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Global public and philanthropic investment in childhood cancer research: systematic analysis of research funding over nine years, 2008 - 2016

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Contributions of authors

EML, EJAF and RA planned the project and the parameters for conducting the grant searches on the Dimensions database. EML conducted the pilot project to categorize grants, and reviewed categorization parameters with EJAF and RA. EML categorized all 7418 grants. EJAF, EML and RA planned the data analysis. EJAF conducted the data analysis and created the figures and tables. EML and EJAF wrote the manuscript. RS and RA reviewed and edited the manuscript.

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SUMMARY

Background: Childhood cancers have long been missing from the global health agenda despite accounting for an estimated 75,000 deaths worldwide in children under 15 years old in 2018 and with more than 90% of childhood cancer deaths occurring in low and middle-income countries. Understanding the current research landscape is essential to ascertain how research resources are allocated to address knowledge gaps in childhood cancer epidemiology, clinical care and the effectiveness of interventions aimed at improving outcomes. We analyse trends in global public and philanthropic funding for childhood cancer research, a useful proxy for global research activity.

Methods: We systematically searched for and analysed the inflation-adjusted amounts (in US Dollars) awarded by, and topics of, 3414 grants from 115 funders across 35 countries between 2008-16; using data from the Dimensions database. Research funding was mapped according to funding source, recipient, tumour type, research focus and pipeline categories; describing trends over time.

Findings: In 2008-16, total global funding for paediatric oncology research was \$2 billion; with a mean of \$227 million per year. Despite a small increase in research infrastructure grants in 2013-14, direct funding for paediatric oncology research has declined since 2011. Most funding supported general childhood cancer research including infrastructure grants (\$772 million; 37.9%), followed by research into leukaemia (\$449 million; 22.0%), central nervous system tumours (\$330 million; 16.2%), and neuroblastoma (\$181 million; 8.9%). The majority of funding was awarded from, and to, United States based institutions (\$1.6 billion; 77.7%); with pre-clinical research receiving \$1.2 billion (59.3%) and \$116 million (5.7%) and \$113 million (5.5%) directly supporting clinical trials and healthcare delivery research, respectively. \$18 million (0.9%) was awarded for prevention research.

Interpretation: Funding for paediatric oncology research is inadequate for a leading cause of child mortality and suffering. There is a bottleneck in funding between pre-clinical biology/aetiology research and clinical trials; with an urgent need for developing new models of care through health systems and healthcare delivery research. New momentum towards achieving universal health coverage for children must be met with major new public and philanthropic commitments to support future research to better understand the distribution, burden and causes of childhood cancer, and to develop innovative prevention and treatment strategies.

Funding: EML and EJAF are Academic Clinical Fellows whose salaries are funded by the National Institute of Health Research (NIHR), which had no role in the in the planning, data analysis or write-up of this work. RS is funded through the UK Research and Innovation GCRF RESEARCH FOR HEALTH IN CONFLICT (R4HC-MENA) program No: ES/P010962/1.

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Research in context

Evidence before this study:

We searched PubMed as well as key research funding networks, including the International Cancer Research Partnership (ICRP), to identify previous analyses of childhood cancer research funding. [There are few](#) publications [that](#) have presented data on funding for paediatric oncology research, [but these include](#) a bibliometric analysis, a report from the ICRP funding network outlining funding by their members, [a report of National Cancer Institute \(NCI\) funding for paediatric cancer](#), and a study restricted to funding from the UK. The 2013 Lancet Oncology series on childhood cancer [and the recent review by Lam et al. published in Science \(2019\)](#) provide a systematic overview of the landscape of global childhood cancer policy priorities including a need for sustainable research funding as a key issue.

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Added value of this study: To our knowledge this is the first global analysis of public and philanthropic funding for childhood cancer research, incorporating data from 115 funders for 3414 research projects, in 35 countries, over a nine year period. We present comprehensive data on funding by the leading funders of childhood cancer research from, mostly, high income settings. Our findings will help inform scientists, policy makers and funding bodies to develop strategic research priorities.

Implications of all the available evidence: Global funding for childhood cancer research is low relative to that for adult cancer or infectious diseases research, heavily biased towards basic sciences and dominated by research into [three tumor types: childhood leukaemia; CNS tumours and neuroblastoma](#). The USA is the predominant funder and recipient of childhood cancer research grants and there is a marked paucity of funding for research in lower-income settings. There is a need for a strategic shift in commitments to global research for childhood cancer, in order to meet the challenges of its rising incidence across the world.

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BACKGROUND

Childhood cancers have long been missing from the global child health agenda; erroneously considered to occur largely in high-income countries, where other causes of childhood mortality and morbidity have been diminished. Estimated age-standardised incidence rates of cancers in children aged 0-14 years (per million person-years) vary from around 50 in sub-Saharan Africa to 100 in South Asia and 150 in North America and northern Europe; however cancer registry coverage in Africa and South Asia is very low.¹ Worryingly, the incidence of childhood cancers appears to be increasing in all settings.^{1,2} Cancer is already the leading cause of non-injury related childhood deaths in the United States of America (USA) and Europe, and in 2018, an estimated 75,000 children worldwide would die from cancer before the age of 15 years.³⁻⁵ Globally, more than 90% of childhood cancer deaths are thought to occur in low- and middle-income country settings.⁶

Over the last decade the integration of clinical trials and better routine clinical care has led to substantial improvements in survival of children with cancer in the North America and western Europe, where the mean 5-year survival has reached 80%.⁷ Progress has been most marked in research for therapies for acute lymphoblastic leukaemia (ALL), yet, the disparity in childhood ALL survival across the world is stark; ranging from less than 60% in China, Ecuador and Mexico to over 95% in Scandinavia.⁷ Furthermore, improvements in survival have varied enormously between childhood cancer types; and across age groups, with teenage and young adult survival lagging behind.⁸ The organization and resourcing, and capability of childhood cancer services also play a major part in better outcomes. Current models of care for childhood cancers range from multidisciplinary specialist input coordinated by tertiary health centres in well-resourced settings, to single handed general pediatric care with limited oncological experience in district hospital settings in low-income countries.⁹

