



Original research

Conditional survival of children, adolescents and young adults (0–24 years) diagnosed with leukaemia during 2000–2014 world-wide: (CONCORD-3)

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ABSTRACT

Background: Population-based survival estimates provide valuable insights into cancer care patterns world-wide. Access to optimal treatment leads to better outcomes, however, treatment pathways vary globally. Conditional survival is the probability that patients who have already survived for a given number of years since diagnosis will live for an additional number of years. It is a useful proxy to assess the success of initial treatment or remission of leukaemia.

Methods: We analysed data for 164,563 patients aged 0–24 years diagnosed during 2000–2014, from 258 population-based cancer registries in 61 countries. Using the Pohar-Perme estimator, we estimated net survival at five years, conditional on surviving at least one year, and at 10 years conditional on surviving five years. To control for background mortality, we used life tables of all-cause mortality by single year of age, sex, country and calendar year. All-ages survival estimates were standardised to the marginal age distribution.

Findings: During 2010–2014, age-standardised five-year conditional net survival ranged from 61.8% in Mexico to 90% or more in 20 countries. By 2010–2014, five-year conditional survival in most high-income countries

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exceeded 90 % for children, but not for older patients, and for acute myeloid leukaemia it was typically 5–10 % lower than for lymphoid leukaemia. Ten-year conditional survival was 90 % or higher in most countries, with less variation world-wide.

Interpretation: World-wide variation in survival was less marked for patients who survived the first year(s) after diagnosis. Notable gains occurred in countries with initially lower five-year survival (e.g., China or Mexico), where legislative changes contributed to improved access to treatment for young patients with cancer. Nonetheless, inequalities persisted between high-income and low- and middle-income countries. Population-based cancer registry data remain essential to monitor further improvements.

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1. Introduction

Cancer in young people (aged 0–24 years) is rare, but it is ranked globally as the fourth leading cause of death in adolescents and young adults [1]. Leukaemia, one of the most common childhood malignancies, also represents about 15 % of malignancies in adolescents [2]. The true burden of leukaemia in young people is not known, especially in low-income and middle-income countries [3].

Over the past decades, significant advances in treatment of cancer for young patients have led to striking improvement in outcomes, especially for children in high-income countries [4]. The third cycle of the CONCORD programme (CONCORD-3) highlighted global variations in five-year survival trends for leukaemia and its morphological sub-types for children, adolescents and young adults diagnosed during 2000–2014 [5]. By 2010–2014, for children, five-year net survival was 80 % or over in North America, Oceania and parts of Europe. Wide international variations in survival still existed, however, and survival was below 60 % in parts of Central and South America, Asia, and Europe. Nonetheless, the survival gap between high-income countries (HIC) and low-income and middle-income countries (LMIC) narrowed for children (0–14 years). Survival disparities between adolescents and children were shrinking. However, survival for young adults (20–24 years) was lowest, with persistent disparities between LMICs and HICs [5].

The poorer outcomes for adolescents and young adults are thought to be influenced by factors such as differences in the sub-types of leukaemia by age, and restricted access to appropriate treatment (i.e., paediatric vs adult protocols) [6–8]. Adolescents and young adults represent a unique demography, often experiencing delayed diagnosis or presenting with more advanced disease than children [7,9]. Further, treatment protocols and pathways vary vastly world-wide contributing to modest gains in five-year survival world-wide.

Population-based survival, measured from the time of diagnosis, is a useful indicator of the overall effectiveness of the health system, because it reflects the survival of all cancer patients [10]. Conditional survival is the probability that patients who have already survived for a given number of years since diagnosis (e.g., one or five years) will live for an additional number of years. Comparisons of these estimates remove the effect of the higher excess mortality that occurs among patients with more severe disease at diagnosis. As a result, they are useful in assessing the success of leukaemia treatment or remission.

Here, we set out to examine world-wide trends in population-based survival up to ten years for young patients diagnosed with leukaemia during 2000–2014 in 61 countries included in CONCORD-3 [5]. We also analysed trends in five-year conditional survival, among patients who survived for at least one year, and ten-year survival among patients who had survived at least five years.

2. Material and methods

Methods of data acquisition and quality control for CONCORD-3 have been described in detail [5,11]. Briefly, we used data from 258 population-based cancer registries in 61 countries and analysed anonymised individual records for 164,563 young people (aged 0–24 years)

who were diagnosed with leukaemia during 2000–2014 and followed through to December 31, 2014.

Leukaemias were defined according to the International Classification of Diseases for Oncology, third edition (ICD-O-3) [12], including its first revision [13]. We included records with morphology codes in the range 9800–9992 and with behaviour code 3 (malignant). Morphology sub-groups were defined using the International Classification of Childhood Cancer (ICCC-3) [14,15], described previously [4]. Morphology was grouped as follows: lymphoid leukaemia (Ia), acute myeloid leukaemia (Ib), chronic myeloproliferative diseases (Ic), myelodysplastic syndrome and other myeloproliferative diseases (Id), and unspecified leukaemias. For lymphoid leukaemias, records were included if the anatomical site was blood, bone marrow, reticulo-endothelial, haematopoietic system not otherwise specified (C42.0–42.1, C42.3–42.4), or unknown primary site (C80.9) [4,14]. In 2010–2014, 68 % of patients were diagnosed with lymphoid leukaemia (group Ia) and 19 % acute myeloid leukaemia group (Ib) [5]. Other subtypes of leukaemia were much less common, ranging from 3.1 % to 6.5 %. This pattern was broadly consistent throughout 2000–14. Therefore, for the analysis by morphology we restricted the focus to the most common sub-types, given the limited data for other sub-types [4].

For CONCORD-3 [11], registries were asked to submit data on the first course treatment as a categorical variable (Yes, No or Unknown). This included information on whether systemic therapy was given (including chemotherapy) within the first six months after diagnosis. Details of drug regimes, dose and duration were not required.

2.1. Statistical analysis

We estimated net survival up to 10 years, by calendar period of diagnosis (2000–2004, 2005–2009 and 2010–2014), and age group.

We used the cohort approach to estimate survival for patients diagnosed during 2000–2004 and 2005–2009 because in most datasets all patients had been followed up for at least 5 years. The cohort approach provides a survival estimate for a group of patients who were diagnosed during the same year or period, are likely to have been treated in similar fashion, and who have all been followed up for at least the duration of survival required, in this case 5 years [16]. We used the period approach for patients diagnosed during 2010–2014, because 5 years of follow-up data were not available for all patients [17]. For ten-year survival, we only present net survival estimates for patients who were diagnosed during 2000–2004, using the cohort approach, as they would have had at least 10 years of follow-up.

Net survival is the cumulative probability of surviving up to a given time since diagnosis (e.g., ten years), after correcting for other causes of death (background mortality) [11]. To control for background mortality, we produced life tables of all-cause mortality rates by sex, single year of age and single calendar year in the general population of each contributing country or jurisdiction during 2000–2014, and where possible, by race/ethnicity (Israel, Singapore, USA, Northern Territory in Australia, and New Zealand) [11,18]. The method of life table construction depended on whether we received raw data (numbers of deaths and populations) or mortality rates, and on whether the raw data

or the mortality rates were by single year of age (complete) or by five-year age group (abridged). Full details on how life-tables were calculated have been published [11,18].

Net survival, with 95 % confidence intervals (CI), was estimated using the Pohar-Perme estimator [19], implemented in the Stata tool *stns* [20].

We also estimated net survival at five years conditional on surviving at least one year after diagnosis (“five-year conditional survival”), as the cumulative probability of surviving a further four years for all patients who were still alive at the end of the first year of follow-up. Similarly, net survival at 10 years, conditional on surviving at least 5 years after diagnosis (“ten-year conditional survival”), is the cumulative five-year net survival for all patients alive at the end of the fifth year of follow-up.

We grouped patients in three age categories: children (0–14 years), adolescents (15–19 years) and young adults (20–24 years). Survival estimates for all ages combined (0–24 years) were standardised by age to maximise comparability between countries and over time. Weights used for age-standardisation were based on the marginal distribution of patients in each age group (0.739, 0.136 and 0.125 for children, adolescents and young adults, respectively) [5]. To examine differences in survival by income group, we classified countries based on World Bank 2016 income classification [21]. Eighteen countries (Algeria, Nigeria, South Africa, Costa Rica, Argentina, Brazil, Peru, Colombia, Ecuador, Mexico, Jordan, Turkey, Malaysia, Thailand, China, India, Bulgaria, Russia Federation) were classified as lower-middle or upper-middle-income, all other countries were grouped as high-income.

