Global childhood cancer survival estimates and priority-setting: a simulation-based analysis

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Summary

Background Accurate childhood cancer survival estimates are crucial for policy makers and clinicians for priority-setting and planning decisions. However, observed survival estimates are lacking for many countries, and when available, wide variation in outcomes is reported. Understanding the barriers to optimising survival can help improve childhood cancer outcomes. We aimed to provide estimates of global childhood cancer survival, accounting for the impact of multiple factors that affect cancer outcomes in children.

Methods We developed a microsimulation model to simulate childhood cancer survival for 200 countries and territories worldwide, accounting for clinical and epidemiologic factors, including country-specific treatment variables, such as availability of chemotherapy, radiation, and surgery. To ensure model results were consistent with reported survival data, we calibrated the model to estimates from the CONCORD-2 and CONCORD-3 studies using an Approximate Bayesian Computation approach. We estimated 5-year net survival for diagnosed cases of childhood cancer in each country and territory and estimated potential survival gains of seven policy interventions focused on improving treatment availability and delivery (ie, increasing the availability of chemotherapy, radiation, general surgery, neurosurgery, or ophthalmic surgery, reducing treatment abandonment, and improving the quality of care to the mean of high-income countries) implemented in isolation or as packages.

Findings Our model estimated that, for diagnosed cases, global 5-year net childhood cancer survival is currently 37·4% (95% uncertainty interval 34·7–39·8), with large variation by region, ranging from 8·1% (4·4–13·7) in eastern Africa to 83·0% (81·6–84·4) in North America. Among the seven policy interventions modelled, each individually provided small gains, increasing global 5-year net survival to between 38·4% (35·8–40·9) and 44·6% (41·7–47·4). 5-year net survival increased more substantially when policy interventions were bundled into packages that improved service delivery (5-year net survival 50·2% [47·3–53·0]) or that expanded treatment access (54·1% [50·1–58·5]). A comprehensive systems approach consisting of all policy interventions yielded superadditive gains with a global 5-year net survival of 53·6% (51·5–55·6) at 50% scale-up and 80·8% (79·5–82·1) at full implementation.

Interpretation Childhood cancer survival varies widely by region, with especially poor survival in Africa. Although expanding access to treatment (chemotherapy, radiation, and surgery) and addressing financial toxicity are essential, investments that improve the quality of care, at both the health-system and facility level, are needed to improve childhood cancer outcomes globally.

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Introduction

Advances in treatment and supportive care over the past six decades have led to increases in 5-year net survival for children (aged 0–14 years) diagnosed with cancer from nearly 0% to 80% in high-income countries such as the UK.[1] Although it is generally known that children who develop cancer in low-income and middle-income countries (LMICs) have not benefited from these gains,[2] the magnitude of the overall survival gap has not been quantified. The best available data, as observed in global population-based cancer registries, was recently published by the CONCORD study[3–5] for a subset of childhood cancers: acute lymphoblastic leukaemia, acute myeloid leukaemia, lymphomas (as a group), and brain tumours.

Highlighting the survival gap, CONCORD estimates of 5-year net survival for acute lymphoblastic leukaemia—the most common childhood cancer—range from less than 10% to over 90%.[5] However, because of the paucity of cancer registry data from resource-limited settings, only a small subset of CONCORD-3 data (7 [2%] of 322 registries) are from low-income and lower-middle-income countries. Disparities in treatment access,[6] quality,[2] and financial toxicity[7] all contribute to the large global variations in childhood cancer outcomes.[2–5,8,9]

Research in context

Evidence before this study

Population-based observed data of 5-year net childhood (0–14 years) cancer survival for acute lymphoblastic leukaemia, lymphomas, and brain tumours from 322 cancer registries globally have been reported in the CONCORD-3 study. The CONCORD-2 study previously provided similar population-based 5-year net-survival estimates for both acute lymphoblastic leukaemia and acute myeloid leukaemia. We searched PubMed for studies on global childhood cancer survival using the search terms "childhood cancer", "survival", and "global" on Feb 28, 2019, without language or publication-date restrictions. We found no other estimates of global childhood cancer survival. Although few data from low-income and lower-middle-income countries are available, they indicate considerable variation in survival by region.

Added value of this study

With major geographic and histological gaps in the observed 5-year net-survival statistics, there are no global estimates of how many children survive cancer. This study provides, to our knowledge, the first estimate of global childhood cancer survival, based on a simulation model for 200 countries and territories and 48 cancer diagnoses. We provide global, regional, and country-level estimates of 5-year net cancer survival for all International Classification of Childhood Cancer (third edition) subgroups and estimate the potential impact of various policy scenarios to help guide priority-setting efforts aimed at improving survival.

Implications of all the available evidence

The estimated gap in childhood cancer 5-year net survival between high-income and low-income countries is more than 70 percentage points. Thus, the most important prognostic factor for whether a child will survive cancer is where he or she lives. Our model-based findings suggest that although improving the availability of treatments and mitigating treatment abandonment are necessary interventions to achieve high survival, they are insufficient if implemented alone. Concurrent improvements in health systems to ameliorate quality of care will also be needed to substantially increase childhood cancer survival worldwide.

To quantify the survival gap and identify opportunities for intervention, we developed a simulation model that synthesises clinical, epidemiological, and health-system data to estimate country-specific childhood cancer survival. Using the model, we aimed to estimate the potential survival gains that could be achieved by addressing barriers to successful treatment, such as availability of treatment modalities and quality of care. These estimates will be used to inform the *Lancet Oncology* Commission on sustainable paediatric cancer care and could assist decision makers as they prioritise policy interventions that have the potential to improve survival and reduce the number of deaths from childhood cancer.

Methods

Study design and data sources

We developed the Global Childhood Cancer (GCC) microsimulation model to simulate childhood cancer incidence[10] and survival for 200 countries and territories for 48 cancer subcategories defined by the International Classification of Childhood Cancer, third edition (ICCC).[11] The survival module of the GCC model, described here, simulates the clinical course of childhood cancer from diagnosis to 5 years after diagnosis, accounting for treatment availability, completion, and quality.

We fit the model to observed data by calibrating our model parameters so that our predicted survival estimates were consistent with population-based survival estimates for each cancer and country produced by the CONCORD programme[3–5] for the global surveillance of cancer survival. We then used a hierarchical approach to infer parameters for countries or diagnoses for which no survival data are available. Using the calibrated model, we estimated current childhood cancer survival for all countries and projected survival gains from expanding access to each treatment modality and improving quality of care. Full details of the methods are in the appendix (pp 2–56).

See Online for appendix

Procedures

We developed a conceptual treatment cascade to account for multiple factors that affect cancer survival from the point of diagnosis to completion of therapy (figure 1). We assumed that a subset of children diagnosed with cancer would achieve 5-year survival based on the availability, completion, and quality of treatment. If any required treatment modalities (chemotherapy, radiation, or surgery) are unavailable, we assumed the child would not survive. We also included a risk of abandoning treatment because of financial toxicity (ie, financial distress related to the cost of medical care). Lastly, we assumed that the quality of care, which depends on a functioning health system with supportive services (eg, nursing standards, integrated referral, and record-keeping) and facility-level activities (eg, infection control and nutritional support), affects survival. We synthesised information from multiple sources to inform country-specific estimates for each step of the cascade (table 1).