Crucially, there is a need to understand paediatric cancer as its own entity, rather than as a continuum of adult oncology. Mismatches between research activity and the most critical knowledge gaps – either in terms of burden or potential for impact, are key emerging issues in many areas of health research including oncology.¹⁰⁻¹⁴ Hence, understanding the current research landscape is essential in order to address existing lacunae in our understanding of the epidemiology, aetiology, management and outcomes of childhood cancer. Judicious investment in research is particularly urgent given that the burden and mortality of childhood cancer appears to be growing in the same places where challenges with data quality and availability are the greatest; with many countries lacking national vital registration data and relying on verbal autopsy for childhood deaths.^{15,16}

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Systematic reviews into the state of childhood cancer research have been conducted and published previously, including the SIOPE European strategic cancer plan for children and adolescents, the 2013 Lancet Oncology series on paediatric cancer [and a recent review by Lam et al. published in Science \(2019\)](#).^{14,17-21} Common themes that have been voiced, beyond the need for new therapies, relate to equitable access to care, addressing the specific needs of adolescent cancer patients, improving the quality of life of pediatric cancer survivors, and to developing preventative strategies specific to childhood cancer types. However, current knowledge about the landscape of funding for paediatric oncology research has so far been limited to bibliometric analyses.^{13,22,23} These approaches reflect a global research map some three to seven years behind what is currently happening. In order to provide both comprehensive input and a more contemporaneous analysis of worldwide research activity we have analyzed the global research funding landscape for paediatric cancer, including categorized funding amounts, number of awards, funders and recipients, and trends over nine years.

METHODS

Data Source and Search Strategy

We conducted a search in the Dimensions database (Panel 1), for all grants awarded for research on childhood cancers. Our search strategy (appendix, pp 1-2) encompassed [keywords](#) related to childhood and specific age groups under the age of 18 as well as all relevant tumour types including those listed under the International Classification of Childhood Cancer (ICCC-3).²⁴ There were no language or geographical restrictions. The last search conducted was in March 2017. We included grants active in the 10 years preceding this date (i.e. active in 2008-17).

Blinded to funding amount and funding organization, titles and abstracts of 7418 resulting grants were manually screened to exclude those without direct paediatric focus, awarded for conferences or symposia, or related to non-malignant conditions. [In line with other funding analyses we](#)

Panel 1: The Dimensions database

- Dimensions is an inter-linked research information system provided by Digital Science (<https://www.dimensions.ai>).
- It uses automated methods to collate funding data from open access web-based sources; as well as manually sourced information directly from funders; updated on a monthly basis.
- [The database allows the use of keywords and Boolean search terms to identify relevant grants; similar to that used for commonly used online databases of scientific publications](#)
- At the time of data collection the database included >3.5 million research projects with aggregate funding of 1.2 trillion US dollars (USD) covering 173 countries and 597 funders
- Available grant information includes the title, abstract, funding amount, start and end dates, as well as the name and location of funders and recipients.
- Grant funding amounts are obtained in their original currencies as well as converted to USD based on the exchange rate at the time of the start date of the grant. In the case that a yearly distribution of the funding amount is provided (e.g. NIH projects), the funding amount is converted for each year's exchange rate.

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excluded basic sciences research that did not demonstrate a genuine paediatric focus in the grant abstract.

^{25,26} Some returned grants did not provide the monetary value of the award, for which we made direct requests from individual funders; reducing the number of grants with missing data from 714 (20.6%) to 204 (6.0%) (Figure 1).

To aid interpretation of our analysis of funding data captured in the Dimensions database, we also conducted a supplementary analysis (see supplementary material), in which we aimed to identify major funders/sources of funding of childhood cancer research that were not included in the Dimensions database at the time of data collection. We employed several complementary strategies as detailed in the supplementary material and Figure 1: a validated scientometric method to analyse the funding organisations acknowledged in childhood cancer research publications; identification of the ten largest public and philanthropic funders of health research worldwide as published in an analysis by Viergever et al. in 2016; direct communication with the ICRP (International Cancer Research Partnership) funding network; and additional online searches for any USA state funders with open access grant data.²⁷

Industry funders (eg. for-profit biotech companies or pharmaceutical companies) were not included in either analysis as reliable sources of data for spending on research are not generally not available. However, grants made to industry as recipients of public or philanthropic funding were not excluded.

Data analysis

Grant categorization

3414 relevant grants from 115 different funders in 35 countries (appendix pp 3-6), were manually categorized according to three sets of criteria: (1) tumour type (as per ICC-3) or as 'general paediatric oncology', (2) research focus, (3) research pipeline. Categories were aligned to established subgroups, such as the Common Scientific Outline (CSO) codes employed by the ICRP where appropriate and are further detailed in panel 2.²⁸ Additional tags were assigned for research grants with significant adult oncology overlap; as well as for those with explicit focus on teenage children. Funders were categorized as public (if predominantly government financed) or philanthropic (eg charities or independent foundations).

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Panel 2: Categorisation

1) Tumour type (as per International Classification of Childhood Cancer (ICCC-3))

- a) [Leukaemias, myeloproliferative diseases, and myelodysplastic diseases](#)
- b) [Lymphomas and reticuloendothelial neoplasms](#)
- c) [CNS and miscellaneous intracranial and intraspinal neoplasms](#)
- d) [Neuroblastoma and other peripheral nervous cell tumors](#)
- e) [Retinoblastoma](#)
- f) [Renal tumours](#)
- g) [Hepatic tumours](#)
- h) [Malignant bone tumours](#)
- i) [Soft tissue and other extraosseous sarcomas](#)
- j) [Germ cell tumours, trophoblastic tumours, and neoplasms of gonads](#)
- k) [Other malignant epithelial neoplasms and malignant melanomas](#)
- l) [Other and unspecified malignant neoplasms](#)
- Or
- m) [General paediatric oncology](#)

2) Research focus (broadly in line with the Common Scientific Outline (CSO) categories employed by the International Cancer Research Partnership (ICRP)).