We did not estimate survival if fewer than ten patients were available for analysis for a given combination of age, morphology sub-group and calendar period. If 10–49 patients were available, we only estimated survival for all ages combined. If 50 or more patients were available, we attempted to obtain age-standardised estimates. If a single age-specific estimate could not be obtained, we merged the data for adjacent age groups and assigned the combined estimate to both age groups before standardisation for age. If two or more age-specific estimates could not be obtained, we present only the unstandardised estimate for all ages combined. We did not merge data between consecutive calendar periods.

Survival estimates from registries where 15 % or more patients were lost to follow-up, or registered from a death certificate or at autopsy, or registered with incomplete dates, were considered less reliable. While survival estimates derived from such data are considered less than ideally reliable for international comparison, they merit inclusion here because of the paucity of survival estimates for leukaemia in children and young people from that country or region. The pooled estimates for countries with more than one registry do not include data from registries for which survival estimates were less reliable. Those estimates are shown with a flag in figures and tables when they are the only available information from a given country or territory. Where relevant, we mention in the text only reliable, age-standardised survival estimates.

2.2. Ethical approval

The Cancer Survival Group maintains approval for processing sensitive personal data for the CONCORD programme from the UK’s statutory Health Research Authority (reference ECC 3–04(i)/2011; last update 18 July 2024), the National Health Service Research Ethics Service (11/LO/0331; 5 June 2024 until end of study), and the Ethics Committee of the London School of Hygiene & Tropical Medicine (28686; 3 April 2025).

3. Results

We analysed data on individual records from 121,328 (73.7 %) children, 22,963 (14.0 %) adolescents, and 20,272 (12.3 %) young adults, from 258 population-based cancer registries in 61 countries, diagnosed with leukaemia during 2000–2014. Data quality indicators

and patients’ characteristics have been described elsewhere [4]. Briefly, histological confirmation was assigned for virtually all patients (164,069; 99.7 %) and overall only 4608 (2.8 %) patients were censored within 5 years of diagnosis, and 3127 (1.9 %) were lost to follow-up [4].

For all leukaemias combined, in 2010–2014, age-standardised five-year conditional net survival varied world-wide, with estimates ranging from 61.8 % in Mexico to between 90 % and 95 % in 20 countries: Puerto Rico, Canada, United States, Singapore, Australia and New Zealand; fourteen countries in Europe (Belgium, Czech Republic, Denmark, Finland, France, Germany, Ireland, Latvia, Netherlands, Norway, Spain, Sweden, Switzerland, United Kingdom) (Table 1, Fig. 1). By contrast, five-year survival was at least 70 % or higher for most countries, but it was below 55 % in Mexico, Ecuador, Peru, China and India, and between 55 % and 69 % in Chile, Brazil and the Russia Federation (Table 1, Fig. 1).

Increases of 20 % or more in five-year conditional survival than five-year survival was present in China (51.8 % vs. 76.1 %), Ecuador (46.8 % vs. 72.7 %), and Russia Federation (62.9 % vs. 85.3 %) (Table 1, Fig. 1). Nonetheless, in majority of these countries, five-year conditional net survival estimates were still below 80 % (Table 1, Fig. 1). Furthermore, five-year conditional survival among individuals who had survived to their first anniversary since diagnosis was 5–10 % higher than five-year survival for 23 countries in Europe, North America and Oceania. Regional variation in survival Europe reduced when taking into account the effect of surviving the first year of diagnosis. The absolute difference between highest and lowest five-year survival of 30 % shrank to 5 % if individuals survived their first year since diagnosis, the improvement was more marked for Eastern Europe countries such as Bulgaria and Russia Federation (Table 1, Fig. 1).

Survival varied by morphological sub-type, in 2010–2014, five-year net survival for children, adolescents and young adults diagnosed with lymphoid leukaemia was 80 % or higher in most parts of Europe, North America and Oceania (Supplementary Table 1, Fig. 2). When restricting the analysis to patients with lymphoid leukaemia who were alive after one year of follow-up, 26 countries saw increases in survival between 5 % and 10 %, majority based in Europe, America (North), Oceania and parts of Asia (Supplementary Table 1 Fig. 2). By contrast, in the great majority of countries five-year net survival for patients with acute myeloid leukaemia was at least 10 % lower than for patients with lymphoid leukaemia, but conditional survival for acute myeloid leukaemia was typically 5–10 % lower than for lymphoid leukaemia. For those alive after one year of follow-up, substantial absolute increases of 25 % or more were noted in six countries namely; Mexico (30.3 vs 55.7 %), Puerto Rico (66.0 vs 100.0 %), China (43.3 vs 79.1 %), Bulgaria (57.7 vs 83.7 %), Czech Republic (53.7 vs 84.7 %) and Spain (53.7 vs 83.2 %) (Supplementary Table 1, Fig. 2). Most countries based in Europe, North America, Oceania and Asia saw increases of 10 % or more. Nevertheless, survival estimates for acute myeloid leukaemia were wide-ranging and less precise than those for lymphoid leukaemia because the estimates were based on lower numbers of patients.

Survival differed by age at diagnosis, we found that in 2010–2014, five-year net survival conditional on surviving one year was highest for children (0–14 years), exceeding 90 % in most of North America, Oceania and Europe, (Supplementary Table 2, Fig. 2). For adolescents (15–19 years), five-year conditional survival ranged from below 50 % in Colombia and Mexico to 90 % or higher in seven countries (Canada, Singapore, Denmark, Switzerland, Lithuania, Ireland and Slovenia). For young adults (20–24 years), five-year conditional survival ranged from 58 % in Costa Rica to over 90 % in two countries Ireland and Norway (Supplementary Table 2, Supplementary Figure 1). The absolute difference between the oldest (20–24 years) and youngest (0–14 years) age group ranged between 10 % and 25 % in 21 countries (Argentina, Peru, Puerto Rico, Canada, United States, China, Israel, Korea, Kuwait, Thailand, Turkey, Austria, Bulgaria, Croatia, Czech Republic, Lithuania, Poland, Portugal, Russian Federation, Switzerland and New Zealand; the difference was greater than 25 % in Costa Rica and Malaysia

Table 1
Age-standardised 1-year, 5-year and 5-year conditional net survival (NS, %):children, adolescents and young adults (0-24 years) diagnosed with all leukaemias combined, by country and calendar period of diagnosis.

