Time from GP visit to hospital app’t was rapid. Delays then started with referral for ultrasound, delay for results, referral for needle biopsy, then results, then op – by which time the small initial lump had grown considerably. The result is damage to the facial nerve which would probably have been avoided if the (operation) had been done much earlier.”
Interval: Patient - 1 month; diagnostic - 4 months.

Diffuse large B-cell lymphoma, aged 60-70 years
Reported symptoms: Swollen gland in neck.
Free text: “I had no ill effects before I was diagnosed. I was working normally. I was my normal weight and I had not lost my appetite and I was eating normally. When I went for the scan and they informed me I had cancer I was in complete shock.”
Interval: Patient - immediate; diagnostic - 3 months.

Diffuse large B-cell lymphoma, aged 70-80 years
Reported symptoms: Tiredness, lump in neck.
Free text: “Initially, the lump appeared and disappeared gradually getting bigger and harder each time. There was no pain or discomfort associated with it at any time.”
Interval: Patient - 3 months; diagnostic - 2 months.

Follicular lymphoma, aged 60-70 years
Reported symptoms: Difficulty walking, backache.
Free text: “In (month) the doctor diagnosed a groin strain. In (month) it was getting worse and another doctor in the practice diagnosed tendonitis and arranged an appointment with a physiotherapist. After a wait I first saw the physiotherapist in (month). At the second visit he said he was unsure what was going on and referred me back to the doctor for an MRI scan. The scan revealed lymphoma and fractured lumbar vertebrae.”

Interval: Patient - 2 months; diagnostic - 3 months.

Follicular lymphoma, aged 60-70 years
Reported symptoms: Hot sweats at night, lump on cheek.
Free text: “I never realised that hot sweats were a problem, as most of my friends have them”.
Interval: Total - 1 month.

Myeloma, aged 50-60 years
Reported symptoms: Stomach-ache.
Free text: “Originally diagnosed as diverticulitis and given antibiotics. Further investigation showed that I was anaemic. The pain was getting worse so I went to (hospital) A&E and blood tests showed a kidney problem. Further investigation revealed the cause of the kidney problem to be multiple myeloma.”
Interval: Patient - immediate; diagnostic - 1 month.

Myeloma, aged 50-60 years
Reported symptoms: Aches in bones/joints, general mood change.
Free text: “I think most of the time my doctor at doctors thought I was just a hypochondriac and putting it on as I suffer from long term post-traumatic stress disorder.”
Interval: Total - 1 year.

Myeloma, aged 60-70 years
Reported symptoms: Backache, tiredness, poor skin and hair.
Free text: “I had two hip replacements in the past. I assumed that the backache (month) was due to something wrong with these. I was prescribed (drug) and later (drug). My doctor sent me for hip x-ray at the hospital only after the physio I was seeing asked (doctor) directly. This came back with no problem with the hips. As regards the backache, this just got worse and worse and still no referral to an ortho was arranged until I had reached rock bottom physically and mentally. The ortho blood tests revealed high calcium levels and I was admitted as an emergency (month).”
Interval: Patient - 1 month; diagnostic - 1 year.

Myeloma, aged 70-80 years
Reported symptoms: Breathless, lack of energy, severe back pain.
Free text: “I contacted my GP in (month) for a severe back pain – X-rays revealed a pressure fracture of a vertebrae in the thoracic region. I was referred to (consultant in orthopaedics) at (hospital) who supplied a spinal brace and effective pain killers. Following a 6 week period and further visit to (orthopaedic consultant at hospital) my GP asked me to supply a blood sample to check how severe my osteoporosis was, as he thought that was the cause of the pressure fracture. This revealed that I was suffering from myeloma and had had it for some time.”
Interval: Total - 22 months.

Myeloproliferative neoplasm, aged 30-40 years
Reported symptoms: Itchiness (mainly legs, also arms, back and chest), red/brown speckles on toes and ankles, migraine.
**Free text:** “Although I was aware of the symptoms for some time I had put them down to other potential causes e.g. itchiness seemed to follow certain foods, speckles on toes/ankles looked like freckles, migraines came when tired following busy periods at work and more recently, in October 2010, becoming a father (when I also felt faint at work on a couple of occasions when particularly tired). The itchiness had become more regular and more severe in that I was unable to sleep on some nights (which could be several nights in a row) obviously adding to the tiredness. However, the symptoms were more of an inconvenience that a particular worry and I didn’t specifically seek medical advice. I just mentioned them when visiting the doctor for an unrelated knee pain. The subsequent blood test (in light of the speckles) uncovered the blood disorder.”

**Interval:** Patient – 18 months; diagnostic – 1 year.

**Myeloproliferative neoplasm, aged 60-70**

**Reported symptoms:** None reported.

**Free text:** “I didn’t seek medical help for my blood disorder – it was detected through the regular blood tests which I have as part of the monitoring of my diabetes.”

**Interval:** Incidental finding – no delay.

**Acute myeloid leukaemia, aged 40-50 years**

**Reported symptoms:** Lower back ache, unexplained bruises, feeling weak and tired.

**Free text:** “On (date), the day I first went to the Doctors, I was able to carry out my normal daily duties e.g. shopping, walking about, cleaning etc. The only reason I went to the Doctors was because of a few unexplained bruises. I had a period at the time which was a lot heavier than my normal ones. This got worse throughout the week, so I think I would have noticed something was wrong had I not already been to the doctors. I was admitted to hospital (day after help-seeking).”

**Interval:** Patient – 2 months; diagnostic – 1 day.