- a) [Biology and aetiology - basic sciences, cancer biology, studies into the origin and progression of cancer, studies into causative factors including epidemiological risk factor studies](#)
- b) [Prevention - research looking to identify interventions which reduce cancer risk \(such as lifestyle, drugs, vaccines\)](#)
- c) [Diagnosis/prognosis - identifying/testing cancer markers and imaging methods that are helpful in detecting and/or diagnosing cancer as well as predicting the outcome or chance of recurrence](#)
- d) [Model systems - development of new animal models, cell cultures or computer simulations](#)
- e) [Treatment - identifying and testing locally or systemically administered treatments; also includes research on immediate complications of cancer treatments \(such as infections, neuropathy, hearing loss\) and research on treatment resistance](#)
- f) [Survivorship - patient care and pain management; beliefs and attitudes that affect behaviour regarding cancer control; ethics, education and communication; supportive and end of life care; quality of healthcare delivery; long-term side effects of cancer treatment \(such as infertility or cardiovascular disease\)](#)

3) Research pipeline

- a) [Pre-clinical research - basic sciences as well as public health research such as surveillance, modelling, bioinformatics](#)
- b) [Clinical trials - phase I, II, or III](#)
- c) [Health care delivery - including survivorship, outcomes, healthcare apps/products, tissue banks, developing a healthcare intervention](#)
- d) [Cross-disciplinary research - awards containing significant components across any two distinct areas along the research pipeline \(a\), \(b\) or \(c\)](#)
- e) [Infrastructure grants - funding for research centres or research staff dedicated to paediatric oncology research](#)

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3414 relevant grants from 115 different funders in 35 countries (appendix pp 3-6), were manually categorized according to three sets of criteria, which were aligned to established subgroups, such as the Common Scientific Outline (CSO) codes employed by the International Cancer Research Partnership (ICRP) where appropriate.²⁴; (1) tumour type (as per ICC-3) or as 'general paediatric oncology' research; (2) research focus (prevention, biology and aetiology, diagnosis and prognosis, treatment, model systems, survivorship (including research on long-term treatment effects, quality of life and communication studies)) and (3) research pipeline (pre-clinical, clinical trials, healthcare delivery (including clinical research related to survivorship, or health system interventions/apps/products and tissue banks), infrastructure (including new research centres or staff) and 'cross-disciplinary' research (those incorporating multiple pipeline categories) (appendix pp 7-8). Additional tags were assigned for research grants with significant adult oncology overlap; as well as those with explicit focus on teenage children. ¶

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Categorization was based on grant summaries, with further information sought online from institutional websites, where required. In an initial pilot analysis, 500 randomly sampled grants (using computer-generated unique random numbers) were categorized by a second researcher; after which minor

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clarifications were made to categorization criteria to ensure consistency and mutual exclusivity. In any further instances of ambiguity grants were discussed and categorization agreed with a second researcher.

Funding analyses

Data analysis was conducted using Stata v14.2. All monetary values were analysed and are presented as United States Dollars (USD; \$). A small number of grants in the database only provided monetary values in pounds sterling (GBP); which were manually converted to USD using the first January exchange rate of the grant start year. All grants were then adjusted for inflation using the Consumer Price Index (CPI) at the beginning of each grant start year, equating all funding amounts to the value of 2010 USD.²⁹

Although the search returned all grants that were active at some point between 2008 to 2017 (10 years), the period of analysis was subsequently restricted to funds available from active grants 2008 to 2016 (nine years), as data were incomplete for 2017. Some active grants during 2008 to 2016 were initiated prior to 2008 and larger grants usually spanned multiple years. In order to demonstrate real funding availability to researchers annually, multi-year grants were assumed to be spread equally across their duration (rather analysing awards by start date; which only reflects new commitments, is skewed by large grants of long duration, and does not take into account ongoing grants).

Therefore, grants with future end dates, or start dates prior to 2008, were restricted to the portion of funding available during the 2008 to 2016 time period (again, making the assumption of constant annual funding for multi-year grants). The grants which did not have data on funding amount available could not be included in monetary analyses but were included in the analysis of number of grants by topic.

Descriptive analyses included number of grants, median grant size (as mean values were highly skewed by large outliers), interquartile range and total funding in USD. These values were presented by funder, country of funder (and World Health Organization (WHO) global region; appendix p 9), country of the primary recipient as well as the research categories describe above.

Where grants had been assigned to multiple tumour types or research focus categories, funding amounts were assumed to be divided equally across categories. To illustrate funding for research by tumour type relative to global burden, we sourced age-standardised incidence rates (world standard) from Steliarova-Foucher et al. (2017).¹

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Our approach to the estimation of financial contributions from additional funders identified in the supplementary analysis is described in detail in the supplementary material.

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FINDINGS

A summary of total funding, median award size, and number of grants are outlined in Table 1, categorized by WHO global region, tumour type, research focus, research pipeline category, and year. All values are in USD, rounded to the nearest \$100.

Overall Funding for Childhood Cancer Research

Total funding for paediatric oncology research from 2008 to 2016 was \$2.0 billion (\$2,040,816,000); making the mean funding available per year \$226.8 million during that time period, with a median award size of \$149,600 (interquartile range (IQR) \$382,400) (Table 1). Between 2008 and 2011, annual funding available from all active grants increased from \$190.5 million to \$237.0 million. However, between 2011 and 2013 there was an overall decrease in funds to \$235.8 million. There was an apparent increase in funding from 2013 to 2015, from \$235.8 million to \$255.3 million, however, this was due to a small number of large research infrastructure grants, representing an increase in research infrastructure investment of \$24 million. Excluding research infrastructure investment the overall direct funding of paediatric oncology research has decreased since 2011 (from \$222.9 million to \$215.3 million in 2015).

New funding commitments (ie. grants starting between 2008 and 2016, including commitments to grants extending beyond 2016) amounted to \$1.4 billion. This equates to \$166.0 million (mean average) of new awards each year; but with considerable year-to-year variability, for example, with \$256.0 million being awarded in 2014 and only \$160.0 million the following year (Figure 2).