	Period of diagnosis	No.	1-year survival		5-year survival		5-year conditional survival		
			NS (%)	95% CI	NS (%)	95% CI	No.	NS (%)	95% CI
AFRICA									
Algeria (2 registries)	2000-2004	101	57.0§	46.6 - 67.5	7.8 §	0.3 - 15.3	47	7.9 §	0.0 - 18.0
	2005-2009	64	79.8 §	69.5 - 90.1	55.6 §	41.8 - 69.4	28	48.8 §	20.3 - 77.4
	2010-2014	40	76.7 §	49.7 - 100.0	28.8 §	0.0 - 69.3	15	37.5 §	0.0 - 78.7
South Africa (Eastern Cape)	2000-2004	20	76.4	39.2 - 100.0	76.4	39.2 - 100.0	3		
	2005-2009	14	80.2	48.8 - 100.0	80.2	48.8 - 100.0	2		
	2010-2014	10	100.0	100.0 - 100.0	75.3	38.4 - 100.0	6		
AMERICA (CENTRAL AND SOUTH)									
‡Argentina (4 registries)	2000-2004	2,321	75.4	71.7 - 79.1	59.9	55.0 - 64.7	1,792	79.5	77.6 - 81.4
	2005-2009	2,341	77.7	74.9 - 80.6	62.3	59.2 - 65.3	1,890	79.4	76.0 - 82.8
	2010-2014	1,998	81.5 §	78.0 - 85.0	67.2 §	63.5 - 70.9	1,545	82.9 §	78.9 - 86.9
Brazil (4 registries)	2000-2004	182	81.1	75.6 - 86.5	62.4	55.5 - 69.3	145	89.4	78.0 - 100.0
	2005-2009	209	78.3	73.1 - 83.6	60.4	54.3 - 66.6	165	76.7	64.7 - 88.7
	2010-2014	123	83.9	77.7 - 90.0	65.7	58.0 - 73.4	97		
Chile (4 registries)	2000-2004	67	81.9	72.7 - 91.1	59.2	47.4 - 70.9	54	72.3	60.5 - 84.1
	2005-2009	199	78.5	72.9 - 84.0	60.2	53.6 - 66.8	152	76.0	69.3 - 82.6
	2010-2014	59	80.7	71.9 - 89.5	58.7	49.5 - 68.0	43	75.9	68.0 - 83.9
Colombia (3 registries)	2000-2004	273	67.7	62.0 - 73.3	42.3	36.3 - 48.4	162	86.4	72.2 - 100.0
	2005-2009	231	73.8	68.2 - 79.4	50.6	43.9 - 57.3	156	84.8	72.1 - 97.5
	2010-2014	102	75.8 §	62.8 - 88.9	49.8 §	36.7 - 62.9	41	76.8 §	57.2 - 96.5
Costa Rica* (5 registries)	2000-2004	208	92.4	89.1 - 95.7	78.7	74.3 - 83.0	192	83.2	78.4 - 88.1
	2005-2009	372	90.7	87.6 - 93.7	76.2	72.2 - 80.2	340	83.1	79.0 - 87.3
	2010-2014	357	89.2	86.0 - 92.5	73.6	69.3 - 77.9	271	84.4	80.4 - 88.4
Ecuador (5 registries)	2000-2004	301	65.7 §	60.4 - 71.0	41.9 §	36.2 - 47.6	180	63.4 §	56.3 - 70.5
	2005-2009	575	68.7	64.9 - 72.5	47.2	43.0 - 51.3	376	67.8	63.0 - 72.6
	2010-2014	590	68.4	64.6 - 72.2	46.8	42.6 - 51.1	390	72.7	68.0 - 77.3
Guadaeloupe	2000-2004								
	2005-2009	10	100.0	100.0 - 100.0	100.0	100.0 - 100.0	5		
	2010-2014	12	55.6	20.7 - 90.6	55.6	20.7 - 90.6	5		
Martinique* (5 registries)	2000-2004	18	88.5	74.0 - 100.0	71.0	50.1 - 91.8	15	80.1	60.6 - 99.7
	2005-2009	21	85.8	71.2 - 100.0	75.4	57.0 - 93.8	18	87.9	72.6 - 100.0
	2010-2014	12	92.3	78.4 - 100.0	82.2	60.5 - 100.0	12	89.0 §	69.7 - 100.0
‡Mexico Childhood	2000-2004								
	2005-2009	1,953	50.4	47.9 - 52.8	45.4	43.1 - 47.7	1,353	62.7	60.0 - 65.4
	2010-2014	5,408	77.0	75.8 - 78.3	45.5	42.6 - 48.4	2,988	61.8	57.9 - 65.7
Peru (Lima)	2000-2004								
	2005-2009								
	2010-2014	570	74.8	71.2 - 78.5	52.1	47.3 - 56.8	397	68.8	63.5 - 74.1
Puerto Rico * (49 registries)	2000-2004	215	85.2	80.7 - 89.7	68.4	62.6 - 74.2	182	79.2	73.5 - 84.9
	2005-2009	185	86.2	81.5 - 90.9	74.6	68.8 - 80.3	156	85.4	80.4 - 90.5
	2010-2014	106	87.9	81.8 - 94.0	81.8	74.9 - 88.7	94	94.5	89.5 - 99.6
AMERICA (NORTH)									
Canada (10 registries)	2000-2004	1,931	89.9	88.2 - 91.5	81.3	79.2 - 83.5	1,739	90.2	88.4 - 92.0
	2005-2009	2,014	92.8	91.4 - 94.2	85.0	83.0 - 86.9	1,864	91.4	89.8 - 93.0
	2010-2014	2,105	93.2	91.7 - 94.7	86.0	84.0 - 88.0	1,616	93.1	91.7 - 94.6
United States (49 registries)	2000-2004	17,475	89.3	88.8 - 89.7	76.7	76.1 - 77.3	15,529	85.5	84.9 - 86.0
	2005-2009	19,221	91.0	90.6 - 91.4	80.8	80.3 - 81.4	17,386	88.6	88.1 - 89.0
	2010-2014	15,550	92.4	92.0 - 92.8	83.3	82.7 - 83.8	12,621	91.1	90.7 - 91.6
ASIA									
China (21 registries)	2000-2004	365	53.8	48.2 - 59.5	38.1	32.5 - 43.7	193	70.2	63.2 - 77.3
	2005-2009	1,080	63.4	60.1 - 66.7	46.3	42.9 - 49.7	658	71.5	67.9 - 75.2
	2010-2014	880	69.4	66.2 - 72.7	51.8	48.1 - 55.4	606	76.1	72.4 - 79.8

(continued on next page)

Table 1 (continued)

