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

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Abstract

Background: Accurate childhood cancer survival estimates are critical for policy-makers and clinicians for priority-setting and planning decisions. However, observed survival estimates are lacking for many countries, and where available, wide variation in outcomes is reported. Understanding the barriers to optimizing 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 influence cancer outcomes.

Methods: We developed a microsimulation model to simulate childhood cancer survival for 200 countries/territories worldwide, taking into account clinical and epidemiologic factors, including country-specific treatment variables, such as availability of chemotherapy/radiation/surgery. To ensure model results were consistent with reported survival data, we calibrated the model to estimates from the CONCORD 2 and 3 studies using an Approximate Bayesian Computation approach. We estimated five-year net survival for diagnosed childhood cancer cases in each country/territory and estimated potential survival gains if seven policy interventions focused on improving treatment availability and delivery were implemented in isolation or as packages.

Findings: Our model estimates that global five-year net childhood cancer survival is currently 37·4% (95% uncertainty interval [UI] 34·7%-39·8%), with large variation by region, ranging from 8·1% (95% UI 4·4%-13·7%) in Eastern Africa to 83·0% (95% UI 81·6%-84·4%) in North America. Among the seven policy interventions modeled, each individually provided limited gains, increasing global five-year net survival to between 38·4% and 44·6%. When bundled into packages of interventions that either improved service delivery or expanded treatment access, five-year net survival increased to 50·2% (95% UI 47·3%-53·0%) and 54·1% (95% UI 50·1%-58·5%), respectively. A comprehensive systems approach consisting of all policy interventions yielded super-additive gains with global five-year net survival of 53·6% (95% UI 51·5%-55·6%) at 50% scale-up and 80·8% (95% UI 79·5%-82·1%) at full implementation.

Interpretation: Childhood cancer survival varies widely by region, with especially poor survival in Africa. While expanding access to treatment (chemotherapy/radiation/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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Research in context

Evidence before this study

Recent population-based observed data of five-year net childhood cancer survival (ages 0-14 years) for acute lymphoblastic leukemia, lymphomas, and brain tumors from 322 cancer registries globally are provided by the CONCORD-3 study. The CONCORD-2 study previously provided similar population-based five-year net survival estimates for both acute lymphoblastic leukemia and acute myeloid leukemia. 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. While limited observed data from low- and lower middle-income countries are available, it is clear that reported survival varies considerably by region.

Added value of this study

With major geographic and histologic gaps in the observed five-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 five-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 five-year net survival between high-income and low-income countries is over 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 while improving the availability of treatments and mitigating abandonment are necessary interventions to achieve high survival, they are insufficient if implemented alone. Concurrent improvements in health systems to achieve better quality of care will also be needed to substantially improve childhood cancer survival worldwide.

Background

Advances in treatment and supportive care over the past six decades have led to increases in five-year net survival for children diagnosed with cancer (ages 0-14 years) from nearly 0% to 80% in high-income countries (HIC) like Great Britain.[1] While it is generally known that children who develop cancer in low-income and middle-income countries (LMIC) have not experienced 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 for a subset of childhood cancers: acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), lymphomas (as a group), and brain tumors.[3-5]

Highlighting the survival gap, CONCORD estimates of five-year net survival for ALL, the most common childhood cancer, range from less than 10% to over 90%.[5] However, due to the paucity of cancer registry data from resource-limited settings, only a small subset of CONCORD-3 data (7/322 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]

In order to quantify the survival gap and identify opportunities for intervention, we developed a simulation model that synthesizes clinical, epidemiologic, and health system data to estimate country-specific childhood cancer survival. Using the model, we 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 can assist decision-makers as they prioritize 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/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 five years post-diagnosis, taking into account 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 for this study by the CONCORD programme for the global surveillance of cancer survival.[3-5] We then used a hierarchical approach to infer parameters for countries/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. We briefly describe our methods below and provide full details in the appendix.