Funding by tumour type

Overall, \$771.8 million (37.9%) was for general paediatric oncology research, without focus on specific tumour types; \$181.6 million (23.5%) of which was investment in research infrastructure (e.g. supporting new research centres and networks). By tumour type, research in leukaemia (and other myeloproliferative and myelodysplastic diseases) was the most funded (\$448.8 million; 22.0%); followed by central nervous system (CNS) tumours (\$329.6 million; 16.2%), and neuroblastoma and peripheral nerve cell tumours (\$181.2 million; 8.9%). 15.2% (\$309.0 million) of total funding was dedicated to research in all other tumour types. For germ cell and hepatic tumours we only identified 28 and 42 grants, with total minimal budgets of \$10.3 million and \$7.2 million, respectively, over the nine-year period (Table 1).

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Figure 2 illustrates the trend in investments by tumour type over nine years [in the context of the overall trend in new grant commitments each year](#). While there was a modest increase in financial support between 2008 and 2011, investment in research focusing on specific cancer types appears to have decreased since 2011. [However](#), funding of general paediatric oncology research increased, mirroring the boost in investment in research infrastructure, [particularly in 2014](#) (Figure 2; appendix pp 10-12). The distribution of investment across tumour types has remained relatively static (Figure 2).

The relationship between burden of disease (estimated number of new cases in 2015) by tumour type, and investment in research (mean annual funding and number of grants), is illustrated in Figure 3. In general, funding per tumour type appears to be aligned to the estimated number of new cases, [except](#) for lymphomas (and reticuloendothelial neoplasms), for which research funding per new case appears substantially lower (Figure 3).

Funding by research focus and pipeline

Figure 4 is a heat-map of funding by research focus (prevention, biology and aetiology, diagnosis and prognosis, treatment, model systems, survivorship), cross-tabulating these categories, by tumour type and pipeline.

While investigation of the biology and aetiology of childhood cancers was awarded \$806.4 million (39.5%) [over the nine year study period](#), \$236.8 million (11.6%) was awarded to survivorship research; [and only \\$111.4 million \(5.5%\) supported diagnosis and prognosis research. We identified only \\$18.1 million \(0.9%\) that was awarded to](#) research with any focus on prevention of childhood cancers (Table 1).

The majority of funding (\$1.2 billion (59.3%)) was for pre-clinical research; [\\$643.8 million of which was investigating the biology and aetiology of childhood cancers \(Figure 4\). We categorized \\$525.3 million \(25.7%\) as being clinical trials or 'cross disciplinary' \(ie. research that included multiple elements of the research pipeline, 43 out of 48 of which included clinical trials\); and \\$115.6 million \(5.7%\) of this was for 141 grants solely awarded solely for Phase I, II or III clinical trials \(Table 1\). 'Cross-disciplinary' grants were much larger awards \(median \\$926,000\) than those solely for clinical trials \(median \\$279,000\). However, despite more funding being awarded for pre-clinical studies overall, the median award was \\$165,900 \(Table 1\). Research on improving health care delivery for children with cancer, received a small proportion of total research funding, amounting to \\$113.0 million \(5.5%\), with a median award size of \\$77,100 \(Table 1\).](#)

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Only 82 (2.4%) grants, allocating \$19.4 million (1.0%), had an explicit focus on cancers in adolescent patients, most of which (\$15.7 million; 80.9%) was for general oncology research, rather than specific tumour types that are more common in this age group; and especially relating to issues around survivorship (\$16.0 million; 83.0%). In comparison, 209 (6.1%) grants funded research with a significant adult oncology, amounting to \$197.6 million (9.7%). Median grant size for those with and without overlap with adult cancer were \$251,700 and \$142,000 respectively.

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Funding by country

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Funders from North America awarded the majority (\$1.7 billion (82.6%); Table 2) of the funding, with \$1.6 billion (77.7% of total funding) originating from funders in the USA. The National Cancer Institute (USA) alone gave \$1.2 billion (59.9%), with the next most significant funder [from our data](#) being the European Commission who gave \$135.2 million (6.6%) in the same time period. In total, funders from Europe awarded \$292.2 million (14.3%) of the total funding. Less than 2% of funding was awarded from funders in Australia and New Zealand (Oceania), Asia and Latin America & The Caribbean (\$37.7 million (1.9%); \$21.0 million (1.0%); and \$4.5 million (0.2%), respectively) [\(Table 2\)](#).

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Figure 5 is a map of countries hosting the primary recipients of the total research funding awarded. The USA was by far the most common hosting country of recipient organizations, receiving \$1.6 billion (77.2%) from 1773 different awards. The next most common recipients were institutions in Canada, receiving 435 grants worth \$98.1 million (4.8%); and the UK, who received fewer grants (261) but more funding overall (\$105.4 million (5.2%)).

The vast majority of grants (3257 (97%)) were 'internal', where funding was awarded and received by organizations in the same country, amounting to at least \$1.9 billion (92%). Overall only \$65.6 million (3.2%) of the funding was awarded directly to organizations outside of North America and Europe of which the majority (\$63.2 million) was sourced from internal funders. Only one relevant grant in our data was directly awarded to an African country (Egypt), with no available funding data from African funders. Similarly, there were no recorded awards directly to or from institutions in South-East Asia. ▼

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Funding by major funders not included in the Dimensions database

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As described in detail in the supplementary material, we identified 80 additional potentially significant funders of childhood cancer research not represented in the Dimensions database at the time of data collection. 45 of these funders were ICRP partners and we identified 35 additional funders from other searches (see supplementary material). In total, these funders represented 14 countries, only one of which (Italy), was not previously represented in our Dimensions database analysis. Sufficient data was available from 56 of the 80 additional funders to estimate funding for one year of childhood cancer research (Figure 1 and supplementary material). After adjustment for inflation, the total additional funding we estimated for one year of childhood cancer research was \$80.29 million USD; with \$32.06 million USD estimated by the ICRP to account for support from additional ICRP partners and \$48.23 million USD identified through our other analyses (see supplementary material).