	Period of diagnosis	1-year survival			5-year survival		5-year conditional survival		
		No.	NS (%)	95% CI	NS (%)	95% CI	No.	NS (%)	95% CI
Cyprus*	2000-2004	14	71.4	48.8 - 94.1	64.3	40.3 - 88.3	7		
	2005-2009	50	88.0	79.1 - 96.9	74.0	62.0 - 86.1	24	84.1 §	73.4 - 94.8
	2010-2014	47	95.8	90.7 - 100.0	87.3	78.3 - 96.3	34	91.4 §	84.5 - 98.3
India (2 registries)	2000-2004	25	56.1	37.1 - 75.0	44.3	25.4 - 63.3	14	79.0	58.2 - 99.7
	2005-2009	84	70.5	53.6 - 87.4	48.5	30.1 - 67.0	60	68.8	48.5 - 89.2
	2010-2014	59	73.0	58.0 - 88.0	50.0	32.8 - 67.1	36	73.0	54.7 - 91.3
Israel *	2000-2004	545	88.5	85.9 - 91.2	77.0	73.6 - 80.4	481	86.7	83.8 - 89.7
	2005-2009	558	89.8	87.3 - 92.3	78.5	75.2 - 81.9	501	87.3	84.5 - 90.2
	2010-2014	469	89.1	86.2 - 91.9	79.7	76.1 - 83.3	423	89.6	86.6 - 92.5
Japan (16 registries)	2000-2004	908	88.3	86.2 - 90.3	69.6	66.6 - 72.5	764	78.3	75.5 - 81.2
	2005-2009	1,579	89.5	88.0 - 91.0	75.1	73.0 - 77.3	1,341	83.6	81.6 - 85.5
	2010-2014	1,094	94.0	92.6 - 95.4	80.7	78.4 - 82.9	996	87.4	85.6 - 89.2
Jordan *	2000-2004	482	84.7 §	81.4 - 88.0	69.5 §	65.2 - 73.8	374	81.8 §	77.9 - 85.8
	2005-2009	479	86.7 §	83.8 - 89.7	78.5 §	74.9 - 82.1	410	90.1 §	87.2 - 93.0
	2010-2014	461	85.3 §	82.2 - 88.4	74.1 §	70.2 - 78.0	324	88.3 §	85.1 - 91.5
Korea *	2000-2004	2,974	80.0	78.5 - 81.4	61.2	59.5 - 63.0	2,342	76.2	74.5 - 77.9
	2005-2009	2,966	84.3	82.9 - 85.6	69.3	67.7 - 71.0	2,486	82.3	80.8 - 83.8
	2010-2014	2,880	89.9	88.8 - 91.0	76.5	75.0 - 78.1	2,051	87.0	85.7 - 88.3
Kuwait *	2000-2004	127	88.6	83.6 - 93.5	79.6	73.0 - 86.3	108	90.3	84.9 - 95.7
	2005-2009	152	87.4	82.2 - 92.6	74.6	67.7 - 81.4	132	84.9	78.8 - 91.0
	2010-2014	112	88.4	82.8 - 93.9	77.7	70.8 - 84.6	99	89.9	84.2 - 95.6
Malaysia (Penang)	2000-2004								
	2005-2009	141	76.7	68.1 - 85.4	63.9	54.3 - 73.5	86	83.4 §	74.5 - 92.3
	2010-2014	119	78.8	71.9 - 85.7	68.3	60.7 - 75.9	94	88.2 §	82.8 - 93.7
Qatar*	2000-2004	48	80.7	68.5 - 92.8	57.4	39.8 - 75.0	21	71.2 §	52.2 - 90.2
	2005-2009	58	84.6	72.8 - 96.4	76.2	60.2 - 92.3	26	91.1 §	79.3 - 100.0
	2010-2014	69	93.7	90.8 - 96.7	81.1	64.1 - 98.0	21	81.2 §	66.5 - 95.9
Singapore *	2000-2004	245	86.1	81.8 - 90.4	68.4	62.8 - 74.1	211	78.3	72.9 - 83.8
	2005-2009	244	90.7	87.2 - 94.2	80.1	75.4 - 84.9	220	87.4	83.1 - 91.7
	2010-2014	228	92.0	88.5 - 95.4	84.0	79.4 - 88.6	173	93.3	90.1 - 96.6
Taiwan *	2000-2004	1,439	83.1	81.2 - 85.1	61.6	59.1 - 64.0	1,187	73.6	71.2 - 76.0
	2005-2009	1,340	86.5	84.7 - 88.3	69.9	67.4 - 72.3	1,148	80.6	78.4 - 82.9
	2010-2014	1,224	89.3	87.6 - 91.0	71.7	69.2 - 74.2	876	81.9	79.6 - 84.2
Thailand (6 registries)	2000-2004	464	59.2 §	54.8 - 63.7	37.9 §	33.4 - 42.3	257	62.7 §	56.8 - 68.7
	2005-2009	624	66.8	63.1 - 70.4	44.5	40.7 - 48.4	407	65.8	61.2 - 70.4
	2010-2014	499	74.0 §	70.2 - 77.8	54.0 §	49.7 - 58.2	297	74.6 §	70.3 - 78.8
Turkey (8 registries)	2000-2004	259	72.3 §	66.9 - 77.7	59.7 §	53.7 - 65.6	174	81.3 §	75.7 - 87.0
	2005-2009	1,205	82.1	79.9 - 84.3	68.5	65.8 - 71.1	968	83.1	80.8 - 85.5
	2010-2014	1,208	86.4	84.6 - 88.3	72.1	69.7 - 74.5	1,024	85.0	83.0 - 87.1
EUROPE									
Austria *	2000-2004	663	89.6	86.7 - 92.6	78.0	74.8 - 81.3	602	86.6	83.6 - 89.6
	2005-2009	723	91.1	88.6 - 93.7	81.5	78.5 - 84.5	677	88.5	85.7 - 91.3
	2010-2014	719	92.9	90.6 - 95.2	82.7	79.8 - 85.7	570	89.9	87.3 - 92.6
‡Belarus Childhood	2000-2004	326	82.9	78.8 - 86.9	71.6	66.7 - 76.5	270	86.4	82.3 - 90.5
	2005-2009	285	89.5	86.0 - 93.1	80.8	76.2 - 85.4	255	90.3	88.6 - 91.7
	2010-2014	362	91.6	88.7 - 94.5	83.9	80.0 - 87.9	257	92.8	89.9 - 95.8
Belgium *	2000-2004	119	89.0	83.3 - 94.6	78.9	71.7 - 86.1	105	88.8	83.0 - 94.5
	2005-2009	583	91.3	89.1 - 93.6	81.1	78.0 - 84.2	524	88.7	86.0 - 91.3
	2010-2014	668	93.7	91.8 - 95.6	85.1	82.3 - 87.9	492	91.6	89.3 - 93.8
Bulgaria*	2000-2004	289	75.9	71.1 - 80.7	50.9	45.3 - 56.6	218	66.9	60.8 - 73.1
	2005-2009	384	80.3	76.4 - 84.1	66.3	61.7 - 70.8	304	81.7	77.5 - 86.0
	2010-2014	304	85.3	81.6 - 89.0	71.7	67.0 - 76.4	208	84.4	80.1 - 88.6

(continued on next page)

Table 1 (continued)

	Period of diagnosis	No.	1-year survival		5-year survival		5-year conditional survival		
			NS (%)	95% CI	NS (%)	95% CI	No.	NS (%)	95% CI
Croatia*	2000-2004	278	88.4	84.7 - 92.0	75.8	71.1 - 80.6	246	85.2	80.9 - 89.6
	2005-2009	239	84.6	80.2 - 89.1	73.8	68.5 - 79.1	202	86.4	81.7 - 91.1
	2010-2014	217	86.5	82.1 - 90.9	76.1	70.9 - 81.3	150	87.7	83.2 - 92.2
Czech Republic*	2000-2004	370	84.2	80.7 - 87.8	75.8	71.7 - 79.9	308	89.1	85.8 - 92.4
	2005-2009	379	85.9	82.6 - 89.2	78.3	74.4 - 82.2	321	90.6	87.5 - 93.6
	2010-2014	267	88.9	85.1 - 92.6	79.6	75.2 - 84.0	211	90.7	87.6 - 93.8
Denmark*	2000-2004	346	91.6	88.6 - 94.6	80.4	76.1 - 84.7	317	87.8	84.2 - 91.5
	2005-2009	330	91.5	88.5 - 94.5	83.4	79.5 - 87.3	300	91.1	87.9 - 94.3
	2010-2014	364	94.4	92.0 - 96.7	87.3	83.8 - 90.8	292	92.4	89.5 - 95.4
Estonia*	2000-2004	68	78.8	70.0 - 87.6	51.6	40.7 - 62.5	53	64.3	51.5 - 77.0
	2005-2009	77	88.8	81.8 - 95.8	75.2	66.1 - 84.4	68	84.5	76.8 - 92.3
	2010-2014	42	89.1	80.1 - 98.0	70.7	58.5 - 82.9	38	86.2	76.7 - 95.6
Finland *	2000-2004	322	92.8	90.0 - 95.6	80.4	76.1 - 84.7	299	86.5	82.7 - 90.4
	2005-2009	354	92.5	89.8 - 95.3	82.3	78.3 - 86.2	327	88.8	85.4 - 92.3
	2010-2014	312	95.2	92.8 - 97.5	86.5	82.8 - 90.2	235	91.2	88.0 - 94.3
‡France (15 registries)	2000-2004	2,625	91.6	90.2 - 93.1	79.3	77.2 - 81.4	2,430	86.4	84.5 - 88.3
	2005-2009	2,671	92.3	90.9 - 93.6	83.1	81.2 - 85.0	2,457	89.6	87.8 - 91.3
	2010-2014	1,587	92.7	90.3 - 95.1	83.4	80.6 - 86.3	1,434	90.9	88.8 - 93.0
Germany (10 registries)	2000-2004	804	91.3	89.2 - 93.4	81.4	78.8 - 84.1	709	88.7	86.4 - 91.0
	2005-2009	1,166	93.4	91.9 - 94.9	84.6	82.6 - 86.7	1,070	90.6	88.8 - 92.3
	2010-2014	824	93.9	92.4 - 95.4	84.4	82.1 - 86.8	637	90.7	88.8 - 92.7
‡Greece National Paediatric	2000-2004	399	90.0	87.1 - 92.9	81.2	77.4 - 85.1	359	90.3	87.2 - 93.4
	2005-2009	411	93.4	91.1 - 95.8	83.0	79.4 - 86.7	384	89.2	87.2 00.0 90.5
	2010-2014	480	90.8	88.1 - 93.4	81.7	78.1 - 85.2	336	90.0	88.6 00.0 91.2
Iceland*	2000-2004	16	100.0	79.4 - 100.0	81.3	62.8 - 99.8	16	81.3	62.8 - 99.8
	2005-2009	26	84.6	71.1 - 98.2	77.0	61.1 - 92.8	22	90.9	79.2 - 100.0
	2010-2014	20	95.8	88.0 - 100.0	92.0	81.8 - 100.0	16	95.7	87.6 - 100.0
Ireland*	2000-2004	271	84.9	80.7 - 89.1	73.8	68.6 - 78.9	229	86.7	82.4 - 91.1
	2005-2009	297	91.3	88.1 - 94.4	84.6	80.5 - 88.7	270	92.7	89.5 - 95.8
	2010-2014	241	89.9	86.2 - 93.6	83.7	79.1 - 88.2	219	95.2	92.4 - 98.0
Italy (44 registries)	2000-2004	1,247	90.6	89.0 - 92.2	78.5	76.2 - 80.8	1,123	86.5	84.5 - 88.5
	2005-2009	1,757	92.7	91.4 - 93.9	82.2	80.4 - 84.0	1,613	88.7	87.1 - 90.2
	2010-2014	714	93.4	91.6 - 95.2	82.8	80.3 - 85.2	654	89.7	87.8 - 91.6
Latvia*	2000-2004	100	82.6	75.4 - 89.8	68.1	59.7 - 76.5	82	82.3	75.4 - 89.1
	2005-2009	75	83.9	76.4 - 91.3	73.1	64.2 - 82.0	63	87.0	79.3 - 94.7
	2010-2014	87	91.8	86.0 - 97.6	81.9	73.7 - 90.1	53	90.8	84.5 - 97.2
Lithuania*	2000-2004	196	78.0	72.2 - 83.7	62.1	55.4 - 68.9	152	79.8	73.4 - 86.1
	2005-2009	169	79.1	73.1 - 85.2	69.2	62.2 - 76.1	131	87.4	81.8 - 93.1
	2010-2014	115	84.2	77.4 - 91.1	73.4	65.1 - 81.6	98	88.5	82.2 - 94.8
Malta*	2000-2004	32	90.6	80.7 - 100.0	65.7	49.5 - 81.8	29	72.5	56.5 - 88.4
	2005-2009	31	87.1	75.5 - 98.7	74.2	59.1 - 89.4	27	85.2	72.1 - 98.4
	2010-2014	15	75.1	54.8 - 95.5	66.7	45.7 - 87.8	11	88.8	74.6 - 100.0
Netherlands*	2000-2004	982	89.1	87.1 - 91.1	75.8	73.1 - 78.4	879	84.7	82.3 - 87.1
	2005-2009	981	89.9	88.0 - 91.8	80.3	77.8 - 82.8	878	89.2	87.2 - 91.2
	2010-2014	863	91.2	89.4 - 93.0	83.7	81.4 - 86.1	676	92.4	90.6 - 94.1
Norway*	2000-2004	282	93.5	90.6 - 96.4	77.3	72.4 - 82.2	264	82.4	77.7 - 87.1
	2005-2009	295	92.2	89.2 - 95.3	83.1	78.8 - 87.3	271	90.0	86.5 - 93.6
	2010-2014	323	91.6	88.6 - 94.7	82.0	77.8 - 86.3	240	90.1	86.7 - 93.6
Poland (16 registries)	2000-2004	1,631	82.2	80.4 - 84.1	67.1	64.9 - 69.3	1,327	80.9	78.9 - 83.0
	2005-2009	1,793	86.9	85.4 - 88.5	74.9	72.9 - 76.8	1,547	86.1	84.4 - 87.8
	2010-2014	1,579	90.2	88.8 - 91.6	79.5	77.6 - 81.4	1,152	88.8	87.3 - 90.4
Portugal (4 registries)	2000-2004	497	88.8	86.1 - 91.5	71.2	67.4 - 75.0	438	79.7	76.1 - 83.3
	2005-2009	503	91.2	88.7 - 93.7	79.8	76.3 - 83.2	455	87.4	84.3 - 90.4
	2010-2014	281	92.8	88.4 - 97.2	79.4	72.2 - 86.7	219	85.6	79.0 - 92.2

