Time trends in 5-year relative survival for major haematological malignancies.

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Rationale

Over the last two decades novel effective treatments for haematological malignancies (HMs) became available, with the development of monoclonal antibodies with specific cellular targets ("targeted therapy") [1-5].

The diffusion of these treatments in the clinical practice has improved remarkably the prognosis of chronic myeloid leukaemia, as well as that of many lymphoid neoplasms and, to a lesser extent, of multiple myeloma [6-8]. Studies documenting these improvements are largely based on hospital series of patients, or derive from controlled clinical studies, whereas there are not many studies investigating whether these prognostic improvements are evident also using population-based cancer registry data [9], which include all cases incident in the cancer registry area and reflect the current clinical practice. Past EUROCARE studies evidenced remarkable differences in survival for HMs across European countries; however, due to changing classification and inclusion criteria over the recent decades, it was not possible to investigate over time changes in survival. The HAEMACARE project, implemented on the EUROCARE database [10], promoted the harmonisation and standardisation of HM cancer registry data, and the uniform adoption of updated International Classification of Disease for Oncology (ICD-O). [11], making now possible to analyse survival
time trends. It is expected that the diffusion of effective treatments reduce the inequalities in survival across European regions that were highlighted by past EUROCARE studies for patients diagnosed in early 2000s.

**Aims**
The aims of our study are:
- To investigate changes over time in survival, analysing age-standardised 5-year relative survival in four consecutive 3-year periods (1996-1998, 1999-2001, 2002-2004, 2005-2007), by European region and by age at diagnosis; analyses will be carried out for specific HMs
- to estimate the relative excess risk of death during first 5 years after diagnosis for the HMs previously selected, after adjusting for period of diagnosis, age at diagnosis and European region

**Material and Methods**
For our analyses, carried out on individual data, we need information on
- date of birth
- date of diagnosis
- date of last follow-up
- vital status
- cancer registry
- morphology, collected according to the 3rd edition of ICD-O (ICD-O-3 [12]), for all adult (≥15 years) patients alive in some points from 1992 to 2007, diagnosed with HMs and followed up to the end of 2008.

In particular, we would like to focus on those HMs for which effective treatments were made available since early 2000s and grouped according to HAEMACARE criteria [11]:

- Hodgkin Lymphoma (HL, ICD-O-3 codes: 9650-9655, 9659, 9661-9667)
- Diffuse Large B-cell lymphoma (DLBCL: 9675, 9678-9684)
- Follicular lymphoma (FL: 9690-9698)
- Chronic Lymphocytic Leukaemia and Small B lymphocytic leukaemia (CLL/SBLL: 9670, 9823)
- Precursor lymphoblastic leukaemia/lymphoma (LBL/L: 9727-9729, 9835-9837)
- Multiple Myeloma/Plamocytoma (MM/P: 9731-9734)
- Acute Promyelocytic Leukaemia (APL: 9866)
Acute Myeloid Leukaemia (excluding APL) (AML: 9840, 9861, 9867, 9870-9874, 9891-9931, 9984, 9987)
Chronic Myeloid Leukaemia (CML: 9863, 9875)
Other Chronic Myeloproliferative Neoplasms (excluding CML) (CMPN: 9950, 9960-9964)
Myelodysplastic Syndromes (MDS: 9980-9983, 9985-9986, 9989)
Poorly specified tumours (NOS), divided in
  Lymphoid malignancy of unknown type: 9590, 9820, 9832; NHL NOS: 9591
  Myeloid malignancy of unknown type: 9800, 9801, 9805, 9860)

Statistical methods
Relative survival [13] is estimated by the period hybrid approach [14]. Relative survival is the ratio of observed survival in the patient group and the expected survival of a comparable group from the general population which is assumed to be free from the cancer under study. The expected survival is estimated using the Ederer II method [15] using cancer registry area-specific official mortality data. Relative survival is age-standardised using the International Cancer Survival Standards [16]. Relative excess risks of death at 5 years since diagnosis are estimated by using generalized linear models assuming that the observed number of deaths followed a Poisson distribution [17]. All the analyses are carried out using the 12th version of STATA Statistical software [18].

Timing
A draft of the paper will be circulated among the EUROCARE Working Group at the end of October or, at least, within mid November.

References
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