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Leukaemia incidence and survival in children and adolescents in Europe during 1978–1997. Report from the Automated Childhood Cancer Information System project

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ABSTRACT

Leukaemias constitute approximately one-third of cancers in children (age 0–14 years) and 10% in adolescents (age 15–19 years). Geographical patterns (1988–1997) and time trends (1978–1997) of incidence and survival from leukaemias in children (n = 29,239) and adolescents (n = 1929) were derived from the ACCIS database, including data from 62 cancer registries in 19 countries across Europe. The overall incidence rate of leukaemia in children was 44 per million person-years during 1988–1997. Lymphoid leukaemia (LL) accounted for 81%, acute non-lymphocytic leukaemia (ANLL) for 15%, chronic myeloid leukaemia (CML) for 1.5% and unspecified leukaemia for 1.3% of cases. Adjusted for sex and age, incidence of childhood LL was significantly lower in the East and higher in the North than in the British Isles. The overall incidence among adolescents was 22.6 per million person-years. The incidence of LL was rising in children (0.6% per year) and adolescents (1.9% per year).

During 1988–1997 5-year survival of children with leukaemias was 73% (95% CI 72–74) and approximately 44% for infants and adolescents. Similar differences in survival between children and adolescents were observed for LL, much less so for ANLL. Survival differed between regions; prognosis was better in the North and West than the East. Remarkable improvements in survival occurred in most of the subgroups of patients defined by diagnostic subgroup, age, sex and geographic categories during the period 1978–1997. For children with ANLL most improvements in survival were observed in the 1990s.

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1. Introduction

Leukaemias comprise approximately one-third of all childhood cancers and one-tenth of adolescent cancers in industrialised countries.[1] As the most frequent and most prevalent childhood malignancy, leukaemias have generated much medical and societal interest. Since the late 1960s effective treatment became available for the largest leukaemic subgroup, acute lymphoblastic leukaemia (ALL),[2] which led to considerable improvement in survival in the following decades, but which varied across Europe.[3] Similar changes have been observed since the late 1980s for children with acute non-lymphocytic leukaemia (ANLL).[4]

Over the study period, several classification systems of leukaemias have been developed, based on morphological,[5] immunological[6] or cytogenetic[7] criteria. Cancer registries apply standard coding of the International Classification of Diseases for Oncology, which has been updated in 2000[8] in agreement with the WHO histological classification.[9] True comparative studies of incidence and survival were hampered by selective inclusion of cases (depending on classification criteria) and incomplete registration or follow-up related to strict interpretation of data privacy rules, especially in central and southern Europe.[4]

The increases in incidence of childhood ALL reported in many populations[10] have been attributed to a variety of factors that are often present simultaneously: higher diagnostic awareness, changing reproductive and perinatal factors, such as increasing parental age at birth, more firstborns or smaller families[11] and higher birth-weights.[12] In addition, changing socio-economic conditions may contribute to rising incidence trends in two ways. On the one hand, delayed exposure to infections, possibly due to widespread vaccinations and better housing[13] may lead to reduced immunity, counteracted by earlier attendance at day care. On the other hand, increasing mobility of populations may stimulate occurrence of childhood leukaemia as uncommon response to (probably) common infectious agent(s).[14,15] Both of these secular changes modify the response of the immune system. Lower death rates from infections may also contribute indirectly to the increase in incidence rates of common childhood leukaemia. By contrast, incidence rates of ANLL have hardly changed and the putative risk factors studied include alcohol use during pregnancy[16] and maternal history of miscarriage.[17]

Survival from leukaemia has improved in industrialised countries since the late 1960s and early 1970s, initially for ALL and since the 1980s also for ANLL.[2–4]

The Automated Childhood Cancer Information System (ACCIS), a collaborative project of European cancer registries, aims to collect, validate, present and interpret data on cancer incidence and survival of children and adolescents in Europe.[18] We now describe incidence and survival of children and adolescents registered with leukaemia in European cancer registries during 1978–1997, according to major morphological subgroups, interpret our findings and suggest avenues for research.

2. Material and methods

Detailed information on the ACCIS database is given elsewhere [Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue]. For this study, the analyses were based on data from the 62 population-based cancer registries in 19 countries listed in Table 1, which contributed to the ACCIS database and met the defined quality criteria for completeness, validity and comparability. Altogether 29,239 childhood and 1929 adolescent cases of leukaemia were extracted from the ACCIS database and included in various analyses. The analyses for children aged 0–14 years were based on data from both paediatric and general cancer registries, while those for adolescents aged 15–19 years were derived from general cancer registries (Table 1). Standard variables for each case included basic demographic data (age, sex, country or region of residence), information on the diagnosis (date and basis of diagnosis, morphology) and follow-up of the patient (date of last contact and vital status). Diagnoses were grouped according to the International Classification of Childhood Cancer (ICCC),[19] in which leukaemia is subdivided into several subgroups: lymphoid leukaemia (LL, subgroup Ia), acute non-lymphocytic leukaemia (ANLL, Ib), chronic myeloid leukaemia (CML, Ic), other specified leukaemias (Id) and unspecified leukaemias (Ie). Among children, more than 98% of the subgroup LL consisted of the acute lymphoblastic leukaemia (ALL, M-9821) and a few cases of 'unspecified lymphoid leukaemia' (M-9820, 1.2%). Subgroup Ia comprised also a few other rare types, the most common of those being chronic lymphocytic leukaemia (0.007%). We therefore used the abbreviations ALL and LL interchangeably to denote subgroup Ia.

The results are reported by gender and age-group (0, 1–4, 5–9, 10–14 and 15–19 years). To examine geographical differences in incidence and survival we grouped cancer registries into five regions (British Isles, East, North, South and West) (Table 1). The populations covered for children and for adolescents differed for all regions except the North as well as Slovenia, Slovakia and Estonia. Using data from the cancer registries with a sufficiently long registration period, time trends were studied by period of diagnosis (1978–1982, 1983–1987, 1988–1992, and 1993–1997). The distribution of cases over the periods and regions, together with selected data quality indicators are shown in Table 2. Detailed data on incidence and survival are given for the most recent period 1988–1997.

Incidence rates were calculated as the average annual number of cases per million person-years and age-standardisation (ASR) was performed by the direct method from age-specific incidence rates for age-groups 0, 1–4, 5–9 and 10–14 years, using the weights of the World standard population. Variations in incidence between the five European regions were examined in a Poisson regression model adjusted for sex and age group, as applicable, with the British Isles as the reference region. Incidence time trends were examined using Poisson regression models of rate on calendar year, adjusted for sex, age group and region (as applicable). Changes in rates were expressed as average annual percent change (AAPC).

Survival was estimated by the actuarial life-table method[20] and confidence intervals were based on computation of standard error according to Greenwood.[21] Differences between survival curves were evaluated using log-rank test or log-rank test for trend. The cases with zero follow-up time were excluded from survival analyses (mostly those registered from