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Table 1 (continued)

	Period of diagnosis	1-year survival			5-year survival		5-year conditional survival		
		No.	NS (%)	95% CI	NS (%)	95% CI	No.	NS (%)	95% CI
Romania (Cluj)	2000-2004								
	2005-2009	16	62.5	40.2 - 84.8	62.5	40.2 - 84.8	10	100.0	69.2 - 100.0
	2010-2014	27	63.1	45.2 - 80.9	63.1	45.2 - 80.9	18	94.6	84.3 - 100.0
Russian Federation (3 registries)	2000-2004	235	70.8	64.8 - 76.8	57.4	51.0 - 63.7	159	82.0	76.2 - 87.9
	2005-2009	235	76.5	71.0 - 82.0	61.5	55.6 - 67.5	178	78.3	72.5 - 84.0
	2010-2014	227	76.8	70.8 - 82.8	62.9	56.7 - 69.2	137	85.3	80.1 - 90.6
Slovakia*	2000-2004	266	82.1	77.4 - 86.7	69.8	64.3 - 75.3	217	85.0	80.3 - 89.6
	2005-2009	304	86.9	83.2 - 90.6	73.4	68.5 - 78.3	261	84.2	79.8 - 88.6
	2010-2014	61	88.9	80.8 - 97.1	76.6	65.5 - 87.7	57	86.3	76.8 - 95.7
Slovenia*	2000-2004	90	88.0	81.9 - 94.1	77.5	69.5 - 85.4	78	88.1	84.9 - 90.8
	2005-2009	104	85.9	79.4 - 92.4	74.6	66.3 - 82.9	88	86.5	79.4 - 93.6
	2010-2014	84	93.5	88.4 - 98.6	79.6	70.8 - 88.4	78	85.0	76.8 - 93.3
Spain (11 registries)	2000-2004	802	86.1	83.5 - 88.6	71.7	68.5 - 75.0	696	83.2	80.2 - 86.2
	2005-2009	1,027	89.0	87.0 - 90.9	77.7	75.1 - 80.3	910	87.3	85.0 - 89.5
	2010-2014	773	87.3	84.0 - 90.6	77.8	73.7 - 81.9	501	91.3	88.2 - 94.5
Sweden*	2000-2004	529	91.2	88.7 - 93.6	79.9	76.5 - 83.3	483	87.5	84.6 - 90.5
	2005-2009	497	90.0	87.4 - 92.6	81.4	78.0 - 84.8	447	90.4	87.7 - 93.1
	2010-2014	584	92.1	89.9 - 94.3	83.3	80.2 - 86.4	420	91.7	89.3 - 94.1
‡ Switzerland (10 registries)	2000-2004	355	92.7	89.8 - 95.5	78.4	73.8 - 83.0	325	84.6	80.4 - 88.8
	2005-2009	330	94.7	92.0 - 97.3	86.0	82.0 - 89.9	314	90.7	87.3 - 94.1
	2010-2014	407	91.6	88.2 - 94.9	85.2	81.1 - 89.3	315	93.3	90.3 - 96.3
United Kingdom (4 registries)	2000-2004	3,397	89.6	88.5 - 90.6	76.7	75.3 - 78.1	3,009	85.3	84.0 - 86.5
	2005-2009	3,506	91.5	90.6 - 92.4	83.0	81.8 - 84.2	3,167	90.6	89.6 - 91.6
	2010-2014	3,721	92.4	91.6 - 93.3	84.6	83.4 - 85.7	2,701	92.3	91.4 - 93.2
OCEANIA									
Australia * (8 registries)	2000-2004	1,543	91.6	90.2 - 93.0	80.7	78.8 - 82.7	1,413	88.0	86.3 - 89.7
	2005-2009	1,596	93.2	92.0 - 94.4	84.5	82.8 - 86.2	1,480	90.4	88.9 - 91.9
	2010-2014	1,520	94.4	93.2 - 95.5	87.7	86.0 - 89.4	1,101	93.9	92.7 - 95.2
New Zealand *	2000-2004	321	89.9	86.7 - 93.2	77.7	73.3 - 82.1	289	85.9	81.9 - 89.9
	2005-2009	331	93.1	90.5 - 95.7	84.9	81.1 - 88.6	306	91.0	87.9 - 94.2
	2010-2014	301	93.0	90.3 - 95.7	84.0	80.2 - 87.8	258	91.2	88.2 - 94.2

Italics denote survival estimates that are not age-standardised; bold indicates age-standardised survival estimates

"five-year conditional survival" - net survival at five years conditional on surviving at least one year after diagnosis