We used published estimates of diagnosed cancer cases by country and ICCC category from the GCC incidence module.[10] These estimates, which take into account geographical variation in cancer incidence and country-specific factors such as demographic trends and health-system barriers, are consistent with reported incidences of diagnosed cancers in registries included in the International Incidence of Childhood Cancer, volume

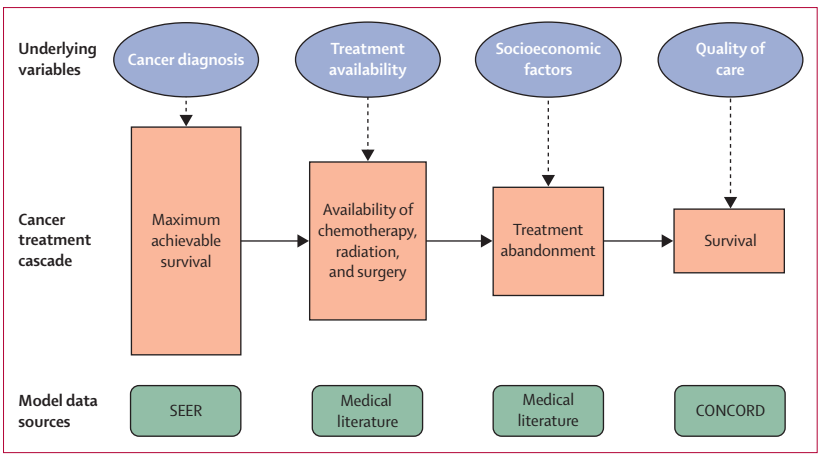

Figure 1: **Conceptual cancer treatment cascade**
This cascade accounts for multiple factors that affect childhood cancer survival from diagnosis to completion of therapy. SEER=Surveillance, Epidemiology, and End Results.

	Data source	Number of model countries reported	Reference
Cancer Diagnosis			
Diagnosed cancer cases	Estimated annual diagnosed cases by ICCC subgroup	200	Ward ZJ et al, 2019[10]
Cancer Survival			
Necessary treatment components	Expert opinion; SEER estimates of chemotherapy or radiation used as proxy for cancer stage	1 (USA)	SEER (appendix pp 3–5)
Maximum achievable survival	SEER 2010–14 5-year relative survival used as initial proxy	1 (USA)	SEER (appendix pp 6, 7)
Population-based survival	5-year net survival by country, derived from cancer registry data	10–64 (varies by diagnosis)	Bonaventure A et al, 2017;[3] Allemani C et al, 2018[5] (appendix p 8)
Cancer Treatment			
Chemotherapy availability	Reported availability of chemotherapy	94	Cohen P et al, 2019[6] (appendix pp 10, 11)
Radiation availability	Radiotherapy coverage	173	Atun R et al, 2015[12] (appendix pp 12, 13)
Surgery availability	Availability of general surgery; neurosurgeon density; and ophthalmologist density	184, 192, 192	Alkire BC et al, 2015[13] (appendix pp 14, 15); World Federation of Neurosurgical Societies, 2016[14] (appendix pp 16, 17); and Resnikoff S et al, 2012[15] (appendix pp 18, 19)
Treatment abandonment	Probability of treatment abandonment	98	Friedrich P et al, 2015[7] (appendix pp 20, 21)

GCC=Global Childhood Cancer. ICCC=International Classification of Childhood Cancer (third edition). SEER=Surveillance, Epidemiology, and End Results.

Table 1: **Overview of country-specific data sources used in the GCC survival module**

For the **Surveillance, Epidemiology, and End Results programme** see www.seer.cancer.gov

three.[16] The GCC incidence module also provides estimates for countries without registries.

For each ICCC diagnosis, we used expert opinion—based on the experience of clinicians with expertise in cancer care in LMICs and specialising in different types of cancer (eg, haematologic cancers, germ-cell tumours, and solid tumours)—to specify which treatment components (chemotherapy, radiation, or surgical specialties) were necessary for survival. Because stage at diagnosis—which determines necessary treatments for some cancers—is not routinely collected in most cancer registries, as a proxy we estimated the probability of requiring chemotherapy or radiation on the basis of reported treatment numbers from the Surveillance, Epidemiology, and End Results (SEER) programme in the USA. We also took into account heterogeneity in treatment needs for diagnoses for which a small proportion of patients require chemotherapy or radiation (appendix pp 3–5).

To account for the curability of different cancer types we estimated maximum achievable survival probabilities using data from SEER 2010–14 to inform the relative probability and variation of survival by diagnosis. Because maximum achievable survival in the model assumes availability of all necessary treatment modalities, no abandonment, and optimal quality of care, we inflated the reported SEER estimates to account for the possibility of non-optimal service delivery in the USA (appendix pp 6–7).

As calibration targets, we obtained country-specific survival estimates for ten morphology groups from CONCORD[3,5] (appendix p 8). For three brain diagnoses (astrocytoma, embryonal, and other), the CONCORD estimates of survival in the USA were higher than those reported in SEER. Specifically, 5-year survival estimates were 80·0% (SEER) versus 82·7% (CONCORD) for astrocytoma, 68·4% versus 69·4% for embryonal brain cancer, and 58·9% versus 96·9% for other brain-cancer diagnoses. Therefore, we adjusted our prior probability distributions of maximum achievable survival for these groups to be consistent with the CONCORD estimates.

We used published country-specific estimates to inform the prior probability distributions of treatment variables in the model (table 1). We estimated priors of the availability of chemotherapy agents on the basis of reported data from a global survey of paediatric oncologists (appendix pp 10–11).[6] Estimates of radiotherapy availability were based on coverage estimates from the *Lancet Oncology* Commission on expanding global access to radiotherapy (appendix pp 12–13).[12]

Data for surgical specialties were drawn from multiple sources. For general surgery, we used estimates from a modelling study of the *Lancet* Commission on global surgery (appendix pp 14–15).[13] For neurosurgery, we used data on neurosurgeon density from the World Federation of Neurosurgical Societies (appendix pp 16–17).[14] Finally, for ophthalmic surgery we used data on the density of ophthalmologists from the World Council of Ophthalmologists (appendix pp 18–19).[15] When sampling country-specific surgery probabilities, we assumed that general surgery was the most available type of surgery, followed by ophthalmic surgery, with neurosurgery the least likely to be available.

To estimate probabilities of treatment abandonment, we used published data from a global survey[7] of paediatric oncologists (appendix pp 20–21). We assumed that only patients requiring chemotherapy, radiation, or both (thus excluding the few surgery-only groups) were at risk of abandoning treatment because of the prolonged nature of these modalities.

Lastly, we included a parameter for quality of care, which has been defined as the "degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge".[17] This parameter allows us to account for health-system and facility-level factors, capturing residual differences in survival not explained by treatment access or abandonment (appendix pp 22–23).

We used a modified Bayesian hierarchical framework[18] with three levels (2016 World Bank income group, region, country) to synthesise all available estimates to generate prior probability distributions for all parameters described. This approach allowed us to regularise the reported data and estimate priors for countries with no data (appendix p 24). These priors were used as initial sampling distributions during calibration.

	Description of policy intervention
Baseline	No change from baseline
Individual policy intervention	
Chemotherapy	Increase availability of chemotherapy to mean of high-income countries
Radiation	Increase availability of radiation to mean of high-income countries
General surgery	Increase availability of general surgery to mean of high-income countries
Neurosurgery	Increase availability of neurosurgery to mean of high-income countries
Ophthalmology	Increase availability of ophthalmic surgery for retinoblastoma to mean of high-income countries
Abandonment	Reduce treatment abandonment to mean of high-income countries
Quality of care	Improve quality of care to mean of high-income countries
Packages of policy interventions	
Expand treatment access	Increase availability of all treatment modalities (chemotherapy, radiation, surgery, and surgical subspecialties) to mean of high-income countries
Improve service delivery	Improve quality of care while reducing abandonment rates to mean of high-income countries
Comprehensive—50%	Expand treatment access and improve service delivery to reduce the difference from mean of high-income countries by 50%
Comprehensive—100%	Expand treatment access and improve service delivery to reduce the difference from mean of high-income countries by 100%

Table 2: **Policy intervention scenarios**

Outcomes

For each country and territory, we modelled the effect of treatment variables on childhood cancer outcomes and estimated 5-year net survival for diagnosed cases for each ICCC subgroup. We also estimated 5-year net survival projections under various policy interventions aimed at improving survival (table 2).

