

Understanding outcomes in leukaemia; why grouping different cancers is misleading

NCIN Data Briefing

Background

Within the blood cancers 'leukaemia' is the name given to a collection of diseases in which abnormal white blood cells fill up the bone marrow, preventing normal blood cells from being made. It has been common practice to present outcome data for all types of leukaemia grouped together (e.g. NCIN UK Cancer e-Atlas), but because of the diversity of these conditions this can be very misleading.

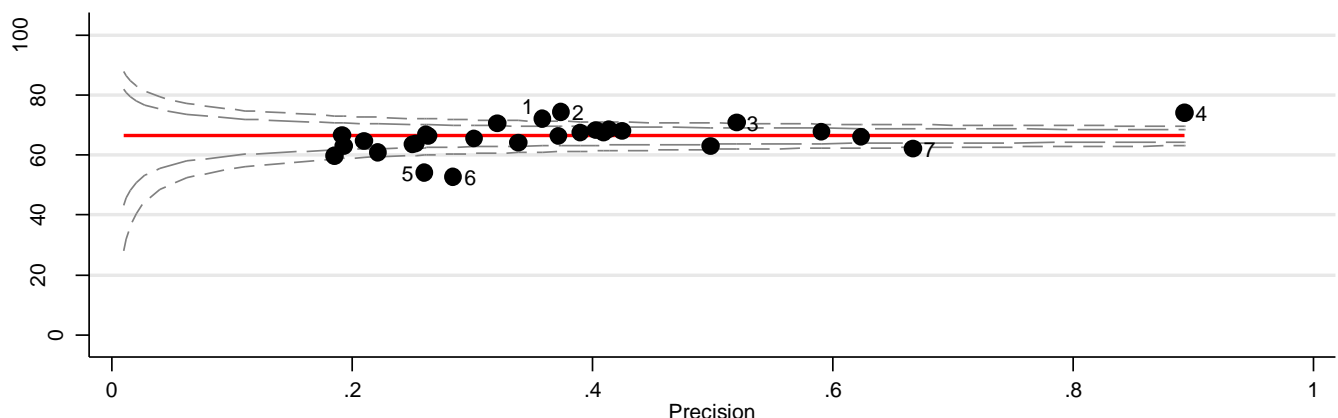
Leukaemia is classified as either *acute* or *chronic* (depending on the apparent maturity of affected cells) and either *lymphoid* or *myeloid* (depending on the cell line they come from). In the *acute* leukaemias there is the possibility of cure, with individuals who survive the illness being subsequently free of the cancer. For *chronic* leukaemias, whilst survival is more likely, current treatments work through controlling but not eliminating the cancer. The commonest forms of leukaemia are Chronic Lymphocytic Leukaemia (CLL) (c.3,000 new cases per year in the UK, more common in the elderly; ICD-10 C91.1) and Acute Myeloid Leukaemia (AML) (c.2,300 new cases per year, more common over age of 60; ICD-10 C92.0, C92.4, C92.5, C93.0, C94.0, C94.2), rarer forms of leukaemia are Acute Lymphoblastic Leukaemia (ALL) (c.700 new cases per year, mainly in children; ICD-10 C91.0) and Chronic Myeloid Leukaemia (CML) (c.570 new cases per year, mainly in older people; ICD-10 C92.1).

To illustrate the problems of grouping outcome data for leukaemia we have examined apparent variability in short term survival from these diseases by English cancer network.

Results

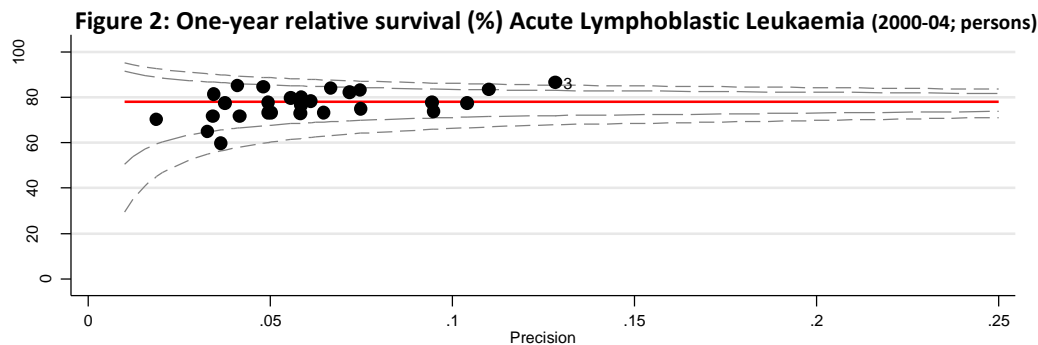
When cases of leukaemia (ALL, AML, CLL, and CML) diagnosed in the time period 2000-2004 were grouped together the average relative one-year survival in England was 66%. The range across 28 English cancer networks was 53-74% and 7 networks were identified as 'outliers' (networks 1, 2, 3, 4, 5, 6, 7) with one-year relative survival rates statistically significantly different from the national average (figure 1).

