Standardized incidence rate of leukaemia as defined by ICD-10 codes C90–95 in children aged 0 to 14 years

This summary is based on national estimates of leukaemia incidence in children aged under 15 years. It also contains information on the environment and health context and policy relevance and an assessment of the situation in the WHO European Region.

**Key Message**

Leukaemia is the most common childhood malignancy. It accounts for 30% of all cancers diagnosed in children under 15 years of age in industrialized countries. Around 2000, the average incidence for this age group in the European Region was 46.7 cases per million per year, with a slightly lower level in eastern than in western European countries. European population-based cancer registries show an average increase in the incidence of childhood leukaemia of 0.7% per year between 1970 and 1999.

Effective preventive measures require knowledge about etiology and cover the early stages of development (in utero). There is a need for focused research to unravel the causes of childhood leukaemia.

**Rationale**

Virtually all childhood cancers have unknown causes. Specific potential environmental causative agents, such as ionizing and nonionizing radiation and environmental chemicals, make only a small contribution to childhood leukaemia. Nevertheless, given public concern about the impact of the environment on childhood leukaemia, the real potential for clustering, the possibility of other environmental risks and our incomplete understanding of how environmental agents react with living tissue, the surveillance of childhood leukaemia is important.

**Presentation of Data**

Fig. 1 shows estimated incidence (age-standardized on the world population) of leukaemia in children aged under 15 years for those countries of the European Region with population-based data available for years around 2000 (1–5). The average age-standardized incidence in participating areas was 46.7 cases per million per year. National estimates ranged from 35 cases per million per year in Israel to 60 cases per million per year in Italy and Malta.
Fig. 1. Estimates of age-standardized incidence of leukaemia in children aged under 15 years in the WHO European Region around 2000

**Note.** Incidence was standardized using the world population. For some countries (Belgium, Italy, Poland, Portugal, the Russian Federation, Serbia, Spain and Turkey), national estimates are based on regional registries.

**Source:** France: National Registry of Haematological Malignancies in Children (unpublished data courtesy of Dr J. Clavel)
Germany: German Childhood Cancer Registry (2)
Greece: Petridou et al. (3)
Hungary: National Paediatric Cancer Registry of Hungary (4)
Italy: Childhood Cancer Registry of Piedmont (unpublished data courtesy of Dr G Pastore); Childhood Tumour Registry of Marche (unpublished data courtesy of Professor F Pannelli); and 19 cancer registries in CI5-IX (1);
Spain: Spanish National Childhood Cancer Registry (unpublished data courtesy of Professor R Peris-Bonet); Childhood Cancer Registry Comunitat Valenciana (unpublished data courtesy of Dr M Vicente & Dr O Zurriaga); and 19 cancer registries in CI5-IX (1)
Switzerland: Swiss Childhood Cancer Registry (5)
United Kingdom: National Registry of Childhood Tumours (unpublished data courtesy of Mr C Stiller)
All other countries: CI5-IX (1).
**Health and Environment Context**

There are various types of leukaemia with different geographical distribution patterns. In Europe, acute lymphoblastic leukaemia (ALL) accounts for around 80% of leukaemia among children aged 0–14 years (6). ALL has an annual incidence of up to 40 cases per million children among industrialized western European countries and up to 30–35 cases per million in eastern European countries, but fewer than 20 per million in sub-Saharan Africa (7). In developed countries, more than 80% of ALL is of the precursor B-cell subtype that is responsible for the pronounced peak of incidence in early childhood and largely accounts for the observed variation in the total incidence of childhood leukaemia among countries (8,9). The second most frequent type of leukaemia in childhood is acute myeloid leukaemia (AML), which accounts for almost 20% of childhood leukaemia in Europe and has a fairly stable worldwide incidence of 5–9 cases per million per year (6,7).

In the majority of cases of childhood leukaemia, the cause is unknown. While a number of causes and highly suspected risk factors have been identified, reviews stress that these are responsible for only a very small number of cases. The known and highly suspected causes include genetic factors (2–3% of cases are associated with Down syndrome) and exposure to ionizing radiation in utero and after birth (10,11). Infectious diseases are likely to have a role in the etiology of childhood leukaemia, especially ALL (11,12). Delayed exposure to infection during early infancy could result in an abnormal response, leading to development of leukaemia. Leukaemia could also be a rare response to a specific although unidentified infectious agent.

Other environmental risk factors have been less clearly identified. The International Agency for Research on Cancer has concluded that extremely low-frequency electromagnetic fields are possibly carcinogenic to humans, based on consistent statistical associations of high-level residential magnetic fields with a doubling of risk of childhood leukaemia (13). Several studies suggest that children exposed to certain hazardous chemicals have an increased risk of leukaemia, with benzene being the most frequently suspected causal agent (11,14). A number of papers have shown statistical associations between the risk of childhood leukaemia and exposure to pesticides during pregnancy or childhood (11,15–18). The risks associated with environmental leukaemogens may be modified by genetic susceptibility (17,19).