Statistical analysis

Calibration involves comparing model predictions with observed data to identify parameter values that achieve a good fit.[19] We briefly describe this process here and provide full details in the appendix (pp 25–56).

We calibrated the model to CONCORD[3–5] country-specific and diagnosis-specific 5-year net survival estimates (appendix pp 28–47), providing 407 targets for model calibration. CONCORD-3 estimates of survival from acute myeloid leukaemia were reserved as a test set to assess model validity and were not used in calibration. We used an Approximate Bayesian Computation approach[20] to fit each country with CONCORD data (65 countries). For each sampled parameter set, we simulated 5-year net survival for the number of cancer cases reported for each CONCORD estimate. If the simulated survival probability was within 1 percentage point of the reported survival estimate, we accepted the parameter set as a sample from the posterior distribution as per the Approximate Bayesian Computation algorithm.[20] If a parameter set was not accepted after one million iterations, the parameter set with the best fit for the country was used. For computational efficiency, we used simulated annealing[21] to direct the sampling.

For each country, we first attempted to fit the model using overall probabilities of chemotherapy availability and treatment abandonment across cancer diagnoses. If the model was unable to fit after 100 000 iterations, we allowed these probabilities to vary by diagnosis (appendix pp 10–11, 20–21). Automatically introducing flexibility in this way allowed us to fit parsimonious models where possible, while accounting for variability in the availability and efficacy of diagnosis-specific chemotherapy regimens and abandonment, if needed.

After fitting each country with calibration targets, we sampled from the posteriors of the hierarchical models to generate parameter values for countries with no CONCORD estimates. This approach allowed us to appropriately reflect country-specific parameter uncertainty while using information from similar countries (ie, similar region and income group) when data were not available. Similar approaches were used by the Global Burden of Disease Study[8] and GLOBOCAN[9] for data imputation. This set of parameter values for all countries and cancers comprised a completed parameter set.

We repeated this process to generate 1000 different parameter sets and scored each set on the basis of how well the model predictions matched the survival targets (according to the distance squared), with each survival target weighted inversely proportional to the width of its confidence interval. We selected the top 100 sets for use in the final model to account for parameter uncertainty.

As a posterior predictive check,[18] we compared our predicted survival from the final model to the reported survival estimates from CONCORD (appendix pp 28–47).[3–5]

For the **World Bank income grouping** see https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups

As a further validity check we compared our predictions of survival for acute myeloid leukaemia to estimates for 48 countries from CONCORD-3 (appendix pp 54–55). These estimates were not used to calibrate the model, so they can serve as an external validity check of our model predictions.

Using the best-fitting 100 parameter sets, we estimated 5-year net cancer survival for each diagnosis. We ran 1000 simulations from 2015 to 2019 to estimate survival over this period, in each iteration sampling a good-fitting parameter set to account for parameter (second-order) uncertainty and simulating the number of diagnosed cases[10] and individual-level survival to account for first-order uncertainty.[22]

To explore the effect of treatment barriers (treatment availability, abandonment, and quality of care), we simulated counterfactual interventions in which we replaced the relevant parameter for each country with the mean estimated parameter among high-income countries (table 2). We also simulated packages of policy interventions to explore the relative impact of expanding treatment access versus improving service delivery, and of a comprehensive approach addressing all treatment barriers. We estimated 5-year net childhood cancer survival for each scenario and report the mean and 95% uncertainty intervals (UI; the 2·5 and 97·5 percentiles) of our simulation results. The GCC model was coded in Java (version 1.8.0), and statistical analyses were done in R (version 3.3.1).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data used in the study. The corresponding author had final responsibility for the decision to submit for publication.

Results

We estimated that, for all cancers combined, global 5-year net survival for children diagnosed in 2015 was 37·4% (95% UI 34·7–39·8), with large variation by region, ranging from 8·1% (4·4–13·7) in eastern Africa to 83·0% (81·6–84·4) in North America (figure 2). Detailed survival estimates by diagnosis and continent for all 48 ICCC categories are presented in figure 3 and reveal large variation within cancer-specific survival, with differences in survival of over 80 percentage points for cancers such as Hodgkin lymphoma and retinoblastoma, which have high survival in North America, but very poor survival in Africa (figure 3; appendix pp 57–257 [country-specific results]).

We found that our estimates have a high degree of accuracy. Our posterior predictive checks revealed that nearly all (99·0%) of our prediction intervals (ie, 95% UIs) overlapped with the 95% CIs of the CONCORD data, and our prediction intervals contained the reported point estimate 87·2% of the time. Our mean predicted survival also fell within the CONCORD 95% CIs 86·4% of the time (appendix pp 28–47). In addition, our external validity checks of acute myeloid leukaemia survival found that our prediction intervals overlapped with the CONCORD-3 95% CIs 97·9% of the time and contained the reported point estimate (ie, coverage probability) 81·3% of time, and our mean predicted survival fell within the 95% CIs 77·0% of the time (appendix pp 54–55). Lastly, we also found that our estimates of quality are highly correlated (r=0·83) with the Global Burden of Disease Healthcare Access and Quality Index (appendix p 56).

We found that among individual policy interventions, efforts to improve the quality of care could yield the largest potential survival gains globally (5-year net survival of 44·6% [95% UI 41·7–47·4]; 7·2% increase),

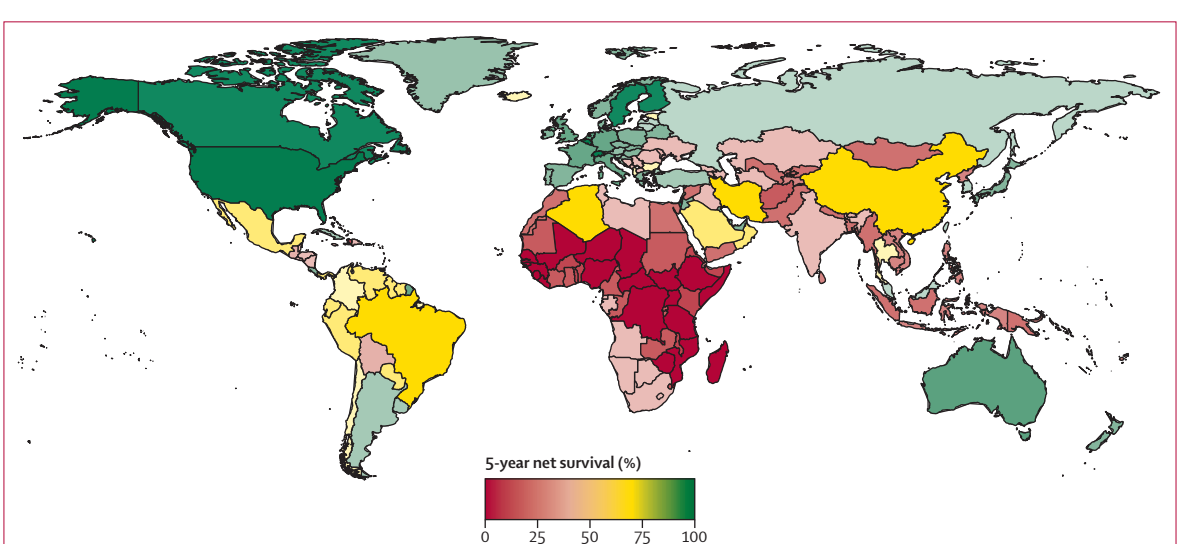

Figure 2: Estimated childhood cancer 5-year net survival by country (2015–2019)