§ Survival estimate considered less reliable, because 15% or more of patients were (a) lost to follow-up or censored alive within five years of diagnosis (or if diagnosed in 2010 or later, before 31 December 2014), or (b) registered only from a death certificate or at autopsy, or (c) registered with incomplete dates, i.e., unknown year of birth, unknown month and/or year of diagnosis or unknown year of last vital status

* Data with 100% coverage of the national population; ‡Data with 100% coverage of the national population for childhood cancers only, data for 15-24 years old are from registries with sub-national coverage

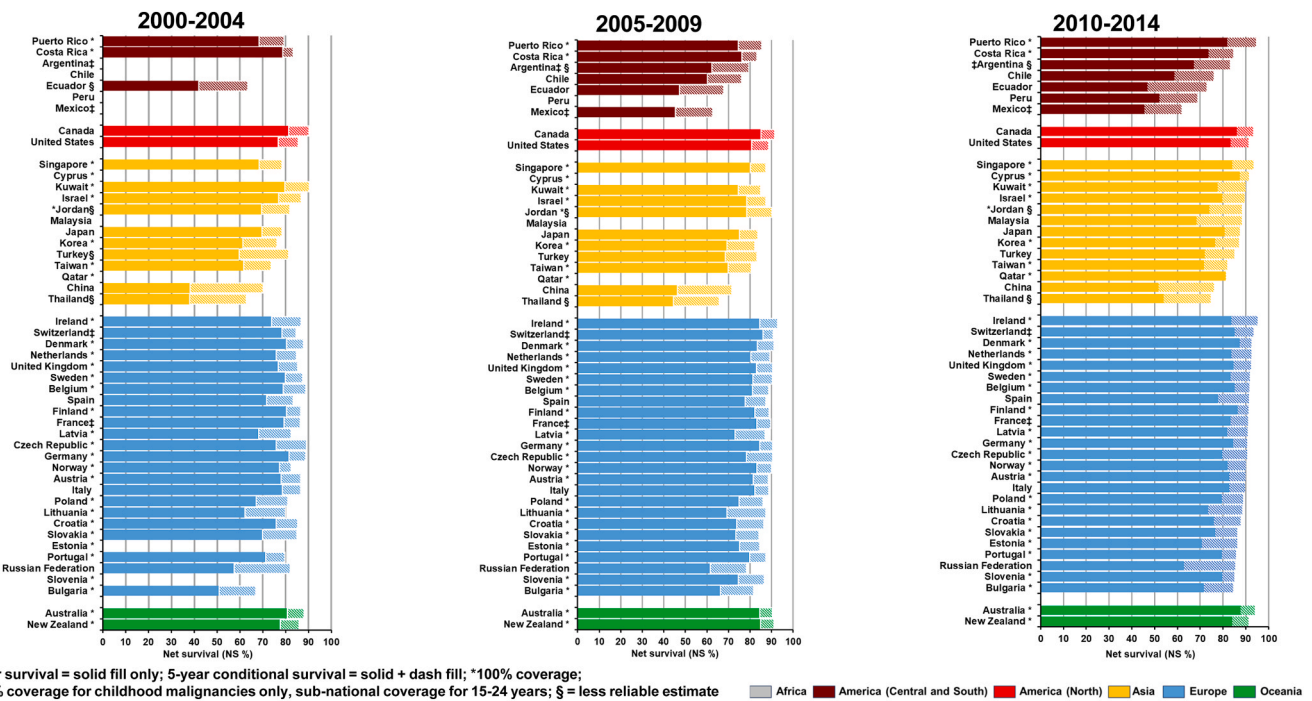


Fig. 1. Age-standardised five-year and five-year conditional net survival (NS, %) for children, adolescents and young adults (0–24 years) diagnosed with leukaemia, during 2000–2014; by continent and country. ‡ Data with 100 % coverage of the national population for childhood malignancies only, data for 15–24 years if available are provided from registries with sub-national coverage. * Data with 100 % coverage of the national population. § National estimate flagged as less reliable because the only available estimates are from a registry or registries in this category. Survival estimates for each population are ranked from highest to lowest within each continent and the ranking of countries for the 5-year conditional survival net estimates for patients diagnosed in 2010–2014 is also used for the 5-year net survival estimates. Only age-standardised estimates are reported, preference was given where standardised estimates were available for conditional estimates. Where data were available for more than one registry in a given country, the survival estimates are derived by pooling the data for that country but excluding data from registries for which the estimates are considered less reliable (see text).

(Supplementary Table 2, Supplementary Figure 1).

Over time, inequalities in survival by age at diagnosis were evident. The gap in five-year survival conditional to surviving one year, for all leukaemias combined, between high-income countries and low-income and middle-income countries persisted throughout the 15-year period (Fig. 3). By 2010–2014, five-year conditional survival for children was 90 % or higher in high-income countries. Survival for children in low-income and middle-income countries was catching up at 80 %, but the gap persisted. Survival for adolescents and young adults still lagged behind survival in children, and the gap was more evident in low- and middle-income countries (Fig. 3).

For patients diagnosed during 2000–2004, age-standardised ten-year net survival for all leukaemias combined ranged from 35 % in China to 81 % in Canada and Iceland (Supplementary Table 5, Supplementary Figure 2). It was at least 70 % in North America, Oceania and most European countries, but tended to be around 5 % lower in Asia. When restricting the estimate to patients who survived to the fifth anniversary after their diagnosis, the differences in survival between countries were smaller. Ten-year survival conditional on surviving five years after diagnosis was 90 % or higher in most countries.

The availability of data on whether or not a first course of systemic treatment was given was limited. Overall such data were available for 77,257 out of 164,563 (46.9 %) patients from 75 registries in 20 countries (Supplementary Table 6). Overall, the proportion of patients with systemic treatment information (i.e. treatment given or not given) varied from 36.9 % in Russian Federation to between 95 % and 100 % in 10 countries. No data on systemic treatment were submitted from registries in Africa or Oceania. The proportion of patients for whom no data on systemic treatment were available ranged from less than 2 % in Kuwait to greater than 60 % in Russian Federation. During the 15-year period, for 12 countries, Canada, United States, Japan, Kuwait, Ireland,

Netherlands, Portugal, Slovenia, Slovakia, Spain, Switzerland and the United Kingdom, 80 % or more of patients had received systemic therapy within the first six months of diagnosis. The median days to the start of treatment overall was within a week, but this data was very limited and available for 12 out of 20 countries (Supplementary Table 6).

4. Discussion

Our study offers the largest world-wide population-based assessment of trends in survival up to ten years, conditional on surviving up to five years since diagnosis, as a proxy of the impact of treatment or remission of leukaemia during the first few years after diagnosis. Using population-based cancer registry data for 164,563 young patients (aged 0–24 years) diagnosed with leukaemia during 2000–2014, we examined five-year conditional survival for patients who had already survived one-year, and ten-year conditional survival for those who survived five years after diagnosis. One-year survival was generally high, reaching 90 % or more in most parts of Europe, Oceania and North America. Overall, survival varied at one year of follow-up after diagnosis and the gaps became more evident with increasing time since diagnosis.

For all leukaemias combined, during 2010–2014, for patients aged 0–24 years living in Europe, North America and Oceania, five-year conditional survival was generally 5 % higher than five-year survival from diagnosis and showed less regional variation, a finding consistent with other studies [22,23]. In Oceania, North America and parts of Asia, the gap in conditional survival between countries was narrower, highlighting the effect of treatment in the first year. The use of well-established treatment protocols in these regions means that patients are more likely to have access to optimal care. Collaborative efforts in Europe, North America and Oceania, through established cooperative trial groups such as the Children’s Oncology Group, have

