

# Early-stage childhood cancers, curative intent

Authors: Pickersgill S, Kaur G, Ahmed S, Watkins D, Coates MM, Økland JM, Haaland ØA, Johansson KA

Date: Sept 21, 2020

Date modified: September 10,2021, November 25,2021

## Description of condition and intervention

Global estimates indicate that about 400000 children and adolescents get diagnosed with cancer annually. Most common types of childhood cancers are Leukemias, Lymphomas, brain cancers and solid tumours, such as neuroblastoma. Childhood leukaemia is the most common type of childhood cancer. There are multiple types of childhood leukaemia, the most common are acute lymphoblastic leukaemia (ALL) and acute myeloid leukaemia (AML). Paediatric lymphoma is the third most common form of cancer in children. There are mainly two types of Paediatric lymphoma. Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). The NHL in children is high grade and distinct from low-grade or intermediate lymphomas as seen in adults. In low- and middle-income country settings, approximately 15 to 45% of children affected with cancer get cured, unlike 80% in high income settings.

Interventions for estimating effects and costs for childhood cancers are:

- Treatment of Burkitt and Hodgkin lymphoma

- Treatment of acute lymphoblastic leukemia

- Treatment of Wilms tumor

## International guidelines

Organization	Indications/recommendations	Applicability
--------------	-----------------------------	---------------

		in LIC & Lower MIC settings

## Intervention attributes

### Type of interventions

Chronic management care

### Delivery platform

This intervention may be delivered at referral and specialty hospital.

### Equity

In addition to considerations like cost-effectiveness and health systems factors, dimensions of equity can be relevant for priority setting. The opportunity for a long and healthy life varies according to the severity of a health condition that individuals might have, so there are inequities in individuals' opportunities for long and healthy lives based on the health conditions they face. Metrics used to estimate the severity of illness at an individual level can be used to help prioritize those with less opportunity for lifetime health. FairChoices: DCP Analytics Tool uses Health adjusted age of death (HAAD), which is a metric that estimates the number of years lived from birth to death, discounting years lived with disability. A high HAAD thus represents a disease less severe in terms of lifetime health loss, while a low HAAD represents a disease that is severe on average, causing early death or a long period of severe disability. It is also possible to estimate the distribution of HAAD across individuals with a health condition. FairChoices shows for each intervention an average HAAD value of the conditions that are affected by respective interventions that have health effects. Additionally, a plot shows HAAD values for around 290 conditions (Johansson KA et al 2020).

### Time dependence

Moderate level of urgency. Treatment outcomes not highly affected by some days of delay.

## Population in need of interventions

Treated population: All prevalent acute lymphoid leukemia among children aged 0-14 (males and females). Assuming that all 57% of prevalent NHL among children aged 0-14 (males and females) are Burkitt lymphoma (Orem, 2007). All prevalent Hodgkin lymphoma among children aged 0-14 (males and females). Assuming all prevalent kidney cancer among children aged 0-14 (males and females) is due to Wilms tumor.

Affected population: All prevalent acute lymphoid leukemia among children aged 0-14 (males and females). Assuming that all 57% of prevalent NHL among children aged 0-14 (males and females) are Burkitt lymphoma (Orem, 2007). All prevalent Hodgkin lymphoma among children aged 0-14 (males and females). Assuming all prevalent kidney cancer among children aged 0-14 (males and females) is due to Wilms tumor.

## Disease state addressed

This intervention targets cancers like acute lymphoid leukaemia, non-Hodgkin lymphoma, Hodgkin lymphoma, kidney cancer.

## Intervention effect and safety

Table 1: Effect and safety of treatment for childhood cancers

Effect of intervention		Certainty of evidence
Mortality (due to condition) Acute lymphoid leukemia (ALL)	Results from a trial in China show event-free survival (EFS) at 4 years was 72.8% for the "Economic Protocol" (Luo, 2008). More intensive regimens obtained slightly better results at higher per patient costs.	See appendix
NHL/Burkitt Lymphoma	A study of children age 2-15 in Blantyre, Malawi with Burkitt lymphoma reported 48% treatment efficacy (continued remission for 265–670 days) for a 28-day chemotherapy treatment schedule with cyclophosphamide and intrathecal methotrexate (Hesseling, 2009). Similar findings were reported in a	

Hodgkin lymphoma	cost-effectiveness study of BL treatment in Uganda; 55% for overall survival rate (Denburg, 2019) and in the pilot study in Malawi; 57% survival rate (Hesseling, 2003). The average treatment efficacy for HL in a cost-effectiveness study in South Africa is 80% (Stefan, 2009). This is supported by a study in India of children under 18 with BL (Chandra, 2008).	
Kidney cancer	Following SIOP 9 protocol in Morocco, treatment resulted in 5-year event-free survival of 56%, 77.4% excluding those lost to follow-up (Madani, 2006).	