Figure 1: One-year relative survival (%) all leukaemias grouped by English cancer network (2000-04; persons)

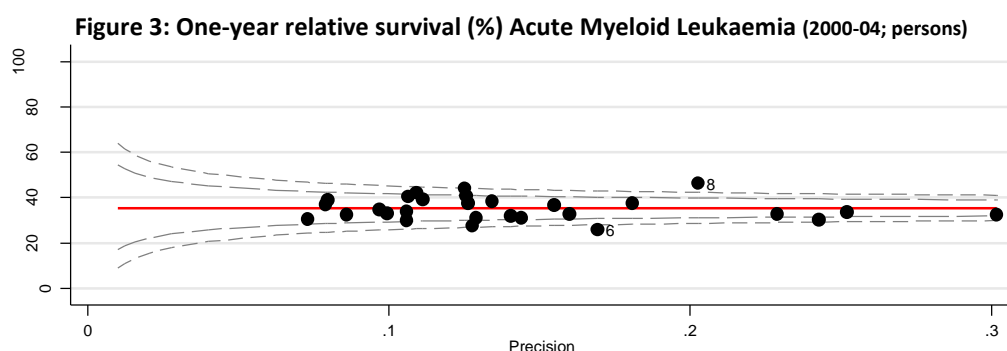


However, different patterns were then seen when each of the leukaemia groups were considered separately.

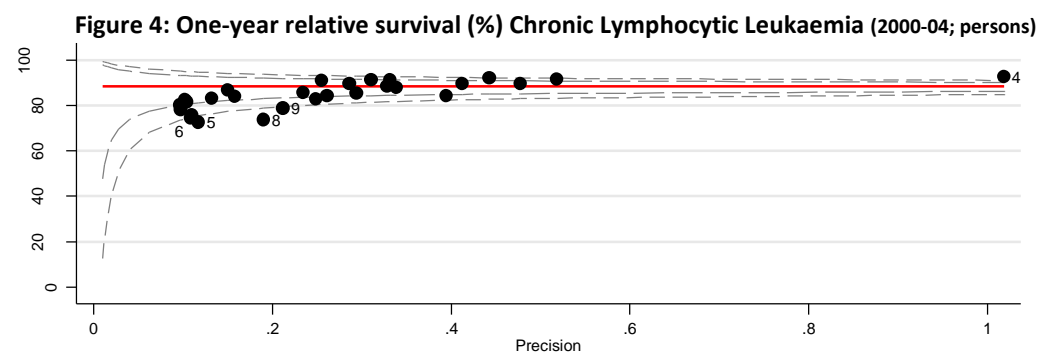
For **Acute Lymphoblastic Leukaemia** the average relative one-year survival was 78%, the range across cancer networks was 60-87% and only one network (network 3) was identified as an 'outlier' (figure 2).



For **Acute Myeloid Leukaemia** the average relative one-year survival was 35%, the range across cancer networks was 26-46% and two networks (networks 6 and 8) were identified as 'outliers' (figure 3).



For **Chronic Lymphocytic Leukaemia** the average relative one-year survival was 88%, the range across cancer networks was 73-93% and five networks (networks 4, 5, 6, 8, 9) were identified as 'outliers' (figure 4).



For **Chronic Myeloid Leukaemia** the average relative one-year survival was 78%, the range across cancer networks was 61-92% and only one network was identified as an 'outlier' (network 10) (figure 5).