5-year net survival (%)	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89	90–100

Diagnosis group	Diagnosis	Maximum achievable survival*	Global	Africa	Asia	Europe	Latin America and Caribbean	North America	Oceania
Leukaemia	Acute lymphoblastic leukaemia†	**96·1% (95·0–97·0)**	56·1% (51·3–60·7)	22·4% (16·2–30·0)	52·6% (45·3–59·7)	**82·8% (80·1–85·2)**	61·4% (57·4–65·1)	**89·8% (88·6–90·9)**	79·0% (69·7–86·6)
	Acute myeloid leukaemia	73·1% (64·1–80·1)	42·9% (38·0–47·7)	20·7% (15·2–27·1)	41·4% (35·1–47·5)	64·7% (59·1–70·1)	52·3% (46·8–60·0)	64·3% (61·5–67·2)	56·8% (45·5–68·2)
	Chronic myeloproliferative diseases	**96·9% (90·4–99·9)**	54·8% (47·4–61·7)	24·1% (16·2–33·1)	54·9% (46·4–63·8)	**85·0% (78·6–90·5)**	68·7% (60·9–76·9)	**90·5% (80·6–97·2)**	69·8% (47·5–87·9)
	Myelodysplastic syndrome and other	65·9% (38·3–97·3)	37·6% (22·5–50·0)	16·7% (9·2–15·6)	41·9% (24·5–54·4)	59·5% (36·2–78·2)	46·7% (28·0–62·2)	61·4% (37·6–79·9)	45·3% (18·5–71·4)
	Unspecified leukaemia	**82·5% (70·5–93·8)**	39·5% (33·0–47·0)	17·7% (11·7–24·6)	43·2% (36·0–52·7)	71·0% (61·1–80·4)	59·3% (50·9–67·0)	71·7% (64·5–79·1)	50·9% (27·6–72·2)
Lymphoma and related	Hodgkin lymphoma	**99·9% (99·6–100)**	44·6% (38·5–51·0)	16·5% (11·3–22·6)	43·7% (33·5–55·2)	**86·3% (82·2–89·8)**	71·7% (65·4–77·1)	**97·7% (96·3–98·9)**	78·2% (56·8–90·1)
	Non-Hodgkin except Burkitt's lymphoma‡	**92·7% (87·7–95·8)**	43·6% (36·4–51·3)	19·2% (13·1–25·7)	53·0% (45·3–61·6)	**82·3% (78·7–86·1)**	66·5% (61·4–71·3)	**89·8% (87·5–91·8)**	75·8% (58·7–87·3)
	Burkitt's lymphoma	**95·8% (91·4–99·0)**	28·6% (20·6–36·9)	17·2% (11·0–23·9)	57·5% (49·1–64·7)	**85·1% (80·1–89·1)**	68·5% (62·1–74·7)	**89·4% (79·6–95·5)**	74·8% (58·5–89·6)
	Lymphoreticular neoplasms	**90·4% (62·2–99·7)**	48·3% (28·0–58·9)	21·6% (13·5–20·5)	53·1% (39·5–61·6)	**80·3% (61·1–89·0)**	64·5% (48·3–73·7)	**84·3% (66·9–94·0)**	69·6% (39·3–92·3)
	Unspecified lymphoma	**92·1% (61·9–100)**	33·9% (25·1–41·9)	17·3% (10·8–24·7)	50·5% (39·4–60·0)	**80·9% (66·0–90·4)**	66·1% (54·0–74·7)	**85·2% (66·7–97·1)**	60·7% (20·8–100)
CNS neoplasms§	Ependymoma	**89·2% (84·0–94·6)**	33·4% (27·8–39·4)	**5·0% (2·4–8·8)**	25·3% (16·9–35·7)	66·9% (62·1–71·5)	37·1% (28·3–46·5)	**83·4% (79·0–87·0)**	54·0% (36·5–67·9)
	Astrocytoma	**85·8% (82·9–88·5)**	33·6% (32·4–39·6)	**8·1% (4·6–12·4)**	22·0% (16·3–28·3)	66·4% (62·8–70·0)	35·1% (27·0–43·4)	**81·1% (78·8–83·0)**	51·8% (35·1–64·2)
	CNS embryonal neoplasms	72·5% (66·4–79·2)	23·6% (20·1–28·0)	**4·4% (2·3–7·4)**	16·0% (11·6–22·0)	51·5% (47·0–56·1)	27·0% (20·7–33·8)	67·1% (62·8–70·8)	37·1% (16·4–51·0)
	Other gliomas	68·0% (60·6–77·0)	23·0% (19·2–26·9)	**4·7% (2·5–7·6)**	16·7% (11·7–21·9)	52·1% (46·4–57·8)	29·8% (22·7–37·9)	58·1% (54·6–61·6)	39·3% (22·6–53·2)
	Other specified CNS neoplasms	**99·9% (99·8–100)**	56·0% (47·7–63·2)	**8·9% (5·0–14·3)**	43·7% (33·3–56·5)	**84·2% (80·4–87·5)**	49·8% (37·7–60·4)	**95·3% (92·1–97·5)**	45·0% (17·1–73·9)
	Unspecified CNS neoplasms	77·3% (48·6–95·4)	18·6% (11·6–25·5)	**2·5% (1·1–4·5)**	18·6% (10·5–27·8)	52·8% (37·7–66·4)	30·3% (21·1–41·3)	67·7% (46·9–85·7)	38·7% (14·5–62·7)
Neuroblastoma	(Ganglio)-neuroblastoma	**88·1% (81·8–91·1)**	40·3% (35·4–45·4)	11·2% (6·5–16·7)	35·0% (28·9–42·0)	71·3% (66·7–75·4)	50·9% (43·4–57·8)	**80·6% (72·9–86·5)**	64·7% (54·0–75·1)
	Peripheral nervous cell tumours	**88·7% (56·4–100)**	25·2% (14·7–33·5)	**6·7% (3·2–12·4)**	24·5% (15·0–35·0)	70·5% (53·9–83·8)	50·9% (37·3–63·4)	**81·5% (58·3–96·8)**	51·1% (12·5–83·3)
Retinoblastoma	Retinoblastoma	**94·0% (85·4–98·0)**	24·0% (17·4–30·6)	**5·2% (3·4–7·7)**	32·1% (24·3–40·5)	77·9% (72·6–82·8)	54·8% (45·0–64·2)	**89·9% (84·4–94·0)**	62·4% (44·6–77·6)
Renal tumours	Nephroblastoma	**97·4% (95·2–98·8)**	27·0% (21·5–32·8)	**5·7% (3·7–8·2)**	27·9% (20·7–35·6)	78·2% (73·5–82·4)	55·8% (48·1–63·8)	**89·2% (80·0–94·8)**	71·0% (54·9–83·9)
	Renal carcinoma	70·8% (40·0–93·3)	24·5% (13·4–36·3)	12·4% (5·9–20·7)	32·0% (18·0–46·4)	63·4% (37·8–82·3)	50·7% (29·8–70·4)	69·5% (40·6–89·6)	46·7% (0–100)
	Unspecified renal tumour	**81·2% (26·0–100)**	16·8% (6·7–26·0)	**8·7% (2·9–16·1)**	31·0% (12·7–45·3)	70·9% (30·1–90·0)	54·9% (24·1–75·5)	78·1% (30·8–100)	57·3% (0–100)
Hepatic tumours	Hepatoblastoma	**91·2% (82·2–97·0)**	37·5% (25·9–43·6)	**7·9% (4·6–12·1)**	37·0% (29·2–43·6)	75·7% (68·6–82·7)	52·0% (41·3–62·4)	**83·8% (73·4–91·4)**	63·6% (41·9–81·1)
	Hepatic carcinoma	63·5% (39·6–85·6)	18·0% (11·5–25·1)	**6·2% (3·6–9·8)**	20·1% (12·0–28·5)	53·0% (35·5–68·9)	35·3% (23·6–50·6)	57·8% (37·9–78·2)	31·2% (6·7–62·5)
	Unspecified hepatic tumour	75·5% (25·9–99·2)	28·0% (13·7–42·9)	**9·2% (4·0–16·9)**	36·4% (17·8–54·1)	68·9% (33·9–91·2)	55·0% (27·5–76·5)	73·8% (29·4–100)	45·9% (0–100)
Bone tumours	Osteosarcoma	74·4% (62·9–83·7)	28·0% (23·3–32·9)	**7·7% (5·1–10·7)**	25·9% (20·1–32·6)	62·5% (54·6–69·2)	44·8% (36·7–52·4)	67·9% (58·0–77·3)	49·7% (32·0–65·3)
	Chondrosarcoma	**85·8% (50·7–99·7)**	23·0% (12·2–32·9)	**5·4% (2·5–8·9)**	29·1% (17·0–40·0)	70·2% (44·0–85·8)	50·4% (29·9–65·8)	78·3% (48·3–96·6)	59·1% (0–100)