Procedures

We developed a conceptual treatment cascade to account for multiple factors that impact cancer survival from the point of diagnosis to completion of therapy (Figure 1). We assume that a subset of children diagnosed with cancer will achieve five-year survival based on the availability, completion, and quality of treatment. If any required treatment modalities (chemotherapy/radiation/surgery) are unavailable, we assume the child will not survive. We also include a risk of abandoning treatment due to financial toxicity (i.e. financial distress related to the cost of medical care). Lastly, we assume that the quality of care, which depends on a functioning health system with supportive services (e.g. nursing standards, integrated referral and record-keeping) and facility-level activities (e.g. infection control, nutritional support), influences survival. We synthesized 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 geographic variation in cancer incidence and country-specific factors such as demographic trends and health system barriers, are consistent with reported rates of diagnosed cancers in the International Incidence of Childhood Cancer, Volume III (IICC-3).[12] 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 LMIC and specializing in different cancer types (e.g. hematologic cancers, germ cell tumours, solid tumors, etc.)) to specify which treatment components (chemotherapy/radiation/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/radiation based on reported treatment numbers from the Surveillance, Epidemiology, and End Results (SEER) program in the US. We also took into account heterogeneity in treatment needs for diagnoses for which a small proportion of patients require chemotherapy/radiation (Appendix pg 3-5).

To account for the curability of different cancer types we estimated maximum achievable survival probabilities using data from SEER 2010-2014 to inform the general level and variation of survival by diagnosis.[13] 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 US (Appendix pg 6-7).

As calibration targets we obtained country-specific survival estimates for 10 morphology groups from CONCORD (Appendix pg 8).[3,5] For three brain diagnoses (Astrocytoma, Embryonal, and Other), the CONCORD estimates of survival in the US were substantially higher than those reported in SEER. Specifically, SEER estimates of five-year survival were 80%, 68·4%, and 58·9%, respectively, compared to CONCORD estimates of 82·7%, 69·4%, and 96·9%. We therefore 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 based on reported data from a global survey of paediatric oncologists (Appendix pg 10-11).[6] Estimates of radiotherapy availability were based on coverage estimates from the Lancet Radiotherapy Commission (Appendix pg 12-13).[14]

Data for surgical specialties were drawn from multiple sources. For general surgery, we used estimates from a modeling study of the Lancet Surgery Commission (Appendix pg 14-15).[15] For neurosurgery, we used data on neurosurgeon density from the World Federation of Neurosurgical Societies (Appendix pg 16-17).[16] Finally, for ophthalmic surgery we used data on the density of ophthalmologists from the World Council of Ophthalmologists (Appendix 18-19).[17] 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 of paediatric oncologists (Appendix pg 20-21).[7] We assumed that only patients requiring chemotherapy and/or radiation (thus excluding the few surgery-only groups) were at risk of abandoning treatment due to 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".[18] 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 pg 22-23).

We used a modified Bayesian hierarchical framework[19] with three levels (World Bank income group, region, country) to synthesize all available estimates to generate prior probability distributions for all parameters described above. This approach allowed us to regularize the reported data and estimate priors for countries

with no data (see Appendix pg 24 for more details). These priors were used as initial sampling distributions during calibration.

Outcomes

For each country and territory, we modeled the effect of treatment variables on childhood cancer outcomes and estimated five-year net survival for each ICCC diagnosis. We also estimated what five-year net survival would be under various policy interventions aimed at improving survival. We report the mean and 95% uncertainty intervals (UI) calculated as the 2·5 and 97·5 percentiles of our simulation results.

Statistical analysis

Calibration involves comparing model predictions with observed data to identify parameter values that achieve a good fit.[20] We briefly describe this process here (see Appendix pg 25-56 for full details).

