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Childhood cancer mortality in Europe, 1970–2007

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ABSTRACT

To update trends in childhood cancer mortality in Europe, we analysed mortality data derived from the World Health Organization for all childhood neoplasms, bone and kidney cancers, non-Hodgkin's lymphomas (NHL) and leukaemias, in 30 European countries up to 2007. Between 1990–1994 and 2005–2007, mortality from all neoplasms steadily declined in most European countries (from 5.2 to 3.5/100,000 boys and from 4.3 to 2.8/100,000 girls in the European Union, EU). In 2005–2007, however, mortality rates from childhood cancers were still higher in countries from Eastern (4.9/100,000 boys and 3.9/100,000 girls) and Southern (4.0/100,000 boys and 3.1/100,000 girls) Europe than in those from Western (3.1/100,000 boys and 2.5/100,000 girls) and Northern (3.2/100,000 boys and 2.5/100,000 girls) Europe. Similar temporal trends and geographic patterns were observed for leukaemias, with declines from 1.7 to 0.9/100,000 boys and from 1.3 to 0.7/100,000 girls between 1990–1994 and 2005–2007 in the EU. For kidney cancer and NHL mortality rates were low and have been declining in larger European countries over the last 15 years. The pattern of trends was less clear for bone cancer, with no systematic downward trends at age 0–14, though some fall was evident at age 15–19. Thus, mortality from childhood cancer continued to decline over more recent years in most European countries. However, the mortality rates in Eastern – but also Southern – European countries in the mid 2000's were similar to those in the Western and Northern European ones in the early 1990's. Some further improvement in childhood cancer mortality is therefore achievable through more widespread and better adoption of currently available treatments.

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1. Introduction

From the 1960's onwards, mortality from childhood leukaemias and other childhood cancers has showed substantial declines in developed areas of the world.^{1–4} In the United States (USA), between 1990 and 2004 death rates declined by 1.3% per year for all neoplasms, and by 3.0% per year for childhood leukaemias.^{5,6} In Western Europe, mortality from all childhood cancers and leukaemias declined by about 60% between

the mid 1960's and the mid 1990's. The downward trends started later (i.e. between the mid 1970's and the late 1980's) and were appreciably smaller (by about 30%) in countries from Eastern Europe.³

To analyse recent patterns in childhood cancer mortality in various European countries, we updated trends up to 2007, and provided an overview of trends for all childhood cancers and leukaemias since 1970 using joinpoint regression analysis.⁷

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2. Materials and methods

We derived cancer death certification data from total cancer, and four cancer sites including bone and articular cartilage, kidney and other urinary sites (predominantly Wilm's tumour), non-Hodgkin's lymphomas (NHL) and leukaemias at age 0–14 (further subdivided in 4 age groups, 0, 1–4, 5–9 and 10–14 years) for 30 European countries for the period 1970–2007 from the World Health Organization (WHO) database.⁸ Giving the higher incidence of bone cancer in adolescents, for this neoplasm we also considered death certification data at age 15–19 years.

For Ukraine and the Russian Federation data were available only for NHL, leukaemias and all cancers. For Albania, Croatia, the Czech Republic, Estonia, Latvia, Lithuania, the Republic of Moldova, the Russian Federation, Slovakia, Slovenia and Ukraine data were available only since the early-mid 1980's. For Portugal data were available only up to 2003; for Albania and Bulgaria up to 2004; for Estonia, Hungary, Slovakia, Spain and Ukraine up to 2005; and for Croatia, Denmark, France, Germany, Italy, Norway, Poland, the Russian Federation, Sweden and Switzerland up to 2006.

During the calendar period considered, three different Revisions of the International Classification of Diseases (ICD) were used.^{9–11} For most countries, there were no major changes in the classification or coding of the cancers considered between various ICD Revisions. We recoded classification of cancer deaths – for all calendar periods and countries – according to the 10th Revision of the ICD. It was impossible to obtain meaningful death certification data for neoplasms of the nervous system, on account of difficulties in histopathological classification and for changes in the classification of neuroblastoma, which is coded in part to the organ affected (chiefly, the adrenal gland, i.e. with cancers of endocrine organs), in part to connective and soft-tissue sarcomas, and in part to the nervous system. In the present analysis, we did not consider mortality from other childhood cancers (i.e. eye (retinoblastoma) and Hodgkin's lymphomas, HL), because of the limited number of deaths in most European countries (less than 10 deaths for each sex registered in the whole Europe).