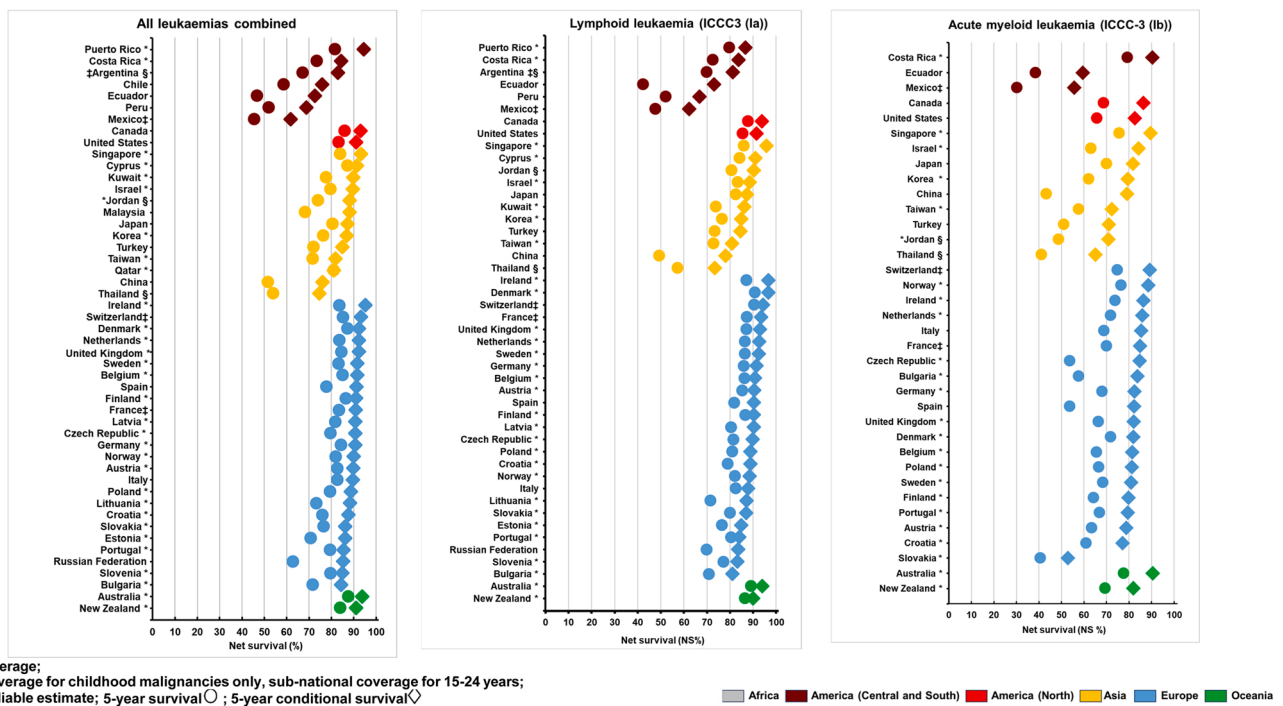


Fig. 2. Age-standardised 5-year net survival and 5-year conditional survival for children adolescents and young adults (0–24 years) diagnosed with leukaemia during 2010–2014; by country and morphology sub-group. ‡ Data with 100 % coverage of the national population for childhood malignancies only, data for 15–24 years if available are provided from registries with sub-national coverage. * Data with 100 % coverage of the national population. § National estimate flagged as less reliable because the only available estimates are from a registry or registries in this category. Survival estimates for each country are ranked from highest to lowest within each continent and the ranking of countries for the 5-year conditional survival net estimates for patients diagnosed in 2010–2014 is also used for the 5-year net survival estimates. Where data were available for more than one registry in a given country, the survival estimates are derived by pooling the data for that country but excluding data from registries for which the estimates are considered less reliable (see text).

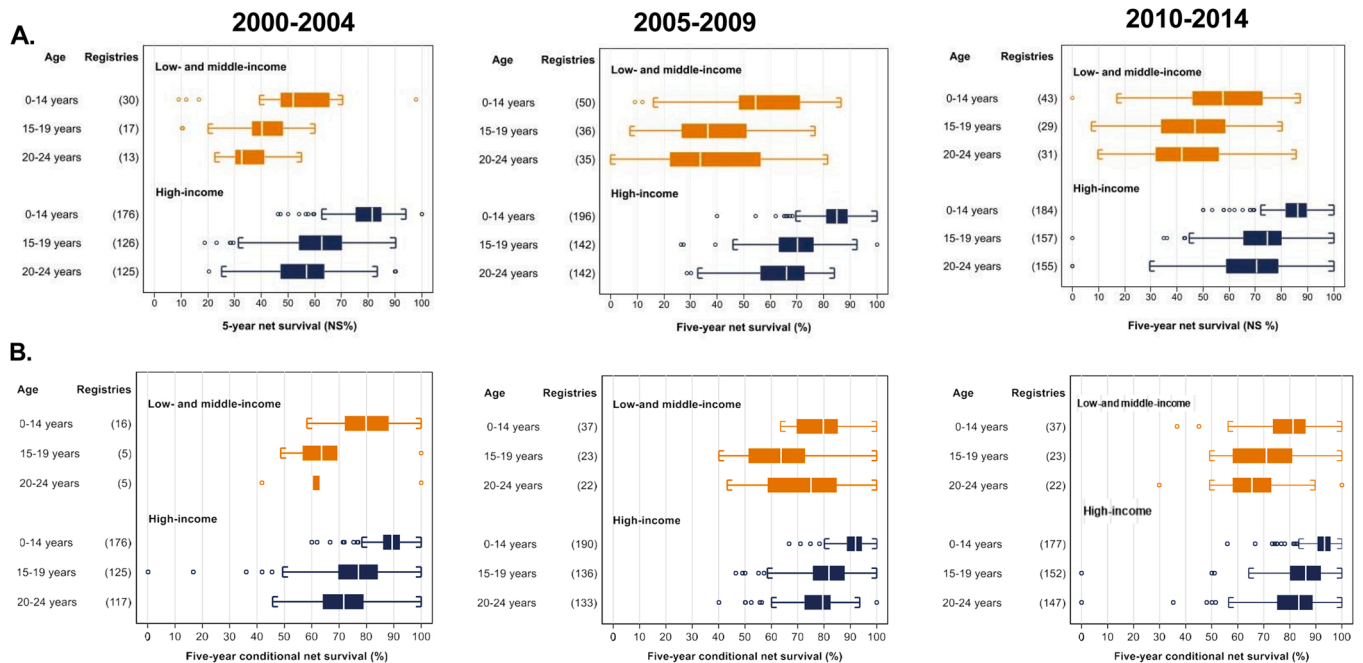


Fig. 3. Five-year (A) and five-year conditional net survival (NS %) (B) for all leukaemias combined, in patients aged (0–24 years) diagnosed during 2000–2014: World Bank income group and calendar period of diagnosis. The number of registries for which suitable estimates could be obtained are shown in parentheses. Each box plot shows the range of net survival estimates among all cancer registries for which suitable estimates could be obtained for patients diagnosed in each calendar period, in each age group. Survival estimates considered less reliable are not included. The vertical line inside each box represents the median survival estimate among all contributing registries (the central value in the range, or 50th centile). The box covers the inter-quartile range (IQR) between the lower and upper quartiles (25th and 75th centiles). Where there are only a few widely scattered estimates, the median might be close to the lower or upper quartile. The extreme limits of the box plot are 1.5 × IQR below the lower quartile and 1.5 × IQR above the upper quartile. Open circles indicate outlier values, outside this range.

led to improved outcomes especially for children. [4,24,25]. Furthermore, improvements over time are also due to better supportive care, and enhanced risk stratification strategies in addition to treatment intensity and optimization, including the employment of hematopoietic stem cell transplantation [26,27].

In addition, the availability of effective targeted therapies since the early 2000s, such as imatinib has contributed to better long-term prognosis [28,29]. Imatinib is a tyrosine kinase inhibitor, primarily used to treat specific types of leukaemia, such as chronic myeloid leukaemia (CML) [28], which accounts for about 3 % of childhood cancers and, to a lesser extent, certain cases of acute lymphoblastic leukaemia (ALL) with the Philadelphia chromosome. Nonetheless, the tight adherence to risk-adapted therapies [30] and the readiness to enrol most children with leukaemia in long-running series of clinical trials has also led to improved prognosis [31–34].

In Europe, the regional variation in five-year survival was smaller when restricted to patients who survived the first year after diagnosis. Greater increases were noted in parts of Eastern Europe (Bulgaria and Russian Federation). This could be due to the fact that countries in parts of Eastern Europe now participate in international clinical trials for childhood leukaemia [35]. Nevertheless, the continuing variation in survival could be driven by the fact that access to appropriate treatment, diagnostic or cancer management facilities is more limited than in the rest of the region.