We calibrated to CONCORD country/diagnosis-specific five-year net survival estimates, providing 407 targets for model calibration. CONCORD-3 estimates of AML survival were reserved as a test set to assess model validity and were not used in calibration. We used an Approximate Bayesian Computation (ABC) approach to fit each country with CONCORD data (65 countries).[21] For each sampled parameter set we simulated five-year net survival for the number of cancer cases reported for each CONCORD estimate. If the simulated survival probability was within one percentage point of the reported survival estimate we accepted the sampled parameters as a draw from the posterior distribution as per the ABC algorithm.[21] If a parameter set was not accepted after one million iterations, the best-fitting parameter set for the country was used. For computational efficiency we used simulated annealing[22] to direct the sampling.

For each country, we first tried 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 (see Appendix pg 10-11 and pg 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 'borrowing' information from similar countries (i.e. region and income group) when data were not available, similar to approaches used by the Global Burden of Disease and GLOBOCAN for data imputation.[8,9] This set of parameter values for all countries and cancers comprises a completed parameter set.

We repeated this process to generate 1,000 different parameter sets and scored each set based on how well the model predictions matched the survival targets (based on 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[19] we compared our predicted survival from the final model to the reported survival estimates from CONCORD. Nearly all (99·0%) of our prediction intervals (i.e. 95% UI) 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 pg 28-47).

As a further validity check we compared our predictions of AML survival to estimates for 48 countries from CONCORD-3. These estimates were not used to calibrate the model, so they can serve as an external validity check of our model predictions. Our prediction intervals (95% UI) overlapped with the CONCORD-3 AML 95% CIs 97·9% of the time, contained the reported point estimate (i.e. coverage probability) 81·3% of time, and our mean predicted survival fell within the 95% CIs 77·0% of the time (Appendix pg 54-55).

Using the best-fitting 100 parameter sets we estimated five-year net cancer survival for each diagnosis. We ran 1,000 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.[23]

To explore the impact 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 vs. improving service delivery, and a comprehensive approach addressing all treatment barriers. We estimated five-year net childhood cancer survival for each scenario. The GCC model was coded in Java (version 1.8.0), and statistical analyses were performed 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 estimate that globally, for children diagnosed in 2015, five-year net survival for all cancers combined was 37·4% (95% UI 34·7%–39·8%), with large variation by region, ranging from 8·1% (95% UI 4·4%–13·7%) in Eastern Africa to 83·0% (95% UI 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. These estimates reveal large variation within cancer-specific survival, with survival gaps of over 80 percentage points for cancers such as Hodgkin lymphoma and retinoblastoma that have high survival in North America but very poor survival in Africa. See Appendix pg 57-257 for complete country-/diagnosis-specific survival estimates.

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

7·2%), followed by expanding access to general surgery (42·7% [95% UI 39·9%-45·6%], 5·3% increase) and chemotherapy (41·9% [95% UI 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 find that increasing the availability of all treatments to the level of HIC has a significant, though still relatively modest effect on global five-year net survival (54·1% [95% UI 50·1%-58·5%]). Similarly, improving service delivery (i.e. simultaneously improving quality of care and reducing abandonment) yields important survival gains, but to a lesser extent (50·2% [95% UI 47·3%-53·0%]).We see however that improving both treatment access and service delivery has a super-additive effect. For example, closing the gap with HIC for all components by 50% is predicted to achieve similar or larger gains in global five-year net survival (53·6% [95% UI 51·5%-55·6%]) compared to 100% scale-up of treatment access or service delivery packages separately (Table 3). Full implementation of all interventions is estimated to increase global five-year net survival to 80·8% (95% UI 79·5%-82·1%).

Discussion

Using rigorous statistical and computational methods to synthesize estimates from multiple sources of data, we developed a model of childhood cancer survival for 200 countries/territories worldwide. We find that childhood cancer survival varies widely by country due to substantial differences in access to multidisciplinary treatment modalities, abandonment rates, and quality of care. As a result, our findings suggest that five-year net survival for all childhood cancers combined varies by up to 75 percentage points between World Health Organization (WHO) sub-regions (Table 3). Furthermore, as net survival only considers deaths from cancer, the gap in total survival is likely even larger given higher risks of competing mortality in LMIC. Although genetic variations are known to impact survival,[24,25] the most important prognostic factor today for whether a child diagnosed with cancer will survive is not related to cancer biology, but is instead the country where they receive treatment.