A number of ecological studies show a positive correlation between leukaemia, particularly ALL, and increasing socioeconomic status (20,21). The reasons for this are not known.

**Policy Relevance and Context**

Environmental issues are often discussed in relation to childhood leukaemia, but the causes of the majority of cases are unknown and there is a lack of major multinational programmes fostering research into potential risk factors for leukaemia in Europe. As a result, there is also a lack of policies aimed directly at reducing the incidence of leukaemia.

The recent Regulation of the European Parliament and the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) is of relevance (22). It considers that the carcinogenicity, mutagenicity and reproductive toxicity of chemical industrial substances are priority criteria when they are submitted to security constraints and declarations authorizing their use. The target of REACH is to substitute progressively substances that are known to be safer for most carcinogenic, mutagenic and toxic industrial substances. Also relevant is Council Directive 97/43/Euratom (23), which aims to protect patients from excessive exposure to radiation for medical use and ensure that there is minimum exposure during pregnancy and early childhood.

**Assessment**

Between 1970 and 1999, there was an average annual increase in the incidence of childhood leukaemia of 0.7% (24). East–west differences were evident, with an average of 39.3 cases per million person-years in eastern European countries and 45.7 in western European countries during that period. The correlation between socioeconomic development and incidence of ALL may be relevant to the differences in rates observed between eastern and western European countries.

As the causes of childhood leukaemia are largely unknown, policies to reduce incidence are difficult to formulate or have limited impact. For example, policies to reduce exposure to ionizing or electromagnetic radiation potentially prevent only a small proportion of leukaemia cases. Thus it is necessary to undertake further coordinated research into environmental influences on leukaemia and environmental–genetic interactions. It is particularly important to monitor childhood leukaemia. National registers with continual follow-up that employ standardized or comparable methods should be universal.
Curing leukaemia is also of great importance. Most childhood leukaemia can be successfully treated, and by the mid-1990s the five-year survival rate had reached 82% for ALL and 53% for AML (6). Further collaborative research and exchange of knowledge about therapies among European countries could enhance the percentage of survivors in children diagnosed with leukaemia. From the public health point of view, mortality from leukaemia is an important co-indicator of the quality of the health care system, but it should be interpreted cautiously because of the tendency for survival to be higher in countries that also have a higher incidence.

### DATA UNDERLYING THE INDICATOR

**Data source**
The main data source used for the previous edition of this fact sheet was the ACCIS project, supported by the European Commission, with the objective of collecting, presenting, interpreting and disseminating data on childhood cancer in Europe (6,24,25). The ACCIS database contains 160 000 records of childhood and adolescent cancer cases registered over the 30-year period 1970–1999 in 78 European population-based cancer registries. For this update, information was taken mainly from Cancer incidence in five continents, Vol. IX (CI5-IX) (1), which was compiled from data supplied by population-based cancer registries covering persons of all ages. In a few countries without complete coverage of the national population in CI5-IX, these data were supplemented or replaced by data from specialized childhood cancer registries (2–5).

**Description of data**
The methodology sheet proposed incidences of number of cases per 100 000 person-years in children and young people aged 0–19 years. In this fact sheet, incidence is given as the number of new cases per million person-years in children aged 0–14 years. This shorter age range has been used since it permits the inclusion of additional countries and allows incidence to be estimated with greater precision in some other countries.

**Method of calculating the indicator**
National estimates of incidence standardized to world standard population aged 0–14 years: number of new cases per million person-years.

**Geographical coverage**
Sixty-five population-based cancer registries in 34 countries of the WHO European Region.

**Period of coverage**
Years around 2000, mostly represented by 1998–2002 but with some variation between registries.

**Frequency of update**
Every five years.

**Data quality**
Data sources differ according to their geographical and time coverage, which has to be borne in mind when comparisons are made. All data originated in cancer registries that contribute to CI5-IX or ACCIS, with quality verified using automatic checking procedures, or were taken from publications in peer-reviewed scientific journals.

From the public health point of view, mortality from leukaemia is an important co-indicator in assessing the quality of health care. Comparable methods of collection, classification, description and registration of information are important to allow comparisons between the incidence of and mortality from leukaemia. Complete national data registries for leukaemia in children and young people aged 0–19 years are crucial. More recent data are essential to assess further the problem of leukaemia. There is room for improved geographical coverage, especially in eastern and southern Europe.

### REFERENCES


FURTHER INFORMATION


Update 2009: Charles Stiller, Department of Paediatrics, University of Oxford, Oxford, United Kingdom.