DISCUSSION

To our knowledge this is the first global analysis of public and philanthropic funding for childhood cancer research, incorporating data from 115 funders, from 35 countries, over a nine year period from 2008-16.

Research and innovation for cost-effective diagnostics, treatment, and methods of service delivery are one of five key action points to drive the global fight to stop cancer, identified by The World Oncology Forum in 2017.^{12,30,31} Yet, our analysis revealed limited investment in cancer research that is primarily focused on children; with only \$226.8 million a year available to predominantly high income setting researchers. This is in context of the \$4.8 billion of reported new investments in cancer research overall in 2008, by 54 funding organizations (<50% the number included in this analysis).²⁶ In the same year, HIV/AIDS and malaria, which are also neglected diseases with high mortality burdens predominantly in low and middle income countries (LMICs), received \$1.3 billion and \$611 million for research and development, respectively.³²

There is a lack of prior estimates with which to compare our results. However, our findings are consistent with data on UK cancer research funding between 2000-13 showing that 3.8% (293 of 7583) awards contained 'paediatrics' as a cross-cutting theme and the investment sum of these grants represented 2.6% of the total funding.¹³ Similarly, a bibliometric analysis estimated that 5% of papers published by the global oncology research community relate to childhood cancer.²² An analysis of National Cancer

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Institute (NCI) investments in childhood cancer estimated awards amounting to \$200 million in 2012; which was larger than our estimate. However, this report used 'percentage relevance' multipliers applied to all NCI grants; including those predominantly supporting adult research.²⁵ Our analysis demonstrates that grants with crossover to adult cancer receive significantly larger awards, whereas we attempted to isolate grants solely awarded for childhood cancer.

The political momentum to accelerate innovation and access for improved cancer outcomes during the time period of analysis has not translated into increasing funding for childhood cancer research. Of great concern is that even the small amount of available funding appears to have stagnated, with overall decreases in the active funding available each year since 2011, other than a small number of large USA-based infrastructure grants. We took grant duration into account, estimating active funds during 2008 to 2016, rather than all funding commitments by start date, allowing us to demonstrate real availability of funding to researchers during the time period of analysis. Compared to other analyses, trends in funding will therefore appear more stable, than analyses by funding start date, and also take into account funding commitments to multi-year grants prior to 2008, which are still ongoing in later years.

Almost half of the total funding for childhood cancer research was focused on just three tumour types: leukaemias, CNS tumours, and neuroblastoma. This was consistent with investments reported from ICRP funders and with prior analyses of NCI funding.^{23,25} While funding by tumour type is broadly aligned to the estimated number of new cases, a notable exception is funding for childhood lymphoma research, which is underfunded relative to global burden (Figure 3). The incidence of endemic Burkitt lymphoma in parts of Africa is up to 50 times higher than that in the USA and Europe and it comprises 30-50% of all childhood cancer in Equatorial Africa.^{33,34} This large difference in incidence may be driving the unmet need for prevention and improved care for this malignancy that predominantly occurs in countries other than those funding and carrying out childhood cancer research.^{34,35}

Funding for germ cell and gonadal tumours also lies below the level expected according to tumour burden (Figure 3). This finding supports earlier calls to address the specific challenges and unmet needs of adolescent cancer patients, with <1% of the total funding specifically focused on adolescence in our analysis.^{8,20} Incidence is only one lens through which to consider the allocation of funds and analyses of tumour type-specific funding against other measures of disease burden, such as survival, mortality or morbidity, would provide additional perspectives. However, currently, there is comparable mortality data for only a limited number of childhood tumour types.^{1,7}

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Our analysis indicates that the majority of childhood cancer research is pre-clinical, with the most common research focus being the biology and aetiology of childhood cancers (Figure 4). There is very limited investment for translation of childhood cancer basic science research into new medicines, technologies, diagnostics and prevention strategies (although understanding aetiology closely feeds into prevention research in the case of childhood cancer), with little evidence of change in this trend over time (appendix Figures 1 and 3, pp 10-11). There are known bottlenecks into clinical trials for individually rare diseases (despite large collective burden), in both study design and the financial incentives for innovation.^{14,36} It is odd that this is still the picture despite Europe's ITCC (Innovative Therapies for Children with Cancer), ENCAA (European Network for Cancer Research in Children and Adolescents) and other translational initiatives, which have been largely mirrored by the US COG (Children's Oncology Group). Our findings suggest that research funding organization strategies are not necessarily aligned with need, or that these initiatives were insufficient to move the research domains.

Particularly striking is the near absence of funders and recipients in South America, South-East Asia and Africa in our data, despite the vast majority of childhood cancer deaths likely occurring in LMIC settings.^{14,37} Funding data from these regions may not have been automatically picked up by the database, particularly if organizations from some countries are less likely to provide open-access data. However, there is likely to be a genuine paucity of funding for research in these regions, which cannot be ignored. There may be some channeling of monetary or technological research support via US or Europe-based institutions, as for other areas of expertise in global health. The simple binary nature of the Dimensions data, representing only one recipient and one funder for each grant over simplifies funding into a linear transaction and does not allow more complex modeling of funding flows between institutions in different regions. However, it is clear that there is insufficient support for research in childhood cancer research in LMICs; and the majority of any existing research not captured here is likely to be directly or indirectly led by principal investigators employed in high income countries. Priorities for new investment would include improvement of surveillance and data collection (e.g. cancer registries) to understand the true burden of childhood cancer in all regions, addressing failures in early diagnosis and high rates of treatment abandonment, as well as supporting the development of health systems for childhood cancer care. In this context the low spends of \$111.4 million on diagnostics and \$113.0 on healthcare delivery, over 9 years, warrants urgent action. Collaborations such as the 5 year India-UK Cancer Research Initiative between CRUK and India's department of Biotechnology (DBT) and the WHO Global Initiative for Childhood Cancer supported by St Jude Children's Research Hospital are promising steps forward.