We obtained estimates of the resident population at age 0–14 and 15–19 years from the same WHO database.⁸ From the matrices of certified deaths and resident population, we computed age-standardised mortality rates at age 0–14 per 100,000 boys and girls, using the direct method on the basis of the world standard population.¹² We computed also age-standardised rates for the European Union (EU) as a whole (defined as the 27 member states as in January 2007, excluding Cyprus, for which data were not available and Belgium, for which data were provided only up to 1997), and for four European subareas, i.e. Eastern (Albania, Bulgaria, Croatia, the Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, the Republic of Moldova, Romania, Slovakia, Slovenia and Ukraine), Southern (Greece, Italy, Portugal and Spain), Western (Austria, France, Germany, the Netherlands and Switzerland), and Northern (Denmark, Finland, Ireland, Norway, Sweden and the United Kingdom) Europe. In a few countries, data were missing for one or more calendar years. No extrapolation was made for the missing data.

We also computed cumulative risk of death at age 0–14 years (i.e. the probability that a child would die from a specific cancer before 14 years of age, in the absence of any competing causes of death) on the basis of age-specific rates for the period 2005–2007 (unless otherwise specified).¹³

To identify significant changes in trend for all childhood neoplasms and leukaemias, we performed joinpoint regression analyses using the software provided by the Surveillance Research Program of the US National Cancer Institute.¹⁴ The aim of this analysis is to identify possible points where a significant change in the linear slope of the trend (on a log-scale) is detected over the study period.⁷ In joinpoint analysis, the best fitting points, called 'joinpoints', are chosen where the rate changes significantly. The analysis starts with the minimum number of joinpoints (e.g. 0 joinpoints, namely a straight line), and tests whether one or more joinpoints (up to 3) are significant and must be added to the model. Each significant joinpoint that indicates a change in the slope (if any) is retained in the final model. To describe linear trends by period, the estimated annual percent change (APC) is then computed for each of those trends by fitting a regression line to the natural logarithm of the rates using calendar year as a regressor variable.

3. Results

Table 1 shows the age-standardised 0–14 years mortality rates from all childhood cancers and leukaemias per 100,000 boys and girls in various European countries and in the EU in the periods 1990–1994, 2000–2004, and 2005–2007, and the average annual number of certified deaths for the most recent period. The histograms of the age-standardised 0–14 years mortality rates in the period 2005–2007 are also presented in Fig. 1. In 1990–1994, mortality rates from all childhood neoplasms varied by about a factor of 3, between the highest rates in Estonia, the Albania, the Republic of Moldova, Romania and Ukraine (over 9/100,000 boys and over 7/100,000 girls), as well as in other Eastern and Southern European countries, and the lowest ones in Ireland (3.6/100,000 boys and 2.6/100,000 girls), and other Northern European countries. Rates were 5.3/100,000 boys and 4.3/100,000 girls in the EU. For almost all countries mortality from all childhood neoplasms steadily declined over the last 15 years. In 2005–2007, the highest mortality rates were in the Republic of Moldova, Romania and Ukraine (over 6/100,000 boys and over 4.5/100,000 girls) and other Eastern European countries, followed by southern European countries, and the lowest ones in Austria, Denmark and Norway (around 2/100,000 boys and 1.3/100,000 girls) and other Northern European countries (Fig. 1). Overall rates were 3.5/100,000 boys and 2.8/100,000 girls in the EU. Similar geographic patterns and temporal trends were observed for leukaemia. In 1990–1994, the highest mortality rates were in Latvia, the Republic of Moldova, Romania and Ukraine (over 2.7/100,000 boys and over 2.4/100,000 girls), followed by other Eastern and Southern European countries, and the lowest ones in Ireland (1.0/100,000 boys and 0.4/100,000 women) and other Northern countries. Overall leukaemia rates in the EU were 1.7/100,000 boys and 1.3/100,000 girls. In 2005–2007, the highest mortality rates from leukaemias were in

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