(Figure 3 continues on next page)

Diagnosis group	Diagnosis	Maximum achievable survival*	Global	Africa	Asia	Europe	Latin America and Caribbean	North America	Oceania
	Ewing's sarcoma and related	82·1% (71·7–90·9)	29·4% (24·3–35·4)	9·3% (5·0–14·6)	22·7% (17·0–29·1)	67·8% (58·5–74·8)	48·8% (40·4–57·3)	75·0% (64·5–84·5)	52·8% (36·0–66·9)
	Other specified bone tumour	67·9% (25·7–91·6)	25·1% (13·3–37·3)	9·4% (4·3–15·7)	29·4% (14·0–43·7)	61·4% (34·9–82·7)	50·0% (28·0–71·7)	66·8% (36·7–89·6)	37·8% (0–75·0)
	Unspecified bone tumour	77·8% (26·0–99·6)	19·9% (8·4–29·7)	10·0% (4·5–17·3)	32·1% (13·8–46·0)	70·1% (30·8–90·0)	56·4% (22·8–77·8)	77·3% (32·9–98·5)	47·4% (0–100)
Soft tissue sarcoma	Rhabdomyosarcoma	79·8% (70·7–86·7)	26·9% (21·7–31·3)	5·6% (3·6–8·0)	26·7% (20·7–32·7)	66·1% (59·4–72·5)	46·9% (39·6–56·0)	73·2% (62·5–80·3)	58·9% (45·2–71·8)
	Fibrosarcoma	87·3% (72·1–97·2)	39·0% (30·1–47·3)	13·7% (9·0–20·0)	46·0% (35·0–56·4)	77·7% (65·5–87·0)	64·4% (53·0–76·5)	85·9% (74·0–94·9)	57·4% (29·0–81·8)
	Kaposi's sarcoma	83·1% (39·0–100)	10·0% (4·4–19·4)	3·8% (1·7–7·6)	37·2% (21·1–54·8)	72·2% (42·9–90·6)	59·0% (33·7–74·6)	80·0% (37·5–100)	56·0% (24·4–84·2)
	Other specified sarcoma	87·5% (80·5–92·9)	27·4% (22·6–32·3)	3·0% (1·7–4·8)	26·4% (19·9–33·9)	69·0% (62·7–75·1)	48·0% (39·0–56·1)	79·9% (72·2–87·1)	52·3% (31·4–70·8)
	Unspecified sarcoma	86·7% (73·3–95·4)	32·6% (24·8–40·0)	12·0% (7·6–17·2)	34·8% (23·9–45·1)	78·7% (69·3–86·7)	64·0% (51·6–75·5)	85·1% (74·7–93·2)	58·8% (31·2–83·3)
Germ-cell tumours	CNS germ-cell tumour	90·4% (78·1–98·0)	33·4% (24·1–41·6)	2·3% (0·8–5·3)	32·0% (21·4–43·0)	66·8% (58·0–75·0)	30·8% (20·9–42·4)	80·9% (69·4–89·9)	43·3% (19·2–65·9)
	Other extragonadal tumour	91·3% (84·3–96·3)	34·9% (22·6–42·2)	7·6% (4·5–11·6)	37·9% (30·4–45·3)	76·6% (69·1–82·8)	55·4% (46·4–64·3)	83·6% (75·3–90·9)	58·9% (35·9–78·7)
	Gonadal germ-cell tumour	98·1% (95·1–99·7)	47·8% (41·3–54·1)	13·4% (8·5–19·2)	44·9% (35·7–53·2)	86·2% (80·4–90·3)	65·3% (53·9–76·0)	94·0% (88·8–97·5)	68·4% (46·8–85·4)
	Gonadal carcinoma	69·5% (28·5–94·3)	19·0% (8·8–28·3)	5·7% (2·2–10·0)	20·9% (9·4–32·1)	56·8% (25·9–80·6)	39·5% (19·5–59·7)	64·3% (25·0–93·9)	43·8% (0–100)
	Unspecified gonadal tumour	86·5% (44·9–99·9)	30·4% (18·6–40·1)	11·4% (6·2–17·5)	36·2% (21·6–48·8)	77·6% (48·8–92·3)	62·0% (39·5–80·6)	84·6% (53·6–100)	60·7% (0–100)
Carcinoma and melanoma	Adrenocortical carcinoma	65·0% (32·2–90·2)	30·7% (16·7–43·4)	9·3% (4·0–17·4)	27·9% (15·4–40·3)	56·3% (32·2–75·7)	42·7% (23·7–59·2)	61·9% (33·3–85·0)	32·4% (0–75·0)
	Thyroid carcinoma	99·9% (99·6–100)	51·9% (44·7–59·1)	11·7% (7·2–16·8)	46·0% (35·5–56·8)	84·1% (78·1–88·8)	66·5% (56·6–76·1)	97·2% (94·6–99·2)	63·4% (33·3–85·4)
	Nasopharyngeal carcinoma	85·8% (53·9–99·4)	26·4% (15·3–36·8)	9·0% (4·5–14·0)	35·0% (23·2–47·0)	73·8% (55·2–86·8)	61·2% (45·8–75·5)	83·2% (61·8–96·4)	55·6% (16·7–92·3)
	Melanoma	99·9% (99·5–100)	60·3% (50·2–67·4)	15·7% (10·0–22·0)	55·0% (41·2–66·3)	91·7% (87·7–95·0)	73·9% (63·1–83·9)	98·2% (96·0–99·7)	79·2% (51·4–93·5)
	Skin carcinoma	80·4% (28·8–99·6)	32·4% (15·1–44·1)	15·0% (6·8–23·3)	33·9% (14·5–48·9)	73·0% (32·8–92·2)	55·7% (27·4–74·7)	78·6% (32·1–100)	59·8% (0–100)
	Other and unspecified carcinoma	89·5% (77·1–97·2)	33·1% (25·7–40·9)	12·3% (8·3–17·5)	37·6% (27·5–48·0)	81·1% (73·4–88·6)	64·8% (54·1–74·6)	88·0% (80·0–95·0)	69·5% (48·3–85·3)
Other and unspecified	Other specified	87·5% (57·4–98·2)	42·0% (29·4–53·1)	14·7% (9·0–21·8)	49·2% (34·1–64·8)	78·6% (59·1–90·7)	63·3% (46·3–77·8)	85·7% (64·8–97·1)	51·8% (20·0–85·7)
	Other unspecified	89·7% (59·6–99·8)	22·5% (14·7–30·6)	10·7% (5·8–17·3)	36·3% (24·0–49·3)	77·4% (55·7–90·2)	60·1% (39·3–76·2)	87·8% (62·7–99·2)	47·3% (18·2–78·9)