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The predominance of funding given, and received, by organizations within the USA (78% and 77% respectively) suggests a vulnerability of global childhood cancer research to changes in the USA's overall national spending on research. The 10-fold difference in contributions between the USA and Europe in our data is noteworthy. However, it is conceivable that we have underestimated European funding in our analysis, as around half of non-commercial funding in the Europe Union is provided by the charitable sector, versus mostly public funding (NIH) from the USA, which is more likely to be openly-accessible.^{40,41} Nevertheless, concerns have been voiced previously regarding the growing gap between the USA and Europe in the funding of non-commercial cancer research.^{40,41}

The Dimensions database provides a unique source of funding data allowing objective and comparable analysis of trends and categories of funding. The key advantage is access to standardized, grant level data, including grant duration where the spread of funding across multi-year grants can be more accurately assessed than relying on reports of new commitments in most funders' annual reports. We are likely to have captured all relevant grants from the funders that were included. For example, we were able to confirm that all relevant grants from the European Union and Cancer Research UK (CRUK) were represented in our data (through personal communication with both organizations).

Whilst it is certain that there are a myriad of diverse smaller funders, the primary focus of our analysis was to highlight key patterns of funding over time, across different countries and across research categories; none of which are likely to be influenced by small contributions from minor funders. However, as identified by other funding analyses, monetary data is not available from many funders, and some known, important funders of childhood cancer research were missing from the Dimensions database.⁴² Our supplementary search for major funders missing from the Dimensions database, and estimation of their annual additional contribution to funding of childhood cancer research lends some context to our main estimates (see supplementary material). As well as estimating the extent of 'missing' funding; we also assessed the likely degree of bias in terms of geography, funding across research focus categories, pipeline categories, and tumour types.

Our estimate of \$80.29 million of additional support for 1 year of childhood cancer research, is relatively small for 57 different funders (ie. those who had available funding data out of the 80 identified) (see supplementary material). In the context of our mean estimate being \$226 million a year, from 115 funders, this could suggest our analysis captured up to 70% of global public and philanthropic funding. Importantly it also supports that most of the largest funders were already included, and that addition of other funders adds diminishing increments to the overall estimate.

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Importantly, the independently conducted ICRP analyses of funding distribution across categories (research focus and tumour types), from funding partners that were not included in the Dimensions analysis, showed a very similar pattern of award allocation. For example, ICRP data corroborated that research for leukaemias, brain tumours and neuroblastoma was the most supported, compared to other tumour types. Although we did not have granular enough data to assess this for the other missing funders; it is encouraging that the ICRP analysis suggests the missing funding data conferred a low risk of bias in the patterns of funding we have reported.

The estimates of funding from missing ICRP partners also suggested a similar pattern of North American funders being the highest contributors to the field. This is consistent with our main analysis and also the dominance of the USA in supporting health research and development globally.⁴³ However, ICRP partners are only from 7 different countries, and our other supplementary searches highlighted more large European funders than those from the USA (see supplementary material). Interestingly, around two thirds of the additional funders were non-governmental organizations, in contrast to our main (Dimensions) analysis which had a predominance of public funders. These observations point to a tendency of open-access funding data to be from governmental funders who are subject to a greater degree of public scrutiny; and therefore more likely to be included in the Dimensions database. In particular the NIH provides a useful online platform (NIH RePORT) for access to information on all grants made through its numerous branches, which has been previously used in isolation for a number of funding analyses^{25,44–46} [refs]. Despite a larger number of the additional funders being European, the mean estimated one year contributions from European funders in our supplementary analysis were considerable less (\$1.9 million vs. \$4.0 million) than from USA funders (see supplementary material). Important future work should include consideration of the ‘efficiency’ of research funding for childhood cancer; as it is unknown how much research costs differ between countries and the degree to which this impacts on public and philanthropic spending.

We only identified one additional funder country in our supplementary search (Italy). In addition, no significant additional funding was apparent from South America, South East Asia or Africa (although a small number of Chinese and Japanese funders were identified that did not provide any data to estimate their contributions) (see supplementary material). This supports our key finding that the majority of childhood cancer research funding is generated and received by only a handful of North American and Western European countries, regardless of the research partnerships with any other regions.

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It is certain that funding amounts reported here, and in our supplementary analyses, are underestimates of the true values to some degree; as the true values will not be captured while a majority of funding organizations have poorly accessible reporting on funding allocations. For those that do have some data available, we found most organizations only report total spend on childhood cancer research, usually in one recent annual report, without clarity on whether this figure reflects new commitments that year or overall funds available to recipients (including prior, ongoing grants); let alone specific topics of research, focus or grant duration. Annual reports are rarely specific and detailed enough to distinguish between new commitments and annualized funding are in general are more likely to present the total new commitments / total new grants awarded in a year, as this a much simpler metric and easier to calculate from an individual organizations' point of view.

These details are crucial for analyses of funding, and it is vital that organizations aim to publish these in conjunction with overall spend, ideally presenting grant-level data, as part of the move towards full transparency. This would allow assessment of national and global trends that could highlight neglected areas, guide future funding priorities and provide insight into the efficacy and efficiency of current funding strategies.

Our analysis only covered available public and philanthropic grants, excluding potential investments from biotech, pharmaceutical and other industries. Industry has been reported to account for 57% of all biomedical research in the USA.⁴³ However, it is completely unknown how much for-profit companies are specifically supporting research for children with cancer. A previous bibliometric analysis detected limited commercial funding of published paediatric cancer research and clinical trials for rare diseases such as childhood cancers.²² However, industry funded studies may be less likely to be published if results are not favourable; and may also be conducted in partnership with academic institutions who are listed as the main sponsors. Despite this, mapping public and philanthropic funding is essential; as industry funding cannot be relied on as a sustainable force for driving improved outcomes for children with cancer, globally.