196 Beyond their importance for policy-making and informing health investment decisions by countries and
197 development agencies, these estimates can provide a baseline assessment to help guide efforts to improve
198 childhood cancer policies and those aimed at building stronger health systems. For example, the WHO
199 Global Initiative for Childhood Cancer, announced in September 2018,[26] aims to increase global childhood
200 cancer survival to 60% by 2030, as measured by six tracer cancer subtypes: ALL, Hodgkin lymphoma, Burkitt
201 lymphoma, retinoblastoma, nephroblastoma, and low-grade gliomas. Our estimates of five-year net
202 survival for ALL (56·1%) and Hodgkin lymphoma (44·6%) suggest moderate improvement is required for
203 these cancers to achieve 60% survival. However, our survival estimates for the other cancers are much
204 lower, with retinoblastoma, Burkitt, and nephroblastoma all around 25% (Figure 3). (It is not possible to
205 estimate survival for low-grade gliomas with the current ICCC categories.)
206 In contrast, we estimate five-year net survival for these cancers to be 90% or higher in North America,
207 highlighting both the opportunity to substantially increase survival and the challenge of achieving these
208 gains in a relatively short period of time. However, given that nearly half of children with cancer may fail to
209 be diagnosed in LMIC,[10] the true overall survival rate is likely even lower. Therefore, in addition to
210 improving treatment, increased efforts to identify all cases in a population and develop stronger health
211 systems with appropriate support services will also be needed to improve survival for all children with
212 cancer.
213 To address the stark global disparities in childhood cancer survival, determining which policy interventions
214 are likely to be most effective is a necessary first step. Individually, our model predicts that single policy
215 interventions alone will yield limited survival gains. While efforts to address any one problem, such as
216 financial toxicity, are necessary to achieve high survival, they are insufficient if implemented alone. In
217 particular, we find that while reducing abandonment results in more children completing therapy, overall
218 survival does not significantly improve due to interdependencies in the availability of treatment modalities
219 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 to reduce treatment-related toxicity.

Our findings instead highlight the importance of complex interdependencies in childhood cancer treatment. We find 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 importance 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 program incentivizing facility childbirth in India succeeded in substantially expanding access to healthcare, but failed to reduce maternal mortality due to a lack of focus on quality.[27] Similarly, improving childhood cancer outcomes worldwide will require paying attention to what happens once children reach healthcare facilities, with investments to measure and improve healthcare quality in addition to expanding access.[28]

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, supportive care-related interventions (e.g. infection control and nutritional programs) designed to reduce death due to comorbidities are critical to improve service delivery and safety. Although generic guidelines promoting the importance of supportive care measures have been published,[29] 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 (e.g. 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-centered and responsive to the patient's needs.

Limitations

While our modeling approach allows us to synthesize data from multiple sources in a way that is consistent with data on treatment availability and reported survival, there are a number of limitations due to the assumptions needed for model development. First, much of our data is based on cross-sectional surveys of treatment access and abandonment that may provide an incomplete snapshot of the reality on the ground. For example, our prior probabilities (i.e. pre-calibration) of abandonment are based on survey data which reported estimates for ALL only,[7] and the survey data used to inform chemotherapy priors may not be representative of the respondents' countries as a whole. However, our approach allowed us to account for uncertainty around all model parameters, as well as their joint distribution. Our 95% uncertainty intervals thus reflect the sensitivity of our results to different parameter estimates. However, it should be noted that while 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 LMIC and small sample sizes in some regions may have affected our results, and contribute to the wide uncertainty intervals we report for some cancers and countries. For example, CONCORD survival estimates were only available for two countries in sub-Saharan Africa (Nigeria and Lesotho), and then only for ALL.