Figure 3: **Estimated childhood cancer 5-year net survival by continent and ICCC diagnosis group (2015–2019)**
Data are % (95% uncertainty interval). ICCC=International Classification of Childhood Cancer (third edition). *Maximum achievable survival estimates are based on adjusted estimates from Surveillance, Epidemiology, and End Results (appendix pp 48, 49). †CONCORD estimates based on lymphoid leukaemia ICCC registry grouping, which includes acute lymphoblastic leukaemia and precursor-cell lymphoblastic lymphoma. ‡CONCORD estimates included Burkitt's lymphoma and Burkitt cell leukaemia with the non-Hodgkin lymphomas. §CONCORD estimates did not include intraspinal tumours.

followed by expanding access to general surgery (42·7% [39·9–45·6]; 5·3% increase) and chemotherapy (41·9% [38·9–45·0]; 4·5% increase; table 3). This general pattern is similar across most regions of the world.

Looking at policy intervention packages, we found that increasing the availability of all treatments to the level of high-income countries would result in global 5-year net survival of 54·1% (95% UI 50·1–58·5; 16·7 percentage-point increase). Similarly, improving service delivery (ie, simultaneously improving quality of care and reducing abandonment) yielded important survival gains, but to a lesser extent (50·2% [47·3–53·0]). We found, however, that improving both treatment access and service delivery has a superadditive effect. For example, reducing the gap with high-income countries

	Baseline	Single intervention—treatment access					Single intervention—service delivery		Intervention packages			
		Chemotherapy*	Radiation†	General surgery‡	Neurosurgery§	Ophthalmic surgery¶	Abandonment‖	Quality of care**	Expand treatment access††	Improve service delivery‡‡	Comprehensive—50%§§	Comprehensive—100%¶¶
Global	37·4% (34·7–39·8)	41·9% (38·9–45·0)	39·1% (36·4–41·5)	42·7% (39·9–45·6)	39·0% (36·3–41·6)	38·4% (35·8–40·9)	41·1% (37·8–44·4)	44·6% (41·7–47·4)	54·1% (50·1–58·5)	50·2% (47·3–53·0)	53·6% (51·5–55·6)	80·8% (79·5–82·1)
Low income	7·4% (5·0–10·7)	10·0% (6·6–14·5)	9·4% (6·4–13·4)	15·5% (10·8–20·6)	7·7% (5·2–11·1)	8·6% (5·9–12·1)	12·2% (8·7–16·5)	14·4% (11·0–18·2)	26·5% (18·3–35·4)	23·9% (20·0–27·8)	29·4% (25·8–33·4)	80·6% (77·2–83·3)
Lower-middle income	24·0% (19·5–29·1)	29·2% (23·4–34·3)	26·1% (21·1–31·6)	31·9% (26·2–38·2)	26·0% (21·1–31·5)	25·5% (20·9–30·8)	28·5% (22·6–34·8)	33·6% (28·7–38·3)	46·5% (38·0–53·9)	40·8% (36·7–45·3)	45·4% (41·7–49·2)	80·6% (78·9–82·1)
Upper-middle income	55·5% (51·5–58·9)	61·5% (55·6–67·1)	56·9% (52·8–60·5)	57·4% (54·1–60·6)	57·5% (54·0–60·4)	55·9% (52·1–59·2)	58·4% (53·7–63·1)	61·9% (55·9–68·1)	68·2% (61·7–73·5)	65·2% (59·5–71·5)	66·9% (64·4–69·1)	80·2% (78·8–81·6)
High income	79·8% (78·7–80·8)	80·6% (79·6–81·7)	80·0% (78·9–81·0)	80·2% (79·2–81·3)	80·3% (79·2–81·3)	79·9% (78·8–80·9)	80·4% (79·4–81·5)	80·2% (79·2–81·3)	81·7% (80·7–82·8)	80·9% (79·9–81·9)	81·3% (80·3–82·4)	82·9% (82·0–83·9)
Africa	11·6% (8·7–14·8)	14·1% (10·5–18·1)	13·4% (10·1–17·1)	19·0% (13·9–25·1)	12·0% (9·0–15·4)	13·1% (9·8–16·9)	16·2% (12·0–21·4)	21·0% (18·0–24·5)	29·0% (21·4–37·6)	30·4% (26·8–34·0)	33·7% (30·2–37·4)	80·9% (77·9–83·5)
Eastern Africa	8·1% (4·4–13·7)	10·5% (5·5–17·5)	10·7% (5·9–18·0)	15·3% (8·7–23·7)	8·3% (4·6–14·1)	8·8% (4·9–14·7)	13·0% (7·5–19·6)	15·4% (11·0–20·8)	26·3% (14·9–41·9)	25·1% (19·6–30·8)	29·7% (24·5–36·0)	80·2% (75·5–83·4)
Southern Africa	19·2% (11·9–26·1)	21·7% (13·9–30·1)	22·3% (14·6–30·5)	22·5% (14·6–31·4)	20·4% (12·8–27·6)	20·8% (13·2–28·2)	23·2% (15·0–31·0)	29·4% (24·8–34·1)	34·8% (24·3–53·3)	36·5% (32·0–41·1)	38·3% (32·7–45·0)	79·1% (75·7–81·7)
Western Africa	8·5% (4·9–13·0)	10·9% (6·3–17·3)	9·4% (5·5–14·4)	17·3% (9·7–28·1)	8·7% (5·0–13·2)	10·8% (6·1–16·7)	13·5% (7·1–22·2)	17·5% (13·4–23·1)	26·2% (15·2–40·3)	28·1% (22·8–34·3)	31·8% (26·4–38·1)	82·0% (78·1–85·0)
Northern Africa	30·3% (18·5–41·6)	33·9% (20·3–46·1)	32·9% (19·9–45·1)	34·8% (20·6–47·7)	32·0% (19·5–44·0)	30·9% (18·8–42·5)	33·3% (20·1–46·7)	47·0% (42·0–51·9)	45·4% (26·8–62·2)	51·8% (47·7–56·1)	50·3% (42·2–58·0)	79·2% (77·3–81·3)
Asia	39·6% (35·1–43·6)	45·8% (40·8–50·8)	41·6% (36·7–45·6)	45·2% (40·5–50·4)	41·8% (37·1–46·4)	40·6% (36·1–44·8)	43·4% (38·0–48·1)	46·9% (42·3–50·9)	59·8% (53·9–66·3)	51·9% (47·1–56·4)	56·4% (53·2–59·3)	80·1% (78·9–81·2)
Eastern Asia	53·8% (46·5–59·4)	61·3% (51·4–72·3)	55·2% (47·4–60·5)	55·7% (49·6–60·6)	55·7% (49·2–61·3)	54·3% (47·3–59·8)	57·0% (48·7–65·8)	59·5% (49·0–70·8)	67·9% (57·5–77·2)	63·0% (52·3–73·9)	65·6% (61·1–69·1)	79·4% (77·5–81·3)
South-central Asia	31·3% (23·2–39·8)	38·0% (28·3–46·4)	33·7% (25·0–42·1)	40·2% (30·7–50·7)	34·3% (25·5–44·0)	32·6% (24·4–41·3)	34·8% (25·9–43·9)	38·8% (31·5–49·1)	58·4% (46·1–69·4)	43·5% (36·7–52·2)	51·5% (45·5–57·7)	80·5% (79·2–81·9)
South-eastern Asia	28·8% (22·2–35·5)	33·6% (25·2–43·1)	30·7% (23·6–38·0)	34·0% (26·7–41·9)	30·0% (23·1–37·0)	30·1% (23·2–37·1)	34·7% (26·3–43·9)	39·0% (33·9–44·1)	46·9% (35·6–58·8)	47·2% (42·8–51·8)	48·4% (43·3–53·8)	79·3% (77·5–81·2)
Western Asia	56·7% (51·9–60·7)	58·7% (53·0–63·4)	58·5% (53·1–62·9)	58·3% (53·4–62·8)	57·8% (52·9–62·1)	56·9% (52·1–61·0)	60·5% (54·8–64·9)	63·8% (60·7–66·5)	64·5% (57·6–70·5)	68·8% (66·3–71·3)	67·1% (63·9–70·1)	81·4% (79·9–82·9)