In Central and South America and in parts of Asia, five-year survival was lower than in other world regions, and the differences in five-year conditional survival were less marked, showing a noticeable effect of surviving during the first year of diagnosis. This may reflect the fact that a considerable proportion of patients with advanced disease die during the first year and those who survive were diagnosed at less-advanced disease [36,37]. During 2010–2014, the absolute difference between five-year survival and five year survival among patients who survived the first year after diagnosis ranged from 10 % in Costa Rica to 25 % in Ecuador.

These variations highlight the heterogeneous nature of cancer management in young patients in Central and South America. For example, during 2010–2014 in Mexico, the absolute difference between five-year survival and five-year conditional survival was greater than 15 %, highlighting the potential impact of treatment during the first year. This difference in survival may be influenced by changes in government legislation in Mexico related to healthcare funding for young patients in the preceding years that improved access to appropriate treatment. In the mid-2000s, the Mexican government introduced legislation that provided financial support for patients without social security to ensure that young patients under the age of 18 would have access to appropriate care and management [4,38–40]. Furthermore, in 2006, the government began funding treatment for children and adolescents with acute lymphoid leukaemia, ensuring that all hospitals that managed young patients adhered to treatment protocols [38,41].

Likewise, for patients diagnosed with leukaemia in China during 2010–2014, five-year conditional survival was 25 % higher than five-year survival. This is probably influenced by better access to appropriate treatment, especially for children and adolescents, following changes in Chinese legislation to provide financial support for young people diagnosed with cancer [42–44]. By contrast, five-year conditional survival for some countries in Asia, such as Cyprus, Japan and Singapore, was approaching the level seen in Europe, North America and Oceania. In Japan, long-standing support since the early 70's through governmental subsidies for children and adolescents with cancer has led to improved outcomes overtime [8,9,45].

Nevertheless, survival in these regions continues to lag behind Europe, North America and Oceania, where most countries are well resourced. Several factors probably contributed to these gaps in survival, including delayed presentation with symptoms, poor nutritional status, inconsistent drug availability, abandonment of treatment, and a lack of appropriate supportive care and specialist treatment [46–48]. Most

countries in low-resource settings adopt treatment guidelines based on the experience of well-resourced countries where these treatments are developed [46,47]. These guidelines may not be as appropriate, because they require supportive care capabilities that may not be readily available in low-resource settings. Lack of appropriate infrastructure can lead to excess deaths due to intensive treatment as well as high rates of treatment abandonment [47–49].

In the past few years, international collaborations have been established whereby institutions in well-resourced settings are paired with an institution in low-resourced settings. Several of such initiatives have been established in Latin America and Asian regions. [47,48] These collaborations aim to facilitate effective cancer-treatment programmes and improve outcomes for patients in these settings [47,48]. In the long-term, population-based survival trends will help assess the success of such initiative in improving outcomes for young people who live in these regions. Often, survival estimates derived from studies conducted in specialist treatment centres can be higher than those derived from population-based data especially in countries with limited resources that have the lowest survival [50,51]. This further emphasises the need for unselected population-based data to provide accurate indicators of the outcome for the entire patient population.

When considering the effect of age at diagnosis on survival, our findings also highlighted evident inequalities. Overall, children experienced better survival, both at time of diagnosis and after surviving the first year. Survival was approaching 90 % by 2010–2014 particularly in North America, Europe and Oceania. Children living in these world regions have benefited from decades of advances in treatment, establishment of designated specialised paediatric oncology centres, enrolment to ongoing clinical trials and standardised treatment protocols [4,24,25,32]. However, the same improvements were not achieved for the older patients aged 15–19 years and 20–24 years. When considering the effect of treatment in the first year, we noted that the gap in survival compared to children reduced by 10 %. Adolescents and young adults often experience delays in diagnosis or present late with more advanced symptoms than children [7,9]. Poorer outcomes in this age-range may be related to a lack of symptom awareness, poorer adherence to treatment or difficulties in health system navigation [52,53]. Furthermore, they often have restricted access to novel treatments due to limited number of clinical trials in this age range, as well as restricted access to optimal treatment strategies [5,9].

There is currently no consensus on the definition of the age range for adolescents and young adults diagnosed with cancer, with the upper limit approaching 39 years in some studies [53]. However, the more commonly used age range are defined as ages 15–24 years or 15–29 years at diagnosis [5,7,52]. For CONCORD-3, we defined adolescents and young adults as those aged 15–24 years at diagnosis, in line with the literature [7,52]. The heterogeneous approaches to defining this patient group highlight the particular difficulties in health system navigation. Previous research has shown that adolescents and young adults who are treated under a paediatric protocol have better prognosis than those treated under adult protocols [8,25,54–56]. This approach is not widely adopted worldwide, leading to gaps in survival between countries. Closing the gap will require commitment to develop integrated models of care, targeted trials and age-appropriate treatment for this patient group [5,53]. Projects such as the Global Initiative for Childhood Cancer (GICC), are a step in the right direction but only include recommendations for patients aged 0–19 years [57].

World-wide, five-year conditional survival for patients diagnosed with acute myeloid leukaemia was lower than for lymphoid leukaemia. In 2010–2014, five-year conditional survival for patients with lymphoid leukaemia was approaching 90 % in most parts of Europe, North America and Oceania. On average, five-year conditional survival for patients with acute myeloid leukaemia ranged from 50 % to 80 %. For countries where five-year survival for acute myeloid leukaemia was lower, an increase in survival became more apparent when taking into account survival after the first year after diagnosis, consistent with other

findings [58]. Acute myeloid leukaemia is an aggressive sub-type of leukaemia and without treatment most patients die within weeks or months after diagnosis [58,59]. Access to optimal care is especially crucial for these patients. Due to sparse data for adolescents and young adults, with fewer patients still alive at one and five years since diagnosis, we could not estimate conditional survival for other morphology sub-types, especially by age. Nevertheless, our results are particularly relevant because they are derived from the largest set of analyses of population-based survival for leukaemia in young people.

For leukaemia, chemotherapy or some form of systemic therapy will often be the main form of treatment. The main goal is to induce remission, and for children this often involves intensive treatment within the first few months of therapy. Submission of data on the initial course of treatment was optional for CONCORD-3 because these data are not routinely collected by most population-based cancer registries. Where data were available, over 80 % of patients had received systemic therapy within six months of diagnosis in 12 countries: Canada, United States, Japan, Kuwait, Ireland, Netherlands, Portugal, Slovenia, Slovakia, Spain, Switzerland and the United Kingdom. It is worth noting that in countries with sub-regional coverage, data on treatment were often submitted by only a single registry. Furthermore, details of drug regimes, dose and duration are not captured adequately in population-based registries making any variation hard to interpret. Treatment data could be captured through efficient record linkage with clinical audit databases.

In conclusion, well-established therapeutic protocols for children with leukaemia have led to improved prognosis over the past few decades. In this study, we have offered an alternative approach to assessing the success of health care systems in managing leukaemia in young people. Conditional survival is a measure that enables an indirect assessment of the success of treatment during the first year(s) after diagnosis. After considering the impact of surviving up to five years since diagnosis, differences in 10-year survival were less marked, especially in countries where survival was low. This highlights the need to understand better what affects the outcomes of young patients in the initial year(s) after diagnosis. Children have benefited the most from national and international collaborative efforts to ensure streamlined treatment protocols, especially in countries that are well resourced. However, important inequities still exist between high-income and low- or middle-income countries. Efforts to extend this to settings with low resources and to adolescents and young adults are on-going. Assessment of these initiatives with data from population-based cancer registries will be crucial to determine the improvements in quality care in this age-group.

CRediT authorship contribution statement

Study design: CA, MPC and NS. Acquisition of statutory and ethical approvals: MPC and CA. Life tables construction: CA and MPC. Data quality controls: NS, CA, MPC. Formal analyses: NS. Writing—original draft: NS, CA, MPC. Review and editing: NS, CA, MPC, CS, RMG, CK, NSJ and JLB provided advice on methods and interpretation of results. All authors checked and contributed to writing the final report. All CONCORD Working Group members had access to the results of all steps of data preparation, quality control and analyses, and contributed to interpretation of the findings. Decision to submit: CA, MPC and NS. Funding acquisition: CA, MPC

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.ejca.2025.115445](https://doi.org/10.1016/j.ejca.2025.115445).

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