In sum, we have demonstrated a low level of funding for childrens' cancer research, with the minimal available funding being limited in scope by topic, and region, and with no evidence of recent acceleration in investment. The setting of strategic research priorities and minimising 'wasteful' research should underpin research funding activity. Childhood cancers represent one of the greatest future opportunities for reducing avoidable death in children and new research in all resource settings is urgently needed. The momentum for universal health coverage must be met with major new public and philanthropic

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We only identified a single new funder country in our supplementary search (Italy) suggesting that our main analysis accurately reflects the geographic spread of major worldwide funders of research in childhood cancer. ¶

<#>Type of funders ¶

In the Dimension database there was a clear predominance of government financed (86%) as compared to philanthropic funders indicating that it are predominantly government funders that lead on transparency and allow data to the level of individual grant information to be publicly available in open access databases such as Dimensions. The pattern was reversed in our additionally identified funder set with two thirds being philanthropic organisations. ¶

Sensitivity analysis.¶

Sum of extra funding in context¶

There are several difficulties with comparing our data estimates with those from 'annual reports' of funders. Most importantly, there are multiple metrics that can be used to report research funding; including both 'new commitments'; or 'annualised'/'active' funding which represents funding apportioned evenly over multiyear grants to depict actual yearly availability of funds for active research. We feel that the latter is more reflective of real funding for childhood cancer research. However, annual reports are rarely specific and detailed enough to distinguish between new commitments and annualized funding are in general are more likely to present the total new commitments / total new grants awarded in a year, as this a much simpler metric and easier to calculate from an individual organizations' point of view.¶

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commitments in global childhood cancer research in order to improve understanding of the distribution, burden and causes of childhood cancers, and to develop innovative prevention and treatment strategies to improve outcomes globally.

Acknowledgements: Data was sourced from Dimensions, an inter-linked research information system provided by Digital Science (<https://www.dimensions.ai>). We thank the ResIn team (Research Investments in Global Health - <http://researchinvestments.org>) for their partnership in carrying out this work and in particular, Michael Head, who reviewed early drafts of the work and provided helpful critique and guidance. [We thank Lynne Davies for her collaboration and help with accessing data from the ICRP.](#)

Declaration of interest: We declare no conflicts of interest.

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Table 1: Summary of funding for childhood cancer research, from active grants between 2008 to 2016, by global region, tumour type, research focus, pipeline categories and year

	Total Active Funding(a,c) 2008-2016 (USD (%))	Number of Active Grants (b) 2008-2016 (n (%))	Median Award Size (USD)(c) and Interquartile range (IQR)	Number of grants where the monetary value of the award was unavailable
ALL	2,040,816,028 (100.00%)	3414 (100.0%)	149,620 (382482)	204
TUMOUR TYPE (as per ICCC-3)				
General Paediatric Oncology	771,837,100 (37.90%)	908 (26.6%)	81,500 (292,602)	30
Leukemias, myeloproliferative diseases, & myelodysplastic diseases	448,754,400 (22.04%)	1001 (29.3%)	170,400 (406,922)	96
CNS & miscellaneous intracranial & intraspinal neoplasms	329,561,100 (16.18%)	618 (18.1%)	185,300 (424,684)	19
Neuroblastoma & peripheral nervous cell tumours	181,231,400 (8.90%)	385 (11.3%)	196,700 (473,921)	31
Malignant bone tumours	86,368,400 (4.24%)	186 (5.4%)	116,300 (282,412)	10
Soft tissue & extraosseous sarcomas	85,910,500 (4.22%)	131 (3.8%)	120,200 (404,735)	7
Lymphomas & reticuloendothelial neoplasms	47,931,000 (2.35%)	110 (3.2%)	149,300 (281,337)	6
Renal tumours	40,334,100 (1.98%)	76 (2.2%)	170,400 (347,756)	5
Retinoblastoma	16,944,300 (0.83%)	42 (1.2%)	155,500 (351,040)	1
Other malignant epithelial neoplasms & malignant melanomas	11,334,400 (0.56%)	37 (1.1%)	83,600 (255,385)	2
Germ cell tumours, trophoblastic tumours, & neoplasms of gonads	10,294,000 (0.51%)	28 (0.8%)	178,100 (291,341)	1
Hepatic tumours	7,139,000 (0.35%)	42 (1.2%)	77,900 (112,219)	4
Other/unspecified malignant neoplasms	2,701,000 (0.13%)	10 (0.3%)	55,600 (972,469)	3
RESEARCH FOCUS				
Biology and aetiology (inc. basic science, cancer biology, epidemiology/risk factors)	806,424,100 (39.51%)	1,536 (45.0%)	153,800 (376,467)	101
Treatment (inc. therapies for cancer, including complications, treatment resistance)	645,795,600 (31.64%)	1,018 (29.8%)	154,100 (377,711)	62
Survivorship (inc. symptom management, end of life care, quality of healthcare delivery, long term side effects of treatment, beliefs and attitudes to care)	236,765,900 (11.60%)	555 (16.3%)	100,000 (356,122)	21
Diagnosis and Prognosis (inc. cancer biomarkers, imaging and predicting outcomes)	111,359,500 (5.46%)	295 (8.6%)	138,600 (310,266)	31
Model Systems (inc. new animal models, cell cultures, computer simulations)	28,854,000 (1.41%)	118 (3.5%)	114,000 (260,893)	5
Prevention (inc interventions to reduce cancer risk including lifestyle, drugs, vaccines)	18,144,400 (0.89%)	35 (1.0%)	172,300 (251,351)	1
PIPELINE				
Pre-clinical (inc. basic sciences, public health research, surveillance, modelling, bioinformatics)	1,209,570,700 (59.27%)	2,621 (76.8%)	165,800 (378,061)	172
Cross-disciplinary (inc. significant components across ≥2 areas)	409,655,900 (20.07%)	49 (1.4%)	926,300 (4,078,303)	1
Infrastructure (inc. research centres/staff dedicated to childhood cancer research)	192,943,500 (9.45%)	246 (7.2%)	48,400 (161,717)	2
Clinical Trials (inc. phase I, II, or III)	115,615,200 (5.67%)	141 (4.1%)	279,000 (767,754)	13
Health Care delivery (inc. survivorship, outcomes, healthcare apps/products, tissue banks, healthcare interventions)	113,009,500 (5.54%)	355 (10.4%)	77,100 (279,114)	15
YEAR				
2008	190,463,300 (9.33%)	823 (24.1%)	101,900 (200,239)	41
2009	203,924,500 (9.99%)	906 (26.5%)	99,500 (196,773)	45
2010	222,759,300 (10.92%)	1069 (31.3%)	94,200 (192,857)	60
2011	237,022,300 (11.61%)	1199 (35.1%)	89,700 (182,897)	74
2012	239,153,200 (11.72%)	1263 (37.0%)	88,800 (180,335)	84
2013	235,831,000 (11.56%)	1274 (37.3%)	85,700 (174,852)	94
2014	253,072,400 (12.40%)	1352 (39.6%)	79,500 (167,787)	100
2015	255,349,700 (12.51%)	1379 (40.4%)	78,400 (153,158)	91
2016	203,240,300 (9.96%)	1373 (40.2%)	62,800 (132,034)	79