(Table 3 continues on next page)

	Baseline	Single intervention—treatment access					Single intervention—service delivery		Intervention packages			
		Chemotherapy*	Radiation†	General surgery‡	Neurosurgery§	Ophthalmic surgery¶	Abandonment‖	Quality of care**	Expand treatment access††	Improve service delivery‡‡	Comprehensive—50%§§	Comprehensive—100%¶¶
(Continued from previous page)												
Europe	74·3% (71·9–76·4)	75·4% (72·9–77·5)	75·2% (72·6–77·4)	74·9% (72·7–76·9)	75·0% (72·8–77·0)	74·4% (72·0–76·4)	75·2% (72·7–77·5)	76·6% (74·8–78·3)	77·9% (75·4–80·1)	77·8% (76·0–79·3)	77·9% (76·3–79·4)	82·2% (81·0–83·3)
Eastern Europe	65·7% (59·9–70·3)	67·4% (61·4–72·5)	67·5% (61·1–72·6)	66·9% (61·6–71·5)	67·1% (61·6–71·7)	65·9% (60·2–70·4)	67·4% (60·7–72·1)	70·4% (66·5–74·3)	72·4% (66·5–77·8)	72·6% (69·1–76·3)	72·7% (69·2–75·9)	81·3% (79·5–83·3)
Northern Europe	80·6% (78·3–82·7)	81·1% (78·9–83·3)	80·8% (78·5–82·9)	80·7% (78·6–82·8)	80·8% (78·6–82·9)	80·6% (78·3–82·7)	80·8% (78·5–82·9)	81·0% (78·7–83·1)	81·8% (79·7–83·8)	81·2% (79·0–83·4)	81·5% (79·5–83·5)	82·5% (80·4–84·6)
Southern Europe	76·2% (73·9–78·7)	77·3% (74·9–79·8)	76·9% (74·4–79·5)	76·5% (74·3–79·0)	76·6% (74·3–79·1)	76·3% (74·0–78·7)	77·2% (74·7–79·8)	78·3% (76·2–80·4)	78·8% (76·3–81·5)	79·4% (77·2–81·5)	79·1% (77·2–81·2)	82·3% (80·4–84·3)
Western Europe	81·6% (79·4–83·6)	82·2% (80·0–84·1)	81·6% (79·5–83·6)	81·8% (79·8–83·7)	81·8% (79·8–83·8)	81·6% (79·4–83·6)	81·8% (79·7–83·8)	81·7% (79·5–83·7)	82·7% (80·9–84·5)	82·0% (79·9–83·9)	82·3% (80·5–84·1)	83·2% (81·6–84·7)
Latin America and Caribbean	55·0% (51·2–58·7)	60·6% (56·2–65·3)	55·9% (52·3–59·5)	57·8% (54·3–60·7)	57·8% (54·3–61·4)	55·6% (51·8–59·3)	58·2% (53·8–62·6)	61·2% (57·0–65·6)	68·4% (63·9–72·7)	64·8% (60·1–69·7)	66·9% (64·6–69·3)	81·0% (79·5–82·5)
Caribbean	45·0% (36·3–54·1)	46·4% (37·5–56·1)	47·2% (37·5–58·1)	48·7% (38·6–59·4)	46·7% (37·7–56·5)	45·4% (36·7–55·0)	48·9% (38·8–57·8)	53·4% (46·5–59·4)	56·3% (43·5–71·5)	59·3% (54·1–64·2)	58·8% (51·8–66·0)	80·7% (77·9–83·3)
Central America	45·4% (35·9–54·1)	53·0% (41·5–62·8)	46·1% (36·6–55·2)	51·7% (46·4–57·3)	49·9% (42·0–57·4)	46·4% (37·6–54·7)	50·1% (40·5–61·1)	50·9% (42·5–58·4)	66·8% (58·8–74·3)	56·0% (46·8–65·7)	61·9% (56·1–66·8)	81·6% (79·4–83·5)
South America	60·2% (54·8–64·2)	65·3% (59·5–69·7)	61·1% (56·0–65·6)	61·3% (56·5–64·8)	62·2% (56·9–66·9)	60·5% (55·2–64·5)	62·6% (56·9–67·6)	66·6% (61·1–72·5)	70·0% (65·2–75·3)	69·3% (63·7–74·2)	69·9% (66·3–72·5)	80·7% (79·0–82·6)
North America	83·0% (81·6–84·4)	83·8% (82·4–85·2)	83·0% (81·6–84·5)	83·0% (81·6–84·5)	83·1% (81·7–84·5)	83·0% (81·6–84·4)	83·1% (81·7–84·5)	83·0% (81·6–84·5)	84·0% (82·6–85·3)	83·1% (81·7–84·5)	83·5% (82·2–84·8)	84·1% (82·8–85·3)
Oceania	64·4% (58·9–69·2)	65·3% (59·5–70·3)	65·2% (59·4–70·3)	66·2% (60·5–71·3)	65·8% (59·9–70·5)	64·7% (59·2–69·6)	65·4% (59·4–70·5)	68·5% (64·1–73·2)	70·6% (63·6–76·8)	70·4% (66·5–74·6)	71·1% (66·4–75·2)	81·5% (78·6–84·5)
Oceania (region)	19·3% (6·7–33·3)	21·6% (7·4–37·1)	22·4% (7·9–38·0)	23·6% (8·1–40·0)	21·4% (7·6–36·6)	20·1% (7·1–34·2)	23·0% (7·6–39·7)	35·3% (26·3–45·6)	35·4% (11·7–58·2)	42·1% (33·2–51·7)	41·2% (29·5–53·1)	78·2% (72·5–83·7)
Australia and New Zealand	79·1% (74·8–83·4)	79·6% (75·3–83·7)	79·2% (74·9–83·4)	80·1% (76·4–83·9)	80·3% (76·2–84·4)	79·3% (75·0–83·7)	79·3% (75·2–83·6)	79·4% (75·3–83·7)	82·1% (78·5–85·6)	79·6% (75·6–83·8)	80·9% (77·3–84·5)	82·6% (79·7–85·8)

Data are % (95% uncertainty interval). *Increase availability of chemotherapy to mean of high-income countries. †Increase availability of radiation to mean of high-income countries. ‡Increase availability of general surgery to mean of high-income countries. §Increase availability of neurosurgery to mean of high-income countries. ¶Increase availability of ophthalmic surgery for retinoblastoma to mean of high-income countries. ||Reduce treatment abandonment to mean of high-income countries. **Improve quality of care to mean of high-income countries. ††Increase availability of all treatment modalities (chemotherapy, radiation, surgery, and surgical subspecialties) to mean of high-income countries. ‡‡Improve quality of care while reducing abandonment rates to mean of high-income countries. §§Expand treatment access and improve service delivery to reduce the difference from mean of high-income countries by 50%. ¶¶Expand treatment access and improve service delivery to reduce the difference from mean of high-income countries by 100%.

