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Original Research

# Emergency admission and survival from aggressive non-Hodgkin lymphoma: A report from the UK's population-based Haematological Malignancy Research Network

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**KEYWORDS**
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**Abstract** ***Background:*** Non-Hodgkin lymphoma (NHL) is often diagnosed after emergency presentation, a route associated with poor survival and an indicator of diagnostic delay. Accounting for around half of all NHLs, diffuse large B-cell lymphoma (DLBCL) is of particular interest since although it is potentially curable with standardised chemotherapy it can be challenging to identify at an early stage in the primary care setting.
***Patients and methods:*** Set within a socio-demographically representative United Kingdom population of around 4 million people, data are from an established patient cohort. This report includes all patients (≥18 years) diagnosed with DLBCL 2004–2011 (n = 1660). Emergency admissions were identified via linkage to Hospital Episode Statistics using standard methods, and survival was examined using proportional hazards regression.
***Results:*** Two out of every five patients were diagnosed following an emergency admission, and this was associated with advanced disease and poor survival ($p < 0.001$). Among the 80% of patients treated with curative chemotherapy, survival discrepancies emerged at the point of diagnosis; the adjusted hazard ratio (emergency versus non-emergency) at one month being 4.0 (95% confidence interval 1.9–8.2). No lasting impact was evident in patients who survived for 12 months or more.

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***Conclusion:*** Emergency presentation impacts negatively on DLBCL survival; patients presenting via this route have significantly poorer outcomes than patients with similar clinical characteristics who present via other routes.


## 1. Introduction

Cancer survival rates are reported to be poorer in Britain than many other European countries, resulting in an estimated 7000 avoidable premature deaths each year [1]. The evidence suggests that diagnostic delay is a major contributor to these differences, and hence the promotion of early diagnosis is being tackled through policy guidance and targets, with progress being audited nationally [2–6]. Nonetheless, despite some positive changes, there is considerable scope for improvement [7].

Emergency presentation is often considered a crude marker of diagnostic delay for cancers that commonly present with early signs and symptoms [8,9]; the analysis of routinely compiled health data confirming that this route to diagnosis is associated with long intervals and poorer outcomes [10]. Among haematological cancers (lymphomas, myelomas and leukaemias), emergency presentation is relatively common [10,11]. While this is clearly the appropriate route for conditions like the acute leukaemias, the reasons why a relatively large proportion of patients with non-Hodgkin lymphomas (NHL) present as an emergency and have poorer survival is less obvious.

As a group, NHLs are challenging to study since they comprise a heterogeneous spectrum of cancers with diverse patterns of onset, treatments and outcomes; the pathways of patients diagnosed with incurable but comparatively indolent subtypes, like follicular lymphoma and marginal zone lymphoma, tend to follow a remitting-relapsing course with periods of observation being interspersed with multiple lines of chemotherapy, whereas those of patients with more aggressive subtypes tend to dichotomise according to whether the cancer is potentially curable or not [12,13]. In this context, diffuse large B-cell lymphoma (DLBCL), which is the commonest haematological malignancy and accounts for around half of all NHLs, is of particular interest since although it is curable with standardised chemotherapy administered over a 6–8 month period, patients who present with advanced disease tend to do less well than those diagnosed at an earlier stage [14–17].

In the general patient population, DLBCL 5-year overall survival is now around 60%, disease/treatment-related deaths being highest in the first few months following diagnosis [14–16,18]. Focussing on deaths occurring within 3 years of diagnosis, the present report uses data from an established United Kingdom (UK) patient cohort to examine the potential impact of emergency presentation on outcome in patients with DLBCL.

## 2. Methods

The study is set within the Haematological Malignancy Research Network (HMRN: www.hmrn.org), a population-based patient cohort instigated in 2004 to generate 'real world' evidence-based data for research and audit purposes [19]. HMRN's catchment population of around 4 million is socio-demographically similar to that of the UK as a whole [20]. Patient care within HMRN is provided by 14 hospitals, clinical practice adheres to national guidelines and all diagnoses (over 2200 new patients annually) are made and coded to the latest World Health Organisation (WHO) classification [12,19,21] by clinical specialists at a single integrated haematopathology laboratory (the Haematological Malignancy Diagnostic Service: www.hmds.info); which was cited in the UK's Cancer Reform Strategy as 'the model for delivery of complex diagnostic services' [2].

HMRN operates with Section 251 support under the National Health Service (NHS) Act 2006, and all patients have prognostic, full treatment and outcome data collected to clinical trial standards. All HMRN patients are 'flagged' for death at the national Medical Research Information Service and are routinely linked to Hospital Episode Statistics Admitted Patient Care (HES-APC) data. Area-based population counts are sourced from the Office for National Statistics; with the income domain of the national index of deprivation being used as a marker of socio-economic status [15,22].

The present report focusses on patients aged 18 years or over who were newly diagnosed with *de novo* DLBCL between September 2004 and March 2011; all of whom were followed up for death for a minimum of 3 years. Primary source information on cancer stage, performance status, disease-associated systemic symptoms (B-symptoms), nodal status and treatment were obtained directly from medical records [15]. Following guidelines outlined by NHS Digital, hospital admissions were constructed from HES-APC. Using a similar approach to the Routes to Diagnosis initiative [10], emergency presentation was defined as an admission within 30 days of diagnosis directly from the accident and emergency (A&E) department (HES-APC admission method codes 21, 28), consultant-led outpatient clinic (code 24), bed