(a) Data shown are estimates of funding for childhood cancer research, from active grants between 2008 to 2016. Grants with future end dates, or start dates prior to 2008, were restricted to the portion of funding available during the 2008 to 2016 time period, with multi-year grants apportioned equally across their duration. Where grants had been assigned multiple tumour types or research focus categories, funding amounts were assumed to be divided equally across categories. (b) Includes grants where the monetary value of the award was not available (c) All monetary values are shown in US Dollars (USD), rounded to the nearest \$100.

Table 2: Summary of funding awarded by funding regions, top funding countries and countries of recipient institutions, for childhood cancer research, from active grants between 2008 and 2016

	Total Active Funding(a) 2008-2016 (USD (%))	Number of Active Grants(a,b) 2008-2016 (n (%))	Median Award Size (USD) and Interquartile range (IQR)	Number of grants where funding amount was unavailable
ALL	2,040,816,028 (100.00%)	3414 (100.0%)	149,620 (382482)	204
WHO GLOBAL REGION (of funder) (c)				
Northern America	1,685,398,103 (82.58%)	2238 (65.6%)	184,399 (488481)	29
Europe	292,198,934 (14.32%)	633 (18.5%)	206,265 (333288)	153
Oceania	37,685,911 (1.85%)	86 (2.5%)	356,214 (430386)	0
Asia	21,014,383 (1.03%)	388 (11.4%)	33,556 (32645)	3
Latin America & The Caribbean	4,518,697 (0.22%)	67 (2.0%)	62,260 (125264)	17
Africa	0 (0.00%)	0 (0.0%)		
TOP FUNDING COUNTRIES (d,e)				
United States	1,586,042,178 (77.72%)	1803 (52.8%)	230,613 (659725)	26
European Union	144,920,812 (7.10%)	57 (1.7%)	1,049,009 (3581471)	0
United Kingdom	100,061,267 (4.90%)	264 (7.7%)	178,988 (323429)	14
Canada	99,355,925 (4.87%)	435 (12.7%)	98,001 (202830)	3
Australia	37,262,534 (1.83%)	84 (2.5%)	356,214 (431447)	0
TOP RECIPIENT COUNTRIES (e,f)				
United States	1576330794 (77.24%)	1773 (51.9%)	234404 (671749)	32
United Kingdom	105398750 (5.16%)	261 (7.6%)	178327 (341137)	14
Canada	98117751 (4.81%)	435 (12.7%)	98477 (199353)	3
Australia	37815595 (1.85%)	89 (2.6%)	321614 (425949)	0
France	31546592 (1.55%)	16 (0.5%)	244367 (3004931)	1
Germany	24315850 (1.19%)	72 (2.1%)	2098976 (3735287)	61
Sweden	23892119 (1.17%)	39 (1.1%)	352971 (400912)	0

(a) Data shown are estimates of funding for childhood cancer research, from active grants between 2008 to 2016. Grants with future end dates, or start dates prior to 2008, were restricted to the portion of funding available during the 2008 to 2016 time period, with multi-year grants apportioned equally across their duration. (b) Includes grants where the monetary value of the award was not available (c) See supplementary material; analysed according to global region of funder country (d) Defined as the countries of funders collectively providing >1% of the total active funding 2008 to 2016 (e) Nb. The German Research Foundation (Germany) had 69 active grants between 2008 and 2016, but funding amount was unavailable so not included here (f) Defined as the countries of institutions collectively receiving >1% of the total active funding 2008 to 2016

Figure 1: Flowchart of data collection

Figure 2: Trends in annual funding available from active grants, and total new commitments, 2008 to 2016, for childhood cancer research, by cancer type

Figure 2 represents annualised active funding (USD, millions) by tumour type, excluding funding for general paediatric oncology, adjusted for inflation, equating all dollars to the value of USD in 2010. Annualised funding calculated by apportioning multiyear grants evenly across their duration (only including years 2008 to 2016). Total funding from new grants (adjusted for inflation) starting each year are also shown (line).

Figure 3: Relationship between mean annual funding, number of active grants, and incidence, by tumour type

Figure 3 illustrates overall mean annual research funding estimated from active grants between 2008 and 2016, categorised by tumour type (assuming equal distribution of funds, where grants covered multiple tumour types) and plotted by estimated age-standardised incidence, where size of bubble represents the number of active grants between 2008 and 2016. Age-standardised incidence rates were sourced from Steliarova-Foucher et al (International Incidence of Childhood Cancer, 2001-2010: a population based registry study, Lancet Onc 2017; 18(6):719-731)

Figure 4: Heat-map representation of funding from active grants 2008 to 2016, by research focus, tumour type and pipeline categories

Figure 4 shows the intersection of funding across categories available from active grants 2008-2016, rounded to the nearest \$100 (USD). Where multiple categories were assigned for tumour type and research focus, funding was assumed to be split equally across categories. See Appendix 3 for category details.

Figure 5: Countries of primary recipient institutions of funding from active grants 2008 to 2016

Figure 5 illustrates overall funding from active grants 2008 to 2016, by country of the primary recipient institution. Unshaded countries represent those for which no grants were identified or awarded.