Table 3: **Estimated childhood cancer 5-year net survival 2015–19 under various policy interventions**

for all components by 50% is predicted to achieve similar or increased gains in global 5-year net survival (53·6% [51·5–55·6]) compared with 100% scale-up of treatment-access or service-delivery packages separately (table 3). Full implementation of all interventions is estimated to increase global 5-year net survival to 80·8% (79·5–82·1).

Discussion

Using statistical and computational methods to synthesise estimates from multiple sources of data, we developed a model of childhood cancer survival for 200 countries and territories worldwide. We found that childhood cancer survival varies widely by country because of substantial differences in access to multidisciplinary treatment methods, risk of abandonment, and quality of care. As a result, our findings suggest that 5-year net survival for all childhood cancers combined varies by up to 75 percentage points between WHO subregions. Furthermore, as net survival only considers deaths from cancer, the difference in total survival is probably even larger given higher risks of competing mortality in LMICs than in high-income countries. Although genetic variations are known to affect survival,[23,24] the most important prognostic factor for whether a child diagnosed with cancer will survive is not related to cancer biology but is instead related to the country where they receive treatment.

Beyond their importance for policy making and informing health-investment decisions by countries and development agencies, these estimates can provide a baseline assessment to help guide efforts to improve childhood cancer policies and those aimed at building stronger health systems. For example, the WHO Global Initiative for Childhood Cancer, announced in September, 2018,[25] aims to increase global childhood cancer survival to 60% by 2030, as measured by six tracer cancer subtypes: acute lymphoblastic leukaemia, Hodgkin lymphoma, Burkitt's lymphoma, retinoblastoma, nephroblastoma, and low-grade gliomas. Our estimates of 5-year net survival for acute lymphoblastic leukaemia (56·1%) and Hodgkin lymphoma (44·6%) suggest moderate improvement is required for these cancers to achieve 60% survival. However, our survival estimates for the other cancers are much lower, with retinoblastoma, Burkitt's lymphoma, and nephroblastoma all around 25%. It is not possible to estimate survival for low-grade gliomas with the current ICCC categories.

By contrast, we estimated 5-year net survival for these cancers to be around 90% or more in North America, highlighting both the opportunity to substantially increase survival and the challenge of achieving these gains in a relatively short period of time. However, given that nearly half of children with cancer might not be diagnosed in LMICs,[10] the true overall survival is probably even lower. Therefore, in addition to improving treatment, increased efforts to identify all cases in a population and develop stronger health systems with appropriate support services will also be needed to improve survival for all children with cancer.

To address the stark global disparities in childhood cancer survival, determining which policy interventions are likely to be most effective is a necessary first step. Individually, our model predicts that single policy interventions alone will yield small survival gains. Although efforts to address any one problem, such as financial toxicity, are necessary to achieve high survival, they are insufficient if implemented alone. We found that even if reducing abandonment resulted in more children completing therapy, overall survival did not significantly improve because of interdependencies in the availability of treatment modalities and quality of care. Although abandonment represents an important actionable opportunity, ensuring patient retention and completion of therapy is inefficient if the quality of care is not also improved.

Our findings highlight the importance of complex interdependencies in childhood cancer treatment. We found that comprehensive packages of policy interventions that improve both treatment access and service delivery yield synergistic survival gains. Thus, a key message is that a systems approach with packages of policy interventions including investments to expand access to multidisciplinary care, reduce financial toxicity, and improve service delivery are necessary to substantially improve cancer survival. In a follow-up analysis, we are estimating the return on investment of implementing such a comprehensive approach, taking into account the costs of health-system strengthening to improve care for children with cancer.

Beyond the interdependence of policy interventions, the model also highlights the important part that quality of care plays in improving childhood cancer outcomes. These findings are not unique to paediatric cancer, as the importance of quality is echoed in results from other areas of global health as well. For example, a conditional cash-transfer programme incentivising facility childbirth in India succeeded in substantially expanding access to health care, but did not reduce maternal mortality because of a lack of focus on quality.[26] Similarly, improving childhood cancer outcomes worldwide will require paying attention to what happens once children reach health-care facilities, with investments to measure and improve health-care quality in addition to expanding access.[27]

The widespread impact of quality, from the patient level to the health system means that a broad range of initiatives is needed. For example, at the facility level, interventions related to supportive care (eg, infection-control and nutritional programmes) designed to reduce death due to comorbidities are crucial to improve service delivery and safety. Although generic guidelines promoting the importance of supportive-care measures have been published,[28] specific quality-improvement initiatives

that reflect the local context need to be designed and evaluated. Improving the quality of care also requires higher-level improvements to the overall health system (eg, workforce planning and efficient referral patterns). A focus on quality at all levels of the health system is thus needed to achieve integrated care that is person-centred and responsive to the patient's needs.

Although our modelling approach allowed us to synthesise data from multiple sources in a way that is consistent with data on treatment availability and reported survival, there are several limitations due to the assumptions needed to develop the model. First, much of our data is based on cross-sectional surveys of treatment access and abandonment, which might provide an incomplete snapshot of the reality on the ground. For example, our prior probabilities (ie, before calibration) of abandonment are based on survey data, which reported estimates for acute lymphoblastic leukaemia only,[7] and the survey data used to inform chemotherapy priors might not be representative of the respondents' countries as a whole. However, our approach allowed us to account for uncertainty around all model parameters and their joint distribution. Our 95% UIs thus reflect the sensitivity of our results to different parameter estimates. However, it should be noted that although these intervals capture the statistical uncertainty around the model parameters and calibration targets, they do not include uncertainty due to other factors, such as our modelling assumptions and potential data-quality issues in the calibration targets used to fit the model.

Second, although we used hierarchical models to incorporate all available observed data, the paucity of registries in LMICs and small sample sizes in some regions might have affected our results and contributed to the wide uncertainty intervals we reported for some cancers and countries. For example, CONCORD[3–5] survival estimates were only available for two countries in sub-Saharan Africa (Nigeria and Lesotho), and then only for acute lymphoblastic leukaemia.

Third, we used a single quality parameter per country as a proxy for many factors related to service delivery, for which we had no data. In some countries, this constraint meant it was not possible to fit all calibration targets. However, our approach allows us to refine and update our model as more specific data become available. Despite being abstract, our estimates of quality are similar to other published estimates and are highly correlated with the Global Burden of Disease Healthcare Access and Quality Index (appendix p 56).[29] Given that our quality parameters were inferred exclusively by model calibration, this high correlation builds confidence in the convergent validity of our estimates.

Lastly, although calibration allowed us to align our model results with observed survival and induce appropriate covariance between model parameters, we assumed that the availability of each treatment modality was independent for each patient since we had no data for the covariance of treatment probabilities for individual patients. In the future, facility-level data would help to refine this assumption and account for correlation between the availability of treatment options for a given patient. Additionally, these types of data could also help inform more specific quality measures to include in the model to track progress more precisely.

Notwithstanding these limitations, using a model-based approach, we provided, to our knowledge, the first global estimate of childhood cancer survival and found large disparities in 5-year net survival as a result of substantial differences in access to multidisciplinary treatment modalities, risk of abandonment, and quality of care. Our findings suggest that although increasing access to treatment is necessary to achieve high survival, it is not sufficient. A comprehensive set of policy interventions, including expanding treatment access, reducing abandonment, and improving quality of care in health systems is needed to reduce the large disparities in childhood cancer survival and substantially reduce childhood cancer deaths worldwide.

Contributors

ZJW, JMY, NB, ALF, and RA designed the study and acquired the data. FG provided insight on morphology groupings and additional survival estimates from the CONCORD programme. ZJW did the analyses. All authors interpreted the results and contributed to the writing of the report.

Declaration of interests

We declare no competing interests.

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