## Model assumptions

Table 2: Summary of model parameters and values used in FairChoices – DCP Analytical Tool

Category	Model parameter	Notes
Intervention		
<b>Cost calculation</b>		
Treated population	Prevalence based	Global Burden of Disease Study 2019
Gender	Both male & female	
Age	0-14 years	
Treated fraction		
Non-Hodgkin lymphoma	0.57	
Hodgkin lymphoma	1	
Acute lymphoid leukemia	1	
Kidney cancer	1	
<b>Effect calculation</b>		
Affected population	Those with condition	
Affected gender	Both male & female	
Affected fraction age	0 to 14 years	
Affected fraction		
Non-Hodgkin lymphoma	0.57	
Hodgkin lymphoma	1	
Acute lymphoid leukemia	1	
Kidney cancer	1	

Comparison	No intervention	
Mortality Reduction (RRR)		
Non-Hodgkin lymphoma	0.48	Sources listed in Table 1
Hodgkin lymphoma	0.8	
Acute lymphoid leukemia	0.728	
Kidney cancer	0.56	

## Intervention cost

The cost of treating Burkitt and Hodgkin lymphoma is estimated to be \$50 in 2006 USD in South Africa for chemotherapy drugs per patient (P. Hesselning et al., 2009). The mean treatment cost for Children with acute lymphoblastic leukemia (ALL) was \$4443 in 2011 USD in Bangladesh (A. Islam et al. 2015). The cost of ALL is used as a proxy to estimate the cost of treatment of Wilms tumor.

## References

Steliarova-Foucher E, Colombet M, Ries LAG, et al. International incidence of childhood cancer, 2001-10: a population-based registry study. *Lancet Oncol.* 2017;18(6):719-731.

World Health Organization. Childhood cancer [Internet] [cited 2021 Nov 25]. Available from: <https://www.who.int/news-room/fact-sheets/detail/cancer-in-children>

Gupta S, Howard SC, Hunger SP, et al. Treating Childhood Cancer in Low- and Middle-Income Countries. In: *Disease Control Priorities*, volume 3. 2015 (<http://dcp-3.org/chapter/900/treating-childhood-cancers-low-and-middle-income-countries>, accessed Nov 2021)

Johansson KA et al 2020: Johansson KA, Coates MM, Økland JM, Tsuchiya A, Bukhman G, Norheim OF, Haaland Ø. Health by disease categories. Distributional Cost-Effectiveness Analysis: Quantifying Health Equity Impacts and Trade-Offs. 2020 Sep 30:105.

Hesseling, P., Molyneux, E., Kamiza, S., Israels, T., Broadhead, R., 2009. Endemic Burkitt lymphoma: a 28-day treatment schedule with cyclophosphamide and intrathecal methotrexate. *Ann Trop Paediatr* 29, 29–34. <https://doi.org/10.1179/146532809X402006>

Denburg, A.E., Laher, N., Mutyaba, I., McGoldrick, S., Kambugu, J., Sessle, E., Orem, J., Casper, C., 2019. The cost effectiveness of treating Burkitt lymphoma in Uganda. *Cancer* 125, 1918–1928. <https://doi.org/10.1002/cncr.32006>

Hesseling, P.B., Broadhead, R., Molyneux, E., Borgstein, E., Schneider, J.W., Louw, M., Mansvelt, E.P.G., Wessels, G., 2003. Malawi pilot study of Burkitt lymphoma treatment. *Med. Pediatr. Oncol.* 41, 532–540. <https://doi.org/10.1002/mpo.10322>

Luo, X.-Q., Ke, Z.-Y., Guan, X.-Q., Zhang, Y.-C., Huang, L.-B., Zhu, J., 2008. The comparison of outcome and cost of three protocols for childhood non-high risk acute lymphoblastic leukemia in China. *Pediatr. Blood Cancer* 51, 204–209. <https://doi.org/10.1002/pbc.21598>

Chandra, J., Naithani, R., Singh, V., Saxena, Y.K., Sharma, M., Pemde, H., 2008. Developing anticancer chemotherapy services in a developing country: Hodgkin lymphoma experience. *Pediatr. Blood Cancer* 51, 485–488. <https://doi.org/10.1002/pbc.21609>

Madani, A., Zafad, S., Harif, M., Yaakoubi, M., Zamiaty, S., Sahraoui, S., Benjelloun, A., Fehri, M., Benchekroun, S., 2006. Treatment of Wilms tumor according to SIOP 9 protocol in Casablanca, Morocco. *Pediatr. Blood Cancer* 46, 472–475. <https://doi.org/10.1002/pbc.20436>

Islam A, Akhter A, Eden T. Cost of treatment for children with acute lymphoblastic leukemia in Bangladesh. *Journal of Cancer Policy.* 2015 Dec 1;6:37-43.

## Appendix

### Literature Review for effectiveness & safety

This literature search is an example of Level 1 search for intervention inputs taken from DCP3 or generated in an ad hoc manner (e.g., quick google search found one study of cervical cancer screening cost-effectiveness that was used to create an effectiveness parameter for that intervention).

Level of evidence of efficacy studies:

1. low (expert opinions, case series, reports, low-quality case control studies)
2. moderate (high quality case control studies, low quality cohort studies)
3. high (high quality cohort studies, individual RCTs)
4. very high (multiple RCTs, metaanalysis, systematic review, clinical practice guidelines).