Third, due to lack of data we used a single quality parameter per country as a proxy for many factors related to service delivery. 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. While abstract, our estimates of quality are similar to other published estimates and are highly

correlated (r=0·83) with the Global Burden of Disease Healthcare Access and Quality Index (HAQI) (Appendix pg 56).[30] Given that our quality parameters were inferred exclusively by model calibration this builds confidence in the convergent validity of our estimates.

Lastly, while calibration allowed us to align our model results with observed survival and induce appropriate covariance between model parameters, due to lack of data we assumed that the availability of each treatment modality was independent for each individual patient. 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. In addition, 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 provide, to our knowledge, the first global estimate of childhood cancer survival and find large disparities in five-year net survival as a result of substantial differences in access to multidisciplinary treatment modalities, abandonment rates, and quality of care. Our findings suggest that while 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 are 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 performed 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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Table 1: Overview of GCC Survival Module country-specific data sources

Model Parameter	Data Source	# Model Countries Reported	Reference
Cancer Diagnosis			
Diagnosed cancer cases	Estimated annual diagnosed cases by ICCC subgroup	200	GCC Incidence Module[10]
Cancer Survival			
Necessary treatment components	Expert opinion; SEER estimates of chemotherapy/radiation used as proxy for cancer stage	1 (US)	SEER[13] (Appendix pg 3-5)
Maximum achievable survival	SEER 2010-2014 five-year relative survival used as initial proxy	1 (US)	SEER[13] (Appendix pg 6-7)
Population-based survival	Five-year net survival by country, derived from cancer registry data	10-64 (varies by diagnosis)	CONCORD[3,5] (Appendix pg 8)
Cancer Treatment			
Chemotherapy availability	Reported availability of chemotherapy	94	Published survey data[6] (Appendix pg 10-11)
Radiation availability	Radiotherapy coverage	173	Lancet Radiotherapy Commission[14] (Appendix pg 12-13)
Surgery availability	Availability of general surgery	184	Lancet Global Surgery Commission[15] (Appendix pg 14-15)
	Neurosurgeon density	192	World Federation of Neurosurgical Societies[16] (Appendix pg 16-17)
	Ophthalmologist density	192	International Council of Ophthalmology[17] (Appendix pg 18-19)
Treatment abandonment	Probability of treatment abandonment	98	Published survey data[7] (Appendix pg 20-21)

Table 2: Policy Intervention Scenarios

Scenario Name	**Description of Policy Intervention**
Baseline	(No change from baseline)
Individual Policy Intervention	
Chemotherapy	Increase availability of chemotherapy to mean of HIC
Radiation	Increase availability of radiation to mean of HIC
General Surgery	Increase availability of general surgery to mean of HIC
Neurosurgery	Increase availability of neurosurgery to mean of HIC
Ophthalmology	Increase availability of ophthalmic surgery for Retinoblastoma to mean of HIC
Abandonment	Reduce treatment abandonment to mean of HIC
Quality of Care	Improve quality of care to mean of HIC
Packages of Policy Interventions	
Expand Treatment Access	Increase availability of all treatment modalities (chemotherapy, radiation, surgery and surgical subspecialties) to mean of HIC
Improve Service Delivery	Improve quality of care while reducing abandonment rates to mean of HIC
Comprehensive – 50%	Expand treatment access and improve service delivery to close the gap with mean of HIC by 50%
Comprehensive – 100%	Expand treatment access and improve service delivery to close the gap with mean of HIC by 100%

HIC = High Income Countries

Table 3: Estimated Childhood Cancer Five-Year Net Survival 2015-2019 (%) Under Various Policy Interventions*

		Single Intervention - Treatment Access					Single Intervention - Service Delivery		Intervention Packages			
Area	**Baseline**	**Chemotherapy**	**Radiation**	**General Surgery**	**Neuro-surgery**	**Ophthalmic Surgery**	**Abandon-ment**	**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)
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/ 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)	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/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)

* Policy interventions are defined in Table 2

\+ Comprehensive 50%/100%: Expand treatment access and improve service delivery to close the gap with mean of HIC by 50%/100%