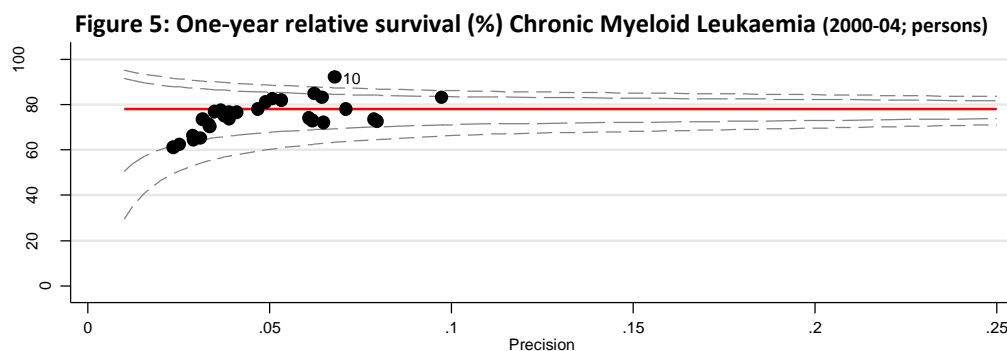
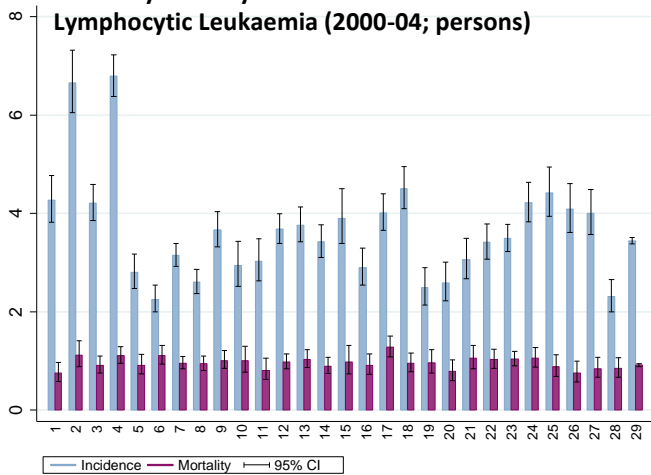


Figure 6: Age and sex standardised incidence and mortality rates by cancer network for Chronic Lymphocytic Leukaemia (2000-04; persons)



For **Chronic Lymphocytic Leukaemia** analysis of survival outcomes between places and across time is further complicated because both diagnostic thresholds and ascertainment of diagnoses by registries have varied across time and between different places. This is a disease where 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.

This is illustrated in figure 6, in which age-standardised incidence and mortality from CLL are shown for 28 English cancer networks and for England combined (network 29). Whilst mortality rates are broadly comparable there is wide variation in apparent incidence. In areas such as networks 2 and 4 high levels of diagnosis by laboratories and ascertainment by cancer registries mean that cases of CLL of all levels of severity

are recorded. In areas such as network 6, ascertainment is much lower, and it is probable that more indolent cancers, with better survival, are disproportionately missing. This variability in registration will lead to spurious differences in relative survival.

Commentary

The 'average' survival reported if all individuals with leukaemia are grouped together does not represent the experience of any of the individual cancers. We have illustrated this using short term survival, but the problem is also apparent if survival over longer time periods is considered. Grouping different forms of leukaemia together is also not helpful in identifying 'outliers'. In these analyses there was one network (network 1) that appeared as an outlier for 'leukaemia' survival, but not for any of individual diseases, and some networks were outliers for specific cancers but not for 'leukaemia' (networks 8, 9 and 10). The variation in cancer registration rates for CLL has a major bearing on apparent outcomes if the leukaemias are grouped together. As CLL generally has a better prognosis than other leukaemias, cancer networks where ascertainment is higher will appear to have better outcomes. Improvements in ascertainment are occurring over time for some leukaemias (CLL) and whilst survival is relatively static for ALL and AML it has improved significantly for CML, it is therefore not sensible to try and interpret time trends in grouped data for different leukaemias. Presenting data by individual disease group for leukaemia means the uncertainty around outcome measures will be greater as the numbers of cases is smaller, but it does allow meaningful comparisons to be made between places and across time. Whilst there may be limited value in grouping leukaemias together when considering measures of the 'burden' of disease such as incidence and prevalence, there is no justification for grouping these cancers when considering outcomes.

Methods

Relative survival reflects the excess mortality among cancer patients, over and above background mortality in the region where they live. Cumulative relative survival up to one year after diagnosis was estimated from calendar year-, age- and sex- specific English life tables using the cohort approach for patients diagnosed during 2000-2004. Funnel plots were used to examine network variation in one-year survival. For each cancer network, the estimate of one-year survival was plotted against the precision for each estimate (taken as the inverse square of its standard error), the value shown on the funnel plot as a horizontal line is the pooled estimate of survival in England. The 95 per cent and 99.8 per cent control limits represent two and three standard deviations, respectively, from the national average at each level of precision. Cancer networks outside the 99.8% control limits were considered to be outliers. Age and sex standardised incidence and mortality was estimated for each cancer network using data from 2000-2004 and the European standard population.

The National Cancer Intelligence Network is a UK-wide initiative, working to drive improvements in standards of cancer care and clinical outcomes by improving and using the information collected about cancer patients for analysis, publication and research. Sitting within the National Cancer Research Institute (NCRI), the NCIN works closely with cancer services in England, Scotland, Wales and Northern Ireland. In England, the NCIN is part of